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ANNUAL REPORT OF THE INTER-AMERICAN DRUG ABUSE CONTROL COMMISSION (CICAD) TO THE GENERAL ASSEMBLY OF THE ORGANIZATION OF AMERICAN STATES AT ITS 32ND REGULAR SESSION, 12-15 NOVEMBER 2001, CARACAS, VENEZUELA, 3 APRIL 2002

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THIRTIETH REGULAR SESSION
November 12-15, 2001
Caracas, Venezuela

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ANNUAL REPORT OF THE INTER-AMERICAN DRUG ABUSE CONTROL COMMISSION (CICAD) TO THE GENERAL ASSEMBLY OF THE ORGANIZATION OF AMERICAN STATES (OAS) AT ITS THIRTY-SECOND REGULAR SESSION

Standards of Care in Drug Abuse Treatment

CICAD continues to help member states develop and put into practice standards of care in drug treatment. This initiative, underway in CICAD since 1997, is designed to help governments develop a consensus in the national health care community around the desirability of establishing standards of care, and then to implement practices and guidelines. A long-term objective, recommended by CICAD's Expert Group on Demand Reduction (March 1998, and again in August 2001), is to develop systems of accreditation for treatment providers.

During 2001, CICAD organized and financed a workshop on the establishment of standards of care in Uruguay. A Spanish-language manual documenting the different experiences of each country in the implementation and adaptation of legislation was published by the Executive Secretariat in October 2000. The English version, published in July 2001, was used as a reference during the meeting of the CICAD Expert Group in Demand Reduction held in August 2001 in Montego Bay, Jamaica.

Caribbean Sub-Regional Group of Demand Reduction Experts

CARICOM and CICAD cosponsored a Sub-Regional Demand Reduction Forum in Georgetown, Guyana on September 17-18. The purpose of the meeting was to bring together individuals from the Caribbean member states to discuss the findings of an assessment relating to a regional demand reduction enhancement program, as well as to develop a strategic approach for carrying out future activities and assessments. The recommendations put forth at the forum were submitted to the Fifth Meeting of the Council for Human and Social Development (COHSOD V) in October 2001, and [to a preparatory meeting for a Caribbean Summit of Heads of Government in December 2001].

Support for the Consultative Group process in Ecuador

As part of its support for Ecuador's Consultative Group process on drugs, the Executive Secretariat provided technical assistance on the development of the demand reduction project portfolio.

C. SUPPLY REDUCTION AND APPLICATION OF CONTROL MEASURES

Expert Group on Chemical (Pharmaceutical Products)

At CICAD XXVIII, the Delegation of Colombia raised concerns regarding the control of pharmaceutical products. The Commission directed the Expert Group on Chemicals to examine this issue. The Group met August 13 - 15 in Washington with representatives from Argentina, Belize, Brazil, Chile, Colombia, Costa Rica, Ecuador, Guatemala, Jamaica, Mexico, Peru, Dominican Republic, St. Kitts and Nevis, Trinidad and Tobago, United States, Uruguay, and Venezuela.

The experts identified 7 general problem areas in controlling pharmaceuticals: the existence and application of adequate legislation, national control systems, the availability and timely exchange of information and the availability of sufficient financial, technical and human resources. The Group developed 10 recommendations for consideration by the Commission and 7 more that were directed to the member states.

The report and recommendations were presented to the Commission by Dr. Maria Cristina Chirolla of Colombia, the Chair of the Expert Group.

The Group presented its final report at the thirtieth regular session. As one of the recommendations the group suggested the creation of a separate Experts Group on Pharmaceutical Products. The Commission decided that the group will meet for the first time In Washington DC, in March 2002, and will be chaired by Colombia.

Chemical Control Software

In response to requests by member states the Executive Secretariat continued its work in the development of a uniform chemical control database designed to assist countries in registering and reporting on precursor imports and exports, maintaining company records and generating pre-export notifications. The software was designed by the chemical control unit of the Ministry of Industry, Tourism, Integration and International Commercial Negotiations (MITINCI) of Peru.

During the first quarter of 2001, MITINCI performed a number of modifications on the software based on consultations with CICAD. These modifications created a general platform that countries could adopt and integrate into their national control systems. Each country may also perform modifications to the program in order to meet their individual needs. In March 2001, CICAD and the DEA hosted a detailed training seminar at MITINCI's headquarters in Lima for representatives from Venezuela's national drug commission (CONACUID) and from the Ministry of Production and Commerce (MPC). Argentina, Bolivia and Panama have also expressed formal interest in acquiring the software and are currently undergoing the preparations for installation.

Study of Maritime Drug Trafficking

In August 2001, the Secretariat conducted a maritime drug trafficking study in Colombia within the framework of its Maritime Cooperation Strategy in the Southeastern Pacific. A previous study was undertaken in Peru in 2000. The study in Colombia, which was conducted in coordination with the Office of Naval Intelligence and the Joint Interagency Task Force – East, focused on drug trafficking activities around coastal areas and waters, including port facilities. It also examined systems, resources, procedures, and capacity to monitor and interdict drug trafficking within the ports and adjacent to the coastline. A final report published in December 2001 made a series of recommendations to the Government of Colombia for consideration in its ongoing national maritime counter drug strategy. A third study will be conducted in cooperation with the Government of Chile in January 2002; the fourth and final study will focus on Ecuador. A regional assessment will also be completed in 2002. The goal of the project is to promote multinational coordination and cooperation.

Maritime Cooperation and Port Security Project

There is an increasing recognition of the role of the private sector in facilitating drug control. This is particularly important in the case of commercial companies active in airports and maritime ports. Governmental port authorities have traditionally been responsible for the administration of maritime ports, but the trend is toward private sector companies assuming these responsibilities.

(GIS) and a computerized image analysis system (IA), using commercial satellite images, aerial photographs, and on-site verification to that end. The GLEAM tool makes it possible to map and evaluate the environmental repercussions of land use, identifies the potential for improvement or development of new infrastructure, evaluates and/or proposes alternative land-use options by identifying the crops with the most potential to bring economic development to a given area, and contributes to the construction of a land-titling database

As a result of the project launched in 1998, in 2001 CICAD delivered the GLEAM project to the Government of Peru, including a work station, field equipment, and training for CONTRADROGAS personnel in the use of the system. With this technology the government of Peru can effectively determine the viability of proposed projects as well as develop new projects in production areas, and those with potential to be used for illicit cultivation.

In Bolivia, the Vice Ministry for Alternative Development, through its Monitoring Office, has been working, in cooperation with CICAD, to compile the necessary information to implement GLEAM over 500,000 hectares of traditional coca production areas identified by the government in the North and South Yungas region. This was done based on a request from the Bolivian Government.

Alternative Development Projects in Indigenous Communities

CICAD, in conjunction with the Foundation ZIO-A'I "Unión de Sabiduría" and the National Alternative Development Plan of Colombia (PNDA), seeks to develop the economy and production component of the Life Plan (Plan de Vida) of the Cofán People and the Indigenous Councils of Valle Guamuez and San Miguel, as a socioeconomic development plan that offers an alternative to coca cultivation for these indigenous communities in the Department of Putumayo, southern Colombia. The project was designed by the communities through the Life Plan and it has become the instrument to ensure the physical and cultural survival of these indigenous communities and to bring social and economic development to their peoples and to the region they inhabit, by seeking, at the same time, to ensure licit alternative development and eradication of coca cultivation from their lands. The purpose of this project is to strengthen the culture, organizations, businesses, and economic development of indigenous communities; identify lands suitable for farming and lands that require environmental restoration; implement a crop, livestock, and animal breeding program, as well as sustainable production systems to enable the recovery of traditional crops in order to provide food security and produce marketable surpluses. The overall objective is to create a strong and sustainable licit economy.

Support for Regional Initiatives

CICAD has been providing financing and participating as technical adviser, along with other Inter-American and International agencies such as the Inter-American Institute for Cooperation in Agriculture (IICA), to the Andean Committee for Alternative Development (CADA). Through this consultation and coordination forum for multilateral dialogue and decision making, the Andean countries exchange information and experiences to develop and apply a regional strategy to enable them to implement joint measures, strengthen bargaining capacity, and promote marketing of alternative products, taking into consideration all sectors of society and agreements among governments. This

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2004 MEMORANDUM OF UNDERSTANDING BETWEEN THE GOVERNMENT OF COLOMBIA AND THE ORGANIZATION OF AMERICAN STATES (OAS) FOR THE EXECUTION OF THE STUDY ON THE EFFECTS OF THE PROGRAM FOR THE ERADICATION OF ILLICIT CROPS BY AERIAL SPRAYING WITH GLYPHOSATE HERBICIDE (PECIG) AND OF ILLICIT CROPS, ON HUMAN HEALTH AND THE ENVIRONMENT, 4 FEBRUARY 2004

(*Archives of the Ministry of Foreign Affairs of Colombia*)

MEMORANDUM OF UNDERSTANDING BETWEEN THE GOVERNMENT OF COLOMBIA AND THE ORGANIZATION OF AMERICAN STATES (OAS) FOR THE EXECUTION OF THE STUDY ON THE EFFECTS OF THE PROGRAM FOR THE ERADICATION OF ILLICIT CROPS BY AERIAL SPRAYING WITH GLYPHOSATE HERBICIDE (PECIG) AND OF ILLICIT CROPS, ON HUMAN HEALTH AND THE ENVIRONMENT

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The Parties to this Memorandum of Understanding, the Government of Colombia through the Ministry of Foreign Affairs, represented by the Minister of Foreign Affairs, Carolina Barco, and the General Secretariat of the Organization of American States ("SG/OEA"), through the Inter-American Drug Abuse Control Commission (hereinafter, CICAD), represented by its Assistant Executive Secretary, Abraham Stein, sign the following Memorandum of Understanding:

CONSIDERING

That the General Secretariat of the Organization of American States (hereafter, "SG/OAS"), is the main and permanent organ of the Organization of American States (hereafter, "OAS"), and is authorized to establish and promote relations of cooperation with member States pursuant to Article 112(h) of the OAS Charter and with its General Assembly resolution AG/RES. 57 (l-O/71).

That CICAD is an agency of the Organization of American States, established by Article 52 of the OAS Charter. This agency is technically autonomous and carries out its duties within the context and scope of the Rio de Janeiro Action Plan against Consumption, Production, and Illicit Trafficking on Drugs and Psychotropic

Substances, the mandates of the General Assembly, and the decisions internally adopted by CICAD.

That the purpose of CICAD is to contribute to eliminate illicit trafficking and drug abuse. Pursuant to its Statutes, it has attributions with regard to the field of prevention, assistance and social rehabilitation of drug-addicts, as well as to that of the prevention, control and punishment of the production and illicit trafficking of drugs and psychotropic substances.

That within the framework of its Hemispheric Strategy, CICAD promotes actions against the illicit crops of raw materials destined for the production of illicit drugs, while always taking into account the preservation of the environment, through the promotion of programs and/or projects to encourage the development of lawful economies in the areas of illicit drug production in Member States.

That the Program for the Eradication of Illicit Crops by Aerial Spraying with Glyphosate Herbicide (PECIG) was implemented in accordance with paragraph g) of Article 91 of Law 20 of 1986, whereby Colombia adopted the National Anti-Narcotics Statute that assigns to the National Narcotics Council the duty to "provide for the destruction of marihuana, coca and other crops from which substances causing dependency may be extracted, using the most adequate means, following a favourable opinion of the agencies entrusted with protecting the health of the population and the preservation and balance of the ecosystem in the country". [The Program] is regulated through resolution 0013 of 2003 and operates in all the regions in the country the presence of illicit crops is evidenced.

That for the Colombian State, the adoption and implementation of the Program for the Eradication of Illicit Crops by Aerial Spraying with Glyphosate Herbicide (PECIG) has become an inexorable necessity in view of the fact of the extended presence of illicit crops in the national territory and the security problems that, in many cases, preclude resort to other eradication methods.

That the Government of Colombia understands the PECIG as the plan of the State for the mitigation of the adverse environmental impact caused by illicit crops and the subsequent processing of illicit drugs.

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That in view of the growing domestic and international concern as to the alleged effects of the Program for the Eradication of Illicit Crops by Aerial Spraying with Glyphosate Herbicide (PECIG), the Governments of Colombia and the United States of America, based on the existing cooperation on the matter between both nations, requested CICAD to conduct a study in order to document such effects in a scientific and independent manner.

That upon the increase of complaints from its nationals in several regions in the country because to the alleged damages caused to agricultural activities, due to the aerial spraying with Glyphosate herbicide, the National Narcotics Council issued, through Resolution 017 of 2001, an expedited procedure aimed at processing such claims, with the purpose of ensuring the protection of their fundamental rights, in accordance with the provisions of the Colombian Constitution.

That, in accordance with Colombian law and abiding by the provisions of the 1961 Single Convention on Narcotic Drugs as amended by its 1972 Protocol and the 1988 United Nations Convention Against Trafficking of Illicit Drugs and Psychotropic Substances as regards the obligation to adopt the necessary measures to eradicate the poppy crops, coca bushes and cannabis plants that are illicitly grown, and in light of the unusual increase of illicit crops in the national territory, the Government of Colombia set out to strengthen its strategy to confront the problem of illicit drugs production and trafficking through forced eradication by aerial spraying with glyphosate herbicide.

STATING the importance of coordinating the efforts of the Parties with the purpose of fulfilling their objectives in light of the international instruments in force in the fight against the world drug problem and related crimes, while observing the principles of the respect for national sovereignty, confidentiality, transparency and veracity in conclusions.

AGREE to conclude the present Memorandum of Understanding that will be governed by the following provisions:

FIRST CLAUSE: Object and purpose

The object and purpose of the present Memorandum of Understanding is to conduct an independent scientific study on the effects of the Program for the Eradication of Illicit Crops by Aerial Spraying with Glyphosate Herbicide (PECIG), and of the herbicides and fungicides used in the production of illicit crops on human health and the environment.

The description of the study is set out in detail in Annex I that is an integral part of the present Memorandum of Understanding that was vetted by the Government of Colombia and the Executive Secretariat of the CICAD. Also annexes to the present Memorandum of Understanding are the documents entitled “Schedule of Activities” and “Operational Plan for conducting the study on the effects of the Program for the

Eradication of Illicit Crops by Aerial Spraying with Glyphosate Herbicide (PECIG) and of illicit crops, on human health and the environment".

SECOND CLAUSE: Framework for cooperation

Cooperation and assistance provided in pursuance of the present project will be carried out in observance of the respect for national sovereignty, confidentiality, transparency and veracity of conclusions.

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THIRD CLAUSE: Study areas

The study will focus on the areas where the Program for the Eradication of Illicit Crops by Aerial Spraying with Glyphosate Herbicide (PECIG) is implemented and, by mutual agreement between the Parties, other areas the assessment of which is considered relevant may be included.

FOURTH CLAUSE: Responsibilities of the Parties

A. CICAD undertakes to:
    1. Supervise and follow-up on the works carried out by the Scientific Assessment Team (SAT) and the Permanent Technical Group for Mobile Monitoring (PTGMM [shortened form PTG]).
    2. Contract, by mutual agreement with the Colombian Government, and supervise the required personnel for conducting the study that is the object of the present Memorandum of Understanding.
    3. Conduct and follow-up on the study that is the object of the present Memorandum of Understanding.
    4. Coordinate and supervise the adequate progress of the activities foreseen in the Proposal for Monitoring of the Aerial Spraying Program in Colombia.
    5. Provide the funds for conducting the corresponding activities in accordance with the established Schedule of Activities. Therefore, the project will not entail any disbursements from the Colombian treasury.
    6. Review and approve periodical reports on the progress of the established work plan.
    7. Periodically inform the Government of Colombia on the progress of the completion of the study that is the object of the present Memorandum of Understanding.
    8. Publicly present the results of the study and widely publicize the corresponding final report that will have been previously presented to the Government of Colombia for its information. The results of the study and

the final report to which this paragraph refers will be presented in Spanish and English.

B. The Government of Colombia undertakes to:
   1. Facilitate the compliance with and implementation of the present Memorandum of Understanding.
   2. Provide any information required for the formulation and implementation of the project as requested by CICAD, including, among others:
      a. Legal background to the PECIG program.
      b. Description of the coverage areas.
      c. Schedule of the spraying program.
   3. Appoint a Liaison who will be entrusted with the following responsibilities:

      a. To facilitate communication between CICAD, implementing personnel and the Government of Colombia.
      b. To arrange the required logistics relating to the mobilization of the personnel to and within the areas under study described in Annex I.
      c. To ensure the timely and coordinated action of the different authorities in charge of providing security to the personnel implementing the study.

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   4. To provide a security detail for the mobilization of the personnel involved in the study to and within its areas, in accordance with the resources allocated for these purposes in the project budget.
      Paragraph 1: Any field visit described in the "Schedule of Activities" shall be conducted by mutual agreement with the Colombian authorities in charge of providing security, and under the terms recommended by such authorities according to the security situation. Pursuant to these same reasons, any scheduled visit may be suspended prior to the agreed date.
      Paragraph 2: Notwithstanding the provisions in paragraph 1, the Parties will endeavor to comply with the entirety of visits described in the "Schedule of Activities", or any other additional visit that may be required for the adequate progress of the study.

FIFTH CLAUSE: Hiring of the manager of the Permanent Technical Group for Mobile Monitoring –GTPMM

The appointment of the Project manager will be made by mutual agreement between the Parties.

SIXTH CLAUSE: Confidentiality

The Parties to this Memorandum of Understanding undertake to preserve the strictest confidentiality while the study is being developed. Neither Party may, without the express prior consent of the other, publish partial results of the study under way.

Once the Parties have learned, under reserve, the results of the study, the final report will be made public and will be widely publicized.

SEVENTH CLAUSE: Termination

The present Memorandum of Understanding may be terminated by mutual agreement or by either Party, through written advance notice of at least three months to the other.

EIGHTH CLAUSE: Settlement of disputes

The Parties undertake to settle controversies that may arise of the interpretation or application of the present Memorandum of Understanding, preferably by mutual agreement. In case a satisfactory solution is not reached, recourse will be had to the exceptional arbitration procedure mutually agreed by the CICAD and the Government of Colombia. If there is no agreement on the procedure, arbitration will be conducted pursuant to UNCITRAL Rules. The arbitral tribunal constituted in accordance with those Rules will rule as amiable mediator or *ex aequo et bono* and its decision will be final and binding.

None of the provisions in this Memorandum of Understanding signifies or shall be construed as a relinquishment of the privileges and immunities enjoyed by the Parties in accordance with international law and practice.

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NINTH CLAUSE: Entry into Force, Duration and Amendments

The present Memorandum of Understanding shall enter into force on the date of its signature and shall be in force for a year that may be extended by mutual agreement between the Parties.

Addition or amendment to this Memorandum of Understanding will be made by mutual agreement between the Parties, following compliance with legal requirements. The instruments registering those modifications will be appended as annexes to the present Memorandum of Understanding and shall become part thereof.

The Schedule of Activities contained in Annex II, will be modified and adjusted taking into account the date of the entry into force of the present Memorandum of Understanding.

The text of the present Memorandum of Understanding between the Government of Colombia and the Organization of American States (OAS) to Conduct a Study on the Effects of the Program for the Eradication of Illicit Crops by Aerial Spraying with Glyphosate Herbicide (PECIG) and of Illicit Crops, on Human Health and the Environment, is done in two copies in Spanish, both equally authentic.

In witness whereof, it is signed in the city of Bogota, D.C., Republic of Colombia on the fourth (4) day of the month of February 2004.

For the Government of Colombia

[signed illegibly]
CAROLINA BARCO
Minister of Foreign Affairs

For the General Secretariat of the Organization of American States

[signed illegibly]
ABRAHAM STEIN
Assistant Executive Secretary of the Inter-American Drug Abuse Control Commission

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ANNEX I
PROPOSAL FOR THE MONITORING OF THE AERIAL SPRAYING PROGRAM IN COLOMBIA

BACKGROUND

Despite the enormous efforts deployed by Colombia, illicit crops, particularly coca crops, continue to affect the Andean region, with 80% of the total production in 2001. During 2001, there was an 11% decrease in coca production in comparison to the previous year. In 2002, the total area of coca crops decreased by 29.5%, going from 144,807 o 102,071 hectares. In the last few years, Colombia has experienced a reversal of the growth trends evidenced up until 2000, corroborating the dynamics and vulnerability of illicit crops. This reduction may be attributed, among others, to the increase in aerial eradication efforts. To deal with the elimination of illicit crops, the Government of Colombia continues with the implementation of the aerial spraying program aimed at the eradication illicit crops.

Aerial spraying began with marijuana crops in the late 70's, then in 1991 poppy crops started to be sprayed and, lastly, in 1994, aerial spraying of coca began. Over time, the issue of aerial spraying as an element of the strategy for reducing crops has polarized the international community. The use of chemical herbicides such as glyphosate has provoked several verbal reproaches and severe criticism on behalf of peasants, peasant organizations and environmental watch groups.

In accordance with Resolution 012 of 2003, the Program for the Eradication of Illicit Crops by Aerial Spraying with Glyphosate Herbicide is to have an Environmental Management Plan, a provision that was regulated by the Ministry for the Environment, Housing and Territorial Development, through Resolution 1054 of 30 September 2003.

This Plan has not assuaged the doubts of the opponents to aerial spraying, wherefore an independent study on such effects is necessary. The results of the studies conducted to date have not provided solid evidence and have been perceived as subjective and unilateral studies. In sum, the controversy continues and it is necessary to have a publicly known study that provides certain results on the matter.

[…]

In light of the growing domestic and international concern as to the environmental and health effects of the Program for the Eradication of Illicit Crops by Aerial Spraying with Glyphosate Herbicide that is conducted in Colombia, the Governments of Colombia and the United States requested the collaboration of CICAD in order to conduct a study documenting such effects.

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To that effect, it is deemed necessary to set out on an independent, objective and impartial assessment of the current aerial eradication program with the purpose of providing verifiable and empirical scientific research. This proposal is an attempt to establish the framework within which to carry out this work, as well as a response to the need to produce an assessment that is scientifically unquestionable in general terms and convincing in the way in which it is publicly perceived.

OBJECTIVES

The objectives of this program are the following:

1) To conduct a scientific study of the aerial spraying program in Colombia, that is notoriously independent and of high quality, on the essential impacts of glyphosate spraying on individuals, fauna, flora and the environment.

2) To conduct a scientific study on the effects of illicit crops inasmuch as their impact on human health and the environment is not known.
3) To establish a method for mobile monitoring that is able to perform random periodic assessments, to research concrete allegations and to respond to specific controversies.
4) To produce project results, as far as possible, within a year as of the start date.
5) To widely publicize the corresponding final report.

AREAS

According to the objectives of the program, the study will focus in the areas where the Program for the Eradication of Illicit Crops by Aerial Spraying with Glyphosate Herbicide (PECIG) is implemented, as follows: In the Amazon Region, Caquetá; Hillside zone, Guaviare; Amazonian Plain, Putumayo; Mountain-range slope, in the region of Catatumbo, the municipality of Tibú, Norte de Santander; in the Magdalena and Mid-Cauca regions, the South of Bolivar, the region of the Colombian massif, the high-Andean forest in the Tolima Province.

Although the areas established by the Government of Colombia are the main objective of this study, the Scientific Assessment Team, in agreement with the Colombian Government, may include other areas the assessment of which is deemed relevant.

PERSONNEL HIRING

The participation of two separate teams in the Program for the Monitoring of Aerial Spraying (PMFA) is foreseen: A Scientific Assessment Team (SAT) and a Permanent Technical Group for Mobile Monitoring. Both teams will work in coordination during the entire process

The Scientific Assessment Team (SAT): CICAD proposes an initial review of the impact of spraying, in particular, of the current aerial spraying protocol. The team will be made up of 4-6 international experts, from different parts of the world. This will be a multinational team with experts on topics such as pathology, environment, tropical horticulture and soils, medicine and veterinary sciences. The members of the team must also be able to present and defend their results in press conferences and other international media events. Thus, at least one member of this team must have experience on project management and press relations.

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The team will not include United States or Colombian nationals, but rather a group of international experts highly regarded in their respective fields. Resort may also be had to the experience of international research institutions, such as the Tropical Agronomy Centre for Research and Teaching (CATIE), the International Atomic Energy Agency (IAEA), the International CAB and the International Centre for Tropical Agriculture (CIAT), as well as to leading international universities in the field. Most of [the team's] work will be conducted from their current locations, through computer or telephone links, or by joint work meetings at a convenient location. Once the assessment has been completed and submitted, the team will be constantly at hand in order to reply to the different queries that may arise.

The Permanent Technical Group for Mobile Monitoring (PTGMM): This group will be in charge of daily operations once the Scientific Assessment Team (SAT) has completed the initial review and operational design. The main work of the PTGMM is to compile and analyse data, according to SAT's instructions on specific project requirements, as well as the occasional complaints or controversies. The PTGMM will be made up of third-country and/or Colombian nationals, under the coordination of a Colombian technician. Personnel selected will submit to the corresponding security studies. The PTGMM will have its seat in Bogotá and be permanently available to travel around the country.

ACTIVITIES

The initial period for the execution of the program will be a year. During this period, CICAD proposes that the team should complete its work on the impacts of aerial spraying and its protocol, and with the information provided by the PTGMM, activities aimed at random monitoring and constant monitoring of aerial spraying activities be carried out.

Likewise, the investigation on the issues relating to the environmental impact of herbicides and fungicides used in the production of illicit crops will be conducted.

The activities foreseen in the project are listed hereafter…

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ANNUAL REPORT OF THE INTER-AMERICAN DRUG ABUSE CONTROL COMMISSION (CICAD) TO THE GENERAL ASSEMBLY OF THE ORGANIZATION OF AMERICAN STATES AT ITS 34TH REGULAR SESSION, 17-20 NOVEMBER 2003, MONTREAL, CANADA, 3 MAY 2004

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ORGANIZATION OF AMERICAN STATES

INTER-AMERICAN DRUG ABUSE CONTROL COMMISSION

cicad

THIRTY-FOURTH REGULAR SESSION
November 17-20, 2003
Montreal, Canada

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ANNUAL REPORT OF THE
INTER-AMERICAN DRUG ABUSE CONTROL COMMISSION (CICAD) TO THE
GENERAL ASSEMBLY OF THE ORGANIZATION OF AMERICAN STATES
AT ITS THIRTY-FOURTH REGULAR SESSION

GENERAL SECRETARIAT OF THE ORGANIZATION OF AMERICAN STATES, WASHINGTON, D.C. 20006

consensus on the nature of and responsibilities for the development of an initial system that can be tested among all participating university sites. Researchers have visited specific ports of entry in both the Dominican Republic and Belize to familiarize themselves with the on-the-ground reality of each country so that they can produce a prototype appropriate for field deployment by national immigration and other governmental agencies. A second technical meeting, held in September 2003 at Carnegie Mellon University in Pittsburgh, served to integrate the separate research components of the project being conducted by the participating universities. This meeting prepared the ground for a technical meeting and initial prototype field test in Belize in December 2003.

PROJECT ON INSTITUTION-BUILDING IN ANDEAN NATIONAL DRUG COMMISSIONS

The main objective of this project, financed by the Spanish Government, is to strengthen the national drug commissions of the Andean countries, which will make possible the development of national drug information and research systems (national observatories), which are the basic tools for strategic planning of national drug policies. The project has continued to move forward despite the region's social and political instability and constant changes of officials and technical staffs of the national institutions involved.

- **Bolivia**
  The project seeks to incorporate national demand reduction data into the existing National Drug Information System (SINALTID). An early 2003 coordination mission introduced new data sources into the system (Vice Ministry of Prevention and Rehabilitation, Ministry of Education, Ministry of Health, and National Statistics Institute, as well as NGOs, universities, and research institutes), to identify the equipment needed by participating institutions, and to define the process for purchasing it. Delivery will take place once the Bolivian Government makes staffing decisions and selects a locale for the Observatory's technical team. A development workshop for the Bolivian Observatory is scheduled for the near future to define a national map of stable indicators along the lines of the SIDUC drug use and CICDAT supply control systems of the Inter-American Observatory on Drugs, pending a positive reply from the Bolivian Government.

- **Colombia**
  Under this project, support is being provided to strengthen the Colombian Drug Observatory, which was organized by the National Drug Council around SIDCO (Drug Information System of Colombia). The project will enable SIDCO to be updated and improved and to have an Internet site. Proposals are also being considered for the development of a national epidemiological surveillance system, put together by the Social Protection Ministry's Office of Public Health.

- **Ecuador**
  Throughout 2002, the project consolidated the development of the Ecuadorian Drug Observatory. In 2003, CICAD has carefully followed the Observatory's progress, primarily because of senior management position changes in the National Drug Commission (CONSEP).

- **Peru**
  Following the definition of the Peruvian Drug Observatory's work plan at a workshop held in November 2002, the process was finalized for procurement and delivery of computer equipment to national institutions participating in the Observatory. Moreover, the technical

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35TH REGULAR SESSION OF CICAD, WASHINGTON, D.C., 27-30 APRIL 2004, SESSION DOCUMENTS

(Available at: http://www.cicad.oas.org/apps/sessions.aspx?lang=ENG&ie=us007
(last visited 7 March 2010))

THIRTY-FIFTH REGULAR SESSION OF CICAD

Washington, D.C. United States
April 27 - 30, 2004

Document No.	Description	Siz
INF.1	Meeting on Maritime Narcotrafficking: Status report on preparations Presentation by Honduras @UpdatedNov 15 2006 10:49AM	4
1264	Annual Report @UpdatedNov 14 2006 3:25PM	27
1294	Agenda @UpdatedNov 14 2006 3:26PM	1
1295	Schedule of Activities @UpdatedNov 14 2006 3:28PM	2
1297	Bolivia Candidacy for the position of Vice Chair of the Commission @UpdatedNov 14 2006 3:29PM	1
1298	Review of requests for assistance from member states, in accordance with funds available, to help them to fulfill the recommendations of the MEM @UpdatedNov 15 2006 11:08AM	11
1299	Report of the ad hoc group on Transnational Organized Crime and its Links to Drug Problems and the work of CICAD Presentation by the Chair of the ad hoc group @UpdatedNov 15 2006 10:51AM	4
1300	Proposals for a Plan of Action for the Development of Hemispheric Cooperation Against the Illicit Trafficking of Drugs and Related Crimes Associated with Transnational Organized Crime @UpdatedNov 15 2006 10:54AM	3
1302	Report of the first meeting of the CICAD Scientific Advisory Committee held in Washington , March 23-25, 2004 Presentation by Dr. Hendrick Harwood, Representative from the Committee @UpdatedNov 15 2006 11:34AM	4

1303	The Health, Enforcement and Education in Partnership (HEP) Approach Held in Fort-de-France, Martinique, March 18-19, 2004 Presentation by Karen Cumberland, HEP National Policy Officer, Canadian Centre on Substance Abuse (CCSA) @UpdatedNov 15 2006 4:18PM	17
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ENVIRONMENTAL AND HUMAN HEALTH ASSESSMENT OF THE AERIAL SPRAY PROGRAM FOR COCA AND POPPY CONTROL IN COLOMBIA

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A report prepared for the Inter-American Drug Abuse Control Commission (CICAD) section of the Organization of American States (OAS)

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PREFACE

This report was prepared for the Inter-American Drug Abuse Control Commission (CICAD) section of the Organization of American States (OAS) in response to requests from the Governments of Colombia, the United Kingdom, and the United States of America. The request was to conduct a science-based risk assessment of the human health and environmental effects of the herbicide, glyphosate, used for the control of the illicit crops, coca and poppy in Colombia.

The initial step in the process was to establish an international panel of experts in human and environmental toxicology, in epidemiology, in agronomic practices, and in ecology (SAT). Because both Colombia and the United States were actively involved in the program for eradication of illicit crops, members of the panel were specifically selected from other countries.

Initially, the panel met to formulate a framework to conduct this risk assessment. The framework was based on those commonly used for risk assessment in a number of jurisdictions and consisted of a problem formulation, characterization of the human health and environmental effects of the substances used in the eradication program, characterization of human and environmental exposures, and the drawing together of these in a risk characterization. During this process, extensive use was made of the scientific and other literature but, where data gaps and uncertainties related to the specific uses in Colombia were identified, studies were initiated to assemble additional data for use in the risk assessment. Some of these studies were carried out in Colombia. The Colombian team (PTG) were contracted specifically to CICAD and worked under the direction of the SAT to collect data in the Colombian Environment. During the conduct of our study, members of the SAT made a number of visits to Colombia to view, at first hand, all aspects of the program, to gather local information and data, and to oversee the local studies of the PTG.

We recognize that the illicit crop eradication program in Colombia has generated considerable local and international interest and is the subject of intense debate for political, social, and other reasons. We have specifically excluded all social, political, and economic issues from our study and the final report is strictly based in science and scientifically based arguments. We believe that the report of the study and its scientific recommendations will be useful in decision making to protect human health and the environment.

After the initiation of this project, additional information on other substances used in the production of coca and poppy and the refining of cocaine and heroin was requested. This request culminated in two separate detailed reports, a Tier-1 and Tier-2 hazard assessment of 67 and 20 substances used for these purposes, respectively. These substances are briefly discussed in the Problem Formulation of this report. We believe that these reports will be useful in comparative hazard assessment and in risk management decision making.

ACKNOWLEDGEMENTS

With an international panel of experts and activities in several countries, a study of this nature requires good co-ordination and organization. We are deeply indebted to Mr. Jorge Rios and Ms. Adriana Henao of the CICAD office for their excellent work in organizing meetings, teleconferences, and field trips. They served the Panel well and frequently worked well beyond the call of duty. We are also very grateful for the contributions of the Colombian Field Team, the PTG. Unfortunately, we cannot name these individuals; however, we extend our most grateful thanks to all of you for all the hard work and the personal risks that you took on behalf of data collection for this project.

Field visits to Colombia by members of the SAT were facilitated and coordinated by the staff of the Ministry of Foreign Affairs and the team was afforded protection by the National Police (Antinarcoticos). We offer our grateful thanks to Brigadier General Luis Gómez, his staff, the pilots, technicians, and the “Junglas” commandos for aiding us in our observations and sampling and for tolerating our scientific curiosity in the face of other priorities. At all times, we were given free and unfettered access to information, we were allowed to take photographs freely, and we were always treated with respect and in a most professional manner.

The SAT members are indebted to Drs. Lesbia Smith, Angus Crossan, Richard Brain, and also to the many students in the Toxicology Program at the University of Guelph for their work on the separate reports on Tier-1 and Tier-2 hazard assessment of other substances used in the production and refining of cocaine and heroin. These data are presented in separate reports.

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EXECUTIVE SUMMARY

This report was prepared for the Inter-American Drug Abuse Control Commission (CICAD) section of the Organization of American States (OAS) in response to requests from the Governments of Colombia, the United States, and the United Kingdom. The request was to conduct a science-based risk assessment of the human health and environmental effects of the use of glyphosate for the control of the illicit crops, coca and poppy, in Colombia. This became the purpose of the study, which was conducted in a number of steps.

The initial step in the process was to establish an international Panel of experts in human, animal, and environmental toxicology, in epidemiology, in agronomic practices, and in ecology (the Scientific Advisory Team - SAT). In the second step, the SAT formulated a framework to conduct this risk assessment. The framework is similar to those commonly used for assessing risks in a number of jurisdictions and consisted of a problem formulation, characterization of the human health and environmental effects of the substances used in the eradication program, characterization of human and environmental exposures, and the drawing together of these in a risk characterization. During the process of conducting the risk assessment, the SAT used scientific literature and government reports but, where data gaps and uncertainties related to the specific uses in Colombia were identified, studies were initiated to assemble additional data for use in the risk assessment. Several of these studies were carried out in Colombia. The Colombian Team (PTG) were contracted specifically to CICAD and worked under the direction of the SAT to collect data in the Colombian environment. During the conduct of our study, members of the SAT made a number of visits to Colombia to view, at first hand, all aspects of the program, to gather local information and data, and to oversee the local studies of the PTG.

The SAT recognized that the growing and production of illicit drugs in Colombia has significant political, social, and economic, implications. However, this study was focused specifically on the human health and environmental significance of the production and eradication of coca and poppy through the use of aerially applied herbicide. The production of coca and poppy as well as the processing and production of cocaine and heroin also involves significant environmental impacts. Both coca and poppy are grown intensively in a process that involves the clearing of land, the planting of the crop and protection against pests such as weeds, insects, and pathogens. All of these activities can impact human health and the environment and some, such as clear-cutting, do so to a significant extent. The total land area used for these activities is small relative to the entire country. However, much of the production takes place in remote areas that are close to or part of the Andean Biodiversity Hotspot.

In Colombia, the herbicide glyphosate is widely used in agriculture and for purposes other than eradication of coca and poppy. Only 10-14% of the total use in Colombia is in the eradication program. Similarly many of the pesticides and other substances used in the production of coca and poppy are also widely used in agriculture. The aerial eradication spray program in Colombia is conducted with modern state-of-the-art aircraft and spray equipment. The spray equipment is similar to that used for forest spraying in other parts of the world and produces large droplets which minimize drift of spray. Identification of target fields and electronic documentation of locations and areas sprayed is conducted with high precision. As a result of the use of best available spray and navigation technology, the likelihood of accidental off-target spraying is small and is estimated to be less than 1% of the total area sprayed.

The physical, chemical, and biological properties of glyphosate and an adjuvant (Cosmo-Flux®) added to the spray mix were characterized through the scientific literature and through new studies specifically conducted for this risk assessment. Glyphosate is a widely-used herbicide that is well characterized in terms of physical, chemical, and biological properties. Glyphosate is not highly mobile in the environment and is rapidly and tightly bound on contact with soil and aquatic sediments. Glyphosate has a very short biological activity in soils and water, does not biomagnify or move through the food chain, and does not leach into groundwater from soil.

Exposures of humans to glyphosate under the conditions of use could not be measured directly in the growers of illicit crops and thus were estimated from literature values with adjustments for the rates of application used in the eradication program in Colombia. Estimated exposures resulting from direct overspray, contact with treated foliage after re-entry to fields, inhalation, diet, and drinking water were small and infrequent. In a special study in five watersheds, weekly analyses of surface waters and sediments over a period of 24 weeks showed that, on most occasions, glyphosate was not present at measurable concentrations; only two samples had residues above the method detection limit of 25 µg/L. As most of the glyphosate used in Colombia is in agriculture, this confirms that, regardless of use pattern, glyphosate is not mobile in environment and it will not move from the treated fields in significant amounts. In analyses of water samples taken from the same five watersheds, several other pesticides were found, including the herbicide 2,4-D and the insecticide endosulfan, the latter a product that is banned in Colombia.

Concentrations of glyphosate in several environmental matrices resulting from the eradication spray program were estimated. Concentrations in air were predicted to be very small because of negligible volatility. Glyphosate in soils that are directly sprayed will be tightly bound and biologically unavailable. Based on observations in other temperate and tropical areas, no residual activity is expected in soil and even the most sensitive organisms, plants, will not be prevented from re-establishing themselves. In Colombia, this is evidenced by the rapid recovery of sprayed fields through successful replanting of coca and/or colonization by invasive species of plants. Concentrations of glyphosate plus Cosmo-Flux® will be relatively large in shallow surface waters that are over-sprayed (maximum instantaneous concentration of 1,052 µg AE/L in water 300 mm deep); however, no information was available on the number of fields in close proximity to surface waters and it was not possible to estimate the likelihood of such contamination.

The toxicity of glyphosate has been rigorously assessed in a number of jurisdictions and in the published literature. Glyphosate itself has low toxicity to non-target organisms other than green plants. It is judged to have low acute and chronic toxicity, carcinogenic, mutagenic, or a reproductive toxicant. With respect to humans, is not considered hazardous, except for the possibility of eye and possibly skin irritation (from which recovery occurs). The toxicity of the formulation as used in the eradication program in Colombia, a mixture of glyphosate and Cosmo-Flux®, has been characterized in specific tests conducted in laboratory animals. The mixture has low toxicity to mammals by all routes of exposure, although some temporary eye irritation may occur. By extrapolation, the spray mixture is also not expected to be toxic to terrestrial mammals and vertebrates. Epidemiology studies conducted in a number of jurisdictions around the world have not suggested a strong or consistent linkage between glyphosate use and specific human health outcomes. A preliminary epidemiology study was conducted in Colombia to assess any linkage between glyphosate and the reproductive outcome, time to pregnancy, in humans. This study did not show any association between time to pregnancy and the use of glyphosate in eradication spraying.

New data from the environmental literature on the toxicity of some formulations of glyphosate suggest that amphibians may be the most sensitive group of aquatic organisms. Special tests of the spray mixture as used in Colombia were conducted using standardized environmental test organisms. These tests revealed that the mixture of glyphosate and Cosmo-Flux® was not toxic to honey bees. The mixture was, however, more toxic to aquatic organisms than formulated glyphosate alone. Extensive studies on the use of glyphosate in agriculture and forestry in temperate and tropical areas have been published in the literature. These have shown that direct effects on non-target organisms other than plants are unlikely to occur. Indirect effects on terrestrial arthropods and other wildlife have, however, been observed. These are the result of habitat alteration and environmental change brought about by the removal of target plants through the effects of glyphosate. Similar effects would be expected regardless of the type of method used to control plants and also occur as a result of clear-cutting, burning, and conversion of natural areas into agricultural lands. Because of the lack of residual activity, recovery of glyphosate-treated areas will be dependent only on the nature of the recolonizing species and the local conditions. Given experience in other tropical regions and in Colombia, this process will be rapid because of good conditions for plant growth. However, return to the conditions of tropical old-growth forest that existed prior to clear-cutting and burning may take hundreds of years. It is important to recognize that the impact here is not the use of glyphosate but the original act of clear-cutting and burning that is the primary cause of the effects on the environment.

The risk assessment concluded that glyphosate and Cosmo-Flux® as used in the eradication program in Colombia did not present a significant risk to human health. Estimated acute worst-case exposures in humans via all routes were less than doses of concern, even for chronic responses. In the entire cycle of coca and poppy production and eradication, human health risks associated with physical injury during clear-cutting and burning and the use of pesticides for protection of the illicit crops were judged to be more important than those from exposure to glyphosate.

For the environment, risks from the use of glyphosate and Cosmo-Flux® to terrestrial animals were judged to be small to negligible. Moderate risks could occur in aquatic organisms in shallow surface waters that are over-sprayed during the eradication program. However, the frequency of occurrence and extent to which this happens are unknown as data on the proximity of surface waters to coca fields were not available. Considering the effects of the entire cycle of coca and poppy production and eradication, clear-cutting and burning and displacement of the natural flora and fauna were identified as the greatest environmental risks and are considerably more important than those from the use of glyphosate.

Strengths and uncertainties in the assessment were identified and used to develop recommendations which were then prioritized. It is recommended that the current application practices for eradication spraying be retained but that additional data be gathered over a longer time period to better characterize the impacts of coca and poppy production in the Andean Biodiversity Hotspot and the possibility of non-target effects in surface waters located close to fields. If shallow waters are routinely found close to fields, it is recommended that other formulants be tested for the purposes of selecting products that present a lower risk to aquatic organisms. Although no association was observed between eradication spraying and reproductive outcomes in humans, additional studies to identify possible risk factors associated with other human activities or environmental factors should be considered.

1 INTRODUCTION

1.1 BACKGROUND

It is estimated that some 200 million people worldwide use illicit drugs. Most of these drugs have natural origins, such as cannabis, cocaine, and the opiates, however, the synthetic drugs such as the amphetamines also comprise a significant proportion of these uses (United Nations 2002). In response to the socio-economic impacts of the production and distribution of illicit drugs, a number of individual nations, as well as multinational organizations, have initiated programs to reduce and eventually eliminate production and distribution (United Nations 2002). While it is recognized that the political, social, and economic impacts of the production, distribution, and use of all of these drugs is significant, the focus of this report is on issues related to the program for reduction and eradication of production of coca and opium poppy and their derivatives, cocaine and the opiates in Colombia, South America.

Coca (*Erythroxylum coca* and related species, Figure 1) are commonly associated with the tropical mountainous regions of South America. However, it has been reported to be grown in Africa, Sri Lanka, Taiwan, and Indonesia (Bray and Dallery 1983). A number of species of coca are found in South America and various varieties grow in the wild or are cultivated in different climatic conditions. It is primarily found in tropical regions with temperatures above 25°C and moderate to high rainfall >1000 mm per year. Currently, it is widely cultivated in Colombia, Bolivia, and Peru, with some cultivation in Ecuador, Venezuela, Brazil, and Argentina as well.

Figure 8 Coca plant

Historically, coca played an important role in culture of the Incas, Quechuas, and many other Andean peoples. Coca also played an important role in the conquest of Latin America by the Spanish when it was used as an incentive and payment for work on railroads, in agriculture, and in mines. More recently, cocaine, derived from the coca plant, has become widely used in many countries. Initially used as a medicinal drug, it was introduced to Europe as cocaine in 1860 as an ingredient of a wine-coca drink which was apparently used by the likes of Sarah Bernhardt, Queen Victoria of England, Thomas Edison, and Pope Leo the XIII. It was also used as a local anesthetic. In 1886, John Pemberton introduced the tonic drink CocaCola® which contained cocaine until 1904 (Gottlieb 1976). Cocaine is now widely used as an illicit addictive drug; global production between 1995 and 2002 was estimated to range from 640 to 950 tonnes used by an estimated 14 million people (United Nations 2002). The illicit growing of coca and its processing into cocaine has become a large and profitable industry that has had significant impacts on social and economic order in a number of producer as well as in consumer nations.

Opium, morphine, and its derivative, heroin, are produced from the poppy, *Papaver somniferum,* which is primarily grown in Asia. Global production of opium in 2002 was estimated to be 1,586 tonnes, of which about 160 tonnes were produced in South America (United Nations 2002). It is estimated that, globally, about 15 million people use opiates and that about 10 million of these use heroin (United Nations 2002). Like coca, the use of opium and morphine has historical roots in the traditional society of the producer regions but became more widely used as a medicinal drug when introduced to other parts of the world. While morphine is still used for medicinal purposes, heroin use is largely illegal and its production and distribution has significant socio-economic impacts in producer and consumer nations.

1.2 IMPACTS OF ILLICIT DRUG PRODUCTION IN COLOMBIA

The growing and production of illicit drugs in Colombia has significant political, social, economic, and environmental impacts. While recognizing the importance of the political, social, and economic aspects of the issue, this report is focused on the human health and environmental significance of the eradication of coca and poppy through the use of aerially applied herbicide.

Although the focus of this study is on the coca and poppy eradication program, it is important to recognize that the actual production of coca and poppy as well as the processing and production of cocaine and heroin involves significant environmental impacts. Both coca and poppy are grown intensively in a process that involves the clearing of land, the planting of the crop and its protection against pests such as weeds, insects, and pathogens.

Depending on the region, the clearing of the land for production purposes may have large and only slowly reversible effects on the environment. As for other forms of agricultural production, the clear-cutting of forests for the purposes of coca and poppy production reduces biodiversity, contributes to the release of greenhouse gases, increases the loss of soil nutrients, and promotes erosion of soils. As production is illegal, it normally takes place in remote locations. As a result, the clearing of land is done with little apparent consideration for the biological and aesthetic value of the ecosystem.

A number of pesticides are used in the production of illicit drugs (Table 1). Herbicides may be used in the initial clearing of the land and later in the suppression of weeds. Similarly, insecticides and fungicides may be used to protect the illicit crops from pests and diseases. To increase yields, fertilizers and other nutrients may also be used. Large quantities of agrochemicals have been seized and confiscated as part of the program to control the production of illicit drugs (Direccion Nacional de Estupefacientes 2002). Although some of these agrochemicals are highly toxic to mammals and may have significant environmental impacts, accurate information on the amounts used, their frequency of use, and the conditions of their use is not available. Because of this, it is not possible to conduct a detailed human health and ecological risk assessment. However, the relevant toxicological and environmental properties of these substances are summarized in two separate reports and several of these are significant potential hazards to human health and the environment (CICAD/OAS 2004a, 2005).

Table 1. Pesticides used in the production of coca

Active ingredient	Toxicological classification[a]	Estimated % of use	Chemical class
Paraquat	II	61.3	Bipyrilidinium herbicide
Glyphosate	IV	19.1	Phosphate herbicide
2,4-D	I	9.7	Phenoxy herbicide
Atrazine	III	4.8	Triazine herbicide
Diuron	III	2.6	Urea herbicide
Carbaryl	II	NA	Carbamate insecticide
Carbendazim	III	NA	Benzimidazole carbamate fungicide
Carbofuran	I	NA	Carbamate insecticide
Chlorpyrifos	II	NA	Organophosphorus insecticide
Copper oxychloride	III	NA	Metal fungicide
Cypermethrin	II	NA	Pyrethroid insecticide
Diazinon	III	NA	Organophosphorus insecticide
Endosulfan	I	NA	Organochlorine insecticide
Lambda cyhalothrin	III	NA	Pyrethroid insecticide
Malathion	III	NA	Organophosphorus insecticide
Mancozeb	III	NA	Carbamate fungicide
Methamidophos	I	NA	Organophosphorus insecticide
Methomyl	I	NA	Carbamate insecticide
Methyl parathion	I	NA	Organophosphorus insecticide
Monocrotophos	I	NA	Organophosphorus insecticide
Prophenophos	II	NA	Organophosphorus insecticide

[a] As classified by the Instituto Colombiano Agropecuaria (ICA) as follows: I (very toxic), II (toxic), III (slightly toxic). Data from (Direccion Nacional de Estupefacientes 2002)

In addition to the use of agrochemicals in the production of coca and poppy, large amounts of chemicals are used in the processing of the raw product into refined cocaine and heroin (Table 2). Processing of the illicit drugs is conducted in remote locations and in the absence of occupational health and environmental regulations and controls. During and after use, these substances may be released into the environment and have significant impacts on human health and the ecosystem. The toxicological and environmental properties of these substances are summarized in a separate Tier-1 Hazard Assessment Report (CICAD/OAS 2004a). Some of these substances have potentially large environmental and human health hazards and a subset of these are dealt with in more detail in Tier-2 Hazard Assessment Report (CICAD/OAS 2005).

Table 2. Identity and amounts of substances seized in Colombia as a result of counter-drug operations[a]

Year	1999	2000	2001	2002
Solid substances (units in Kg)				
Activated charcoal	36,681	49,323	84,141	93,057
Ammonium chloride	480	7	450	350
Ammonium nitrate	-	-	2,390	9,350
Ammonium sulfate	-	-	-	900
Calcium carbonate	500	150	255	1,570
Calcium chloride	7,371	33,073	56,985	146,040
Cement, grey	142,818	197,646	502,857	1,053,372
Cement, white	-	-	-	18,700
Lime	24,807	49,783	155,507	220,259
Potassium chloride	2,290	4,766	1,456	34,750
Potassium hydroxide	375	1,425	-	4,700
Potassium nitrate	2	-	2,150	2,390
Potassium permanganate (sum)	71,284	171,798	51,641	80,639
Sodium bicarbonate	52	4,827	8,538	9,939
Sodium carbonate	531,095	248,136	59,521	128,571
Sodium chloride	28,154	17,046	31,594	35,161
Sodium hydroxide	73,776	69,100	111,540	122,619
Sodium hypochlorite	-	16	4,208	1,720
Sodium sulfate	5,755	970	1,852	8,667
Urea	62,685	37,995	226,394	360,237
Liquid substances (units in L)				
Butyl Acetate	23,732	469	13,089	11,908
Ethyl Acetate	97,723	76,156	23,289	15,336
Acetone	1,666,474	894,070	1,546,651	1,841,860
Hydrochloric Acid	144,804	62,303	126,884	140,650
Sulfuric Acid	303,732	200,404	241,903	277,538
Isopropyl Alcohol	59,379	6,938	16,408	19,330
Ammonia	131,104	154,180	102,512	431,485
Acetic Anhydride	9,938	284	10,855	1,045
Chloroform	465	1,457	1	273
Ethyl Ether	205,984	67,704	53,989	110,098
Gasoline	621,686	1,034,880	2,013,650	2,612,820
Hexane	35,963	4,497		16,991
Kerosene	127,316	90,855	159,818	210,408
Methyl ethyl ketone MEK	88,402	69,209	10,674	41,332
Methanol	269,027	14,107	2,961	3,512

Table 2. Identity and amounts of substances seized in Colombia as a result of counter-drug operations[a]

Year	1999	2000	2001	2002
Methyl isobutyl ketone MIBK	55,943			2,086
Thinner	226,657	78,156	100,829	203,459
Toluene	3,630	208	19	6,469
Acetic acid	11	14	208	212
Nitric acid	59	6	1	5,300
Isobutyl alcohol	170		3	1,136
Petroleum ether				35,579
Methylene chloride	416	4	45	4,182
Fuel oil	32,082	325,250	346,460	948,083
Solvent No 1	203,603	116,498	435,816	280,921
Solvent No 2	6,505	3,819	5,621	11,942

[a] These substances are mainly used in the refining of cocaine, opium, and heroin. It is estimated that only 20% of the total amounts used are seized. Therefore, total use may be as much as 5-times greater than indicated in the table. Data from (Direccion Nacional de Estupefacientes 2002)

1.3 THE PROGRAM TO CONTROL ILLICIT DRUG PRODUCTION AND DISTRIBUTION IN COLOMBIA

The growing of coca and poppy and the distribution of cocaine and opium/heroin in Columbia has been the focus of a national control and eradication program starting in the 1970s. The program involves a number of Departments and Agencies of the Colombian Government and is coordinated by the Direccion Nacional de Estupefacientes (DNE), an agency of the Ministry of the Interior and Justice. The program has three main foci; the control of production of coca and poppy; the control of the processing, purification, and transport of the cocaine and heroin; and the seizure and forfeiture of the profits of illicit drug production (Direccion Nacional de Estupefacientes 2002).

The aerial eradication program in Colombia is the responsibility of the Antinarcotics Directorate of the Colombian National Police (DIRAN-CNP), supported by data gathering from other nations such those in North America and Europe. The DIRAN conducts regular flights with aircraft that spray coca and opium poppy crops with herbicide. The DIRAN reviews satellite imagery and flies over growing regions on a regular basis to search for new coca and opium poppy growth and to generate estimates of the illicit crops through high resolution low-altitude imagery and visual observation. The DIRAN selects the locations of the illicit crops that are to be sprayed with input from the DNE or the Government of Colombia's Plan Colombia Office. For example, at this time, certain existing or future alternative development projects or national parks may not be sprayed as a matter of policy.

Several concerns have been raised about the use of glyphosate and adjuvants in the eradication of coca and poppy plants. These concerns range from damage to other crops to adverse effects on the environment and human health. In response to this, the

Government of Colombia appointed an independent environmental auditor who reviews the spray and no-spray areas with the DIRAN, and regularly monitors the results of spraying through field checks and analysis of data from the computer system.

The objectives of this assessment and report are to provide a science- and data-based study of the eradication program with a key focus on the environment and human health, to collect data for use in the assessment, to address specific concerns that have been raised, and to make the results known to the public and the scientific community. As with all risk assessments, we have followed a framework based on those used in other jurisdictions (NRC 1986, USEPA 1992, 1998). This framework consists of a Problem Formulation, Effects and Exposure Assessment, and Risk Characterization for both humans and the environment.

2 PROBLEM FORMULATION

The problem formulation is a key step in the process of the risk assessment and places the use of the substances being assessed into a local context. It is recognized that the growing of illicit crops such as coca and poppy as well as the refining of the cocaine and heroin involves considerable impacts on the environment through clearing of forests and the use of a number of substances for promoting crop growth and refining of the drugs (Figure 2). Although the identity of the substances is known, the quantities used, and their manner of use is largely unknown and exposures in workers cannot be easily estimated. While the hazard of these substances is known (CICAD/OAS 2004a, 2005), the risks cannot be estimated as the logistics of collecting the human and environmental exposure data are very difficult and not without other risks. Because of this and as it was the initial mandate of the Panel, the focus of this risk assessment is on the use of glyphosate and adjuvants for control of the illicit crops. In this case, the locations and amounts of application are known with accuracy and environmental risk can be estimated.

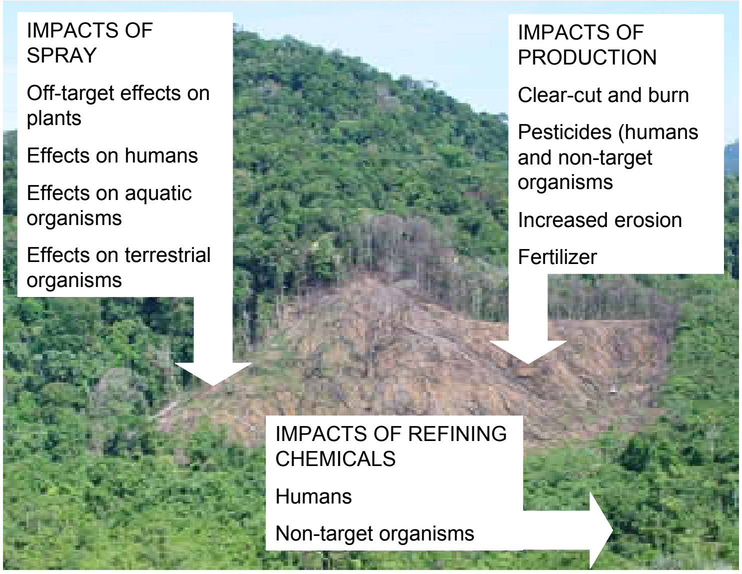


Figure 9 Diagrammatic representation of potential impacts of coca production, refining, and spraying.

In humans, there are no specific biomarkers for exposure to glyphosate that can be used to estimate historical exposures. For logistical reasons, it was not possible to measure exposures resulting from eradication spraying directly in the field. For that reason, in epidemiology studies, indirect measures of exposures such as ecological studies, where the indicator variable or exposure is a defined by eradication spraying and crops production patterns, must be used.

2.1 STRESSOR CHARACTERIZATION

The potential stressors in this risk assessment are glyphosate, its formulants, and adjuvants, such as surfactants, that are added to the spray formulation to modify its efficacy. The properties of glyphosate and these substances are described in the following sections.

2.1.1 Glyphosate

Glyphosate is one of the most widely used pesticides on a global basis. Uses include agricultural, industrial, ornamental garden and residential weed management. In agriculture, the use of glyphosate is increasing and use in soybeans is probably greater since the introduction of glyphosate-tolerant crops (Wolfenbarger and Phifer 2000). Other agricultural uses for glyphosate-based products include its use by farmers as a routine step in pre-plant field preparation. Non-agricultural users include public utilities, municipalities, and regional transportation departments where glyphosate is used for the control of weeds or noxious plants. The environmental and human-health properties of glyphosate have been extensively reviewed in the literature (Giesy et al. 2000, Solomon and Thompson 2003, Williams et al. 2000) and by regulatory agencies (NRA 1996, USEPA 1993a, 1997, 1999, World Health Organization International Program on Chemical Safety 1994). The following sections highlight key issues with regard to those properties of glyphosate that are fundamental to the assessment of risks associated with the coca and poppy eradication programs in Colombia.

2.1.1.1 Structure and chemical properties

The chemical name of glyphosate (acid) is N-(phosphonomethyl) glycine (MW = 167.09) and that of the most common technical form, the isopropylamine salt (IPA) is N-(phosphonomethyl) glycine isopropylamine salt (MW = 226.16). The Chemical Abstracts Registry (CAS) number of the acid is 114370-14-8 and for the IPA salt is 1071-83-6. The chemistry of glyphosate is important in determining its fate in the environment. Glyphosate (Figure 3) is a weak organic acid comprising a glycine moiety and a phosphonomethyl moiety. Chemically and physically, glyphosate closely resembles naturally occurring substances and it is not chemically reactive, not mobile in air or soils, does not have great biological persistence, and does not bioaccumulate or biomagnify through the food chain (CWQG 1999, Giesy et al. 2000, USEPA 1993a, Williams et al. 2000, World Health Organization International Program on Chemical Safety 1994).

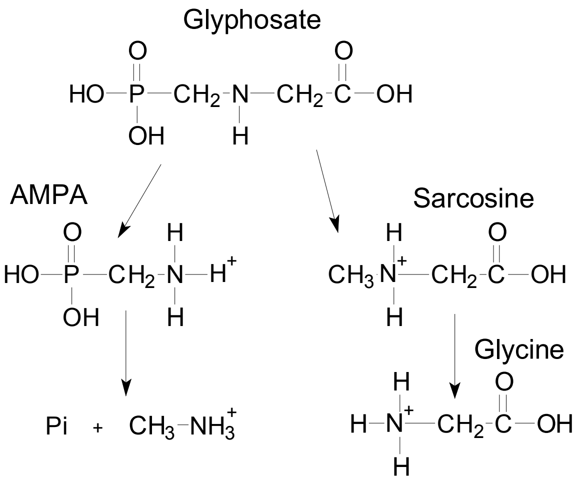


Figure 10 The structure of glyphosate and its major metabolic and breakdown products. From (Liu et al. 1991)

Glyphosate is readily ionized and, as the anion, will be strongly adsorbed to organic matter in soils of normal pH (Figure 4). It thus has low mobility in soils and is rapidly removed from water by adsorption to sediments and suspended particulate matter.

2.1.1.2 Mechanism of action of glyphosate

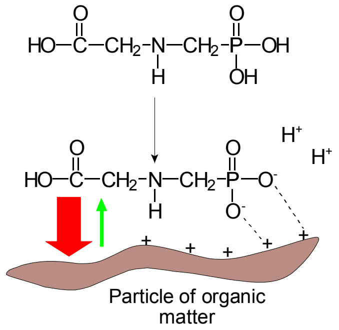


Figure 11 Binding of glyphosate to soil particles

The mechanism of action of glyphosate is via the inhibition of the enzyme 5-enolpyruvyl shikimate-3-P synthetase, an essential enzyme on the pathway to the synthesis of the aromatic amino acids in plants (Devine et al. 1993). This inhibition results in decreases in the synthesis of the aromatic amino acids, tryptophan, phenylalanine, and tyrosine, as well as decreased rates of synthesis of protein, indole acetic acid (a plant hormone), and chlorophyll. The death of the plant is slow and is first seen as a cessation of growth, followed by chlorosis and then necrosis of plant tissues. Inhibition of 5-enolpyruvyl shikimate-3-P synthetase is specific to plants. Many animals obtain their aromatic amino acids from plants and other sources and do not possess this pathway of synthesis. For this reason, glyphosate is relatively non-toxic to animals but is an effective herbicide in plants.

2.1.1.3 Global and local registration and use

Glyphosate has been registered since 1971 and is currently widely used as a broad-spectrum, non-selective, post-emergence herbicide in a number of countries around the world (World Health Organization International Program on Chemical Safety 1994). It is rapidly translocated from the leaves of treated plants to other parts of the plant, including the growing tips of stems and roots, and to underground storage organs, such as rhizomes and tubers. It is very effective for the control of perennial weeds and is more efficacious than many other non-selective herbicides that only affect the above-ground parts of the plant. Applied to soil, glyphosate shows low activity because the strong binding to soil organic matter makes the substance biologically unavailable to plants. Glyphosate has been used extensively in Colombia and many other countries for agricultural and other purposes for many years. Use of glyphosate in the coca and poppy spray program is shown in Table 3 and represents a relatively small fraction of the total use in Colombia.

Table 3. Use glyphosate in eradication spraying in Colombia 2000 to 2004

Year	Amount sold in Colombia (L)[a]	Amount used in the eradication of illicit crops (L)[b]	Percent of total amount sold
2000	7,037,500	603,970	8.6%
2001	9,473,570	984,848	10.4%
2002	NA	1,061,538	11%[c]
2003		1,381,296	14%[c]
2004		1,420,130	14%[c]

[a] Data from (ICA 2003). [b] Data from (Direccion Nacional de Estupefacientes 2002, Policia Nacional Direccion Antinarcoticos 2005). [c]Estimated from total used in 2001 but likely less than this value.

2.1.1.4 Environmental fate

The environmental fate of glyphosate has been extensively reviewed (CWQG 1999, Giesy et al. 2000, NRA 1996, World Health Organization International Program on Chemical Safety 1994); only key issues relevant to water and soil/sediment are summarized below.

As a result of its specific physicochemical properties, glyphosate is immobile or only slightly mobile in soil. The metabolite of glyphosate, aminomethyl phosphoric acid (AMPA, Figure 3), is somewhat more mobile in soil but is rapidly broken down, resulting in minimal amounts leaching in normal agricultural soils. The strong binding of glyphosate to soil results in almost immediate loss of biological activity, however, the bound residues do break down sufficiently rapidly that accumulation will not occur, even over many years of regular use. Contamination of groundwater from the normal use of glyphosate is unlikely except in the event of a substantial spill or other accidental and uncontrolled release of large amounts into the environment.

The great water solubility of glyphosate and its salts suggests that it would be mobile in water, however, strong and rapid binding to sediments and soil particles, especially in shallow, turbulent waters, or those carrying large loads of particulates, removes glyphosate from the water column (Tooby 1985). In normal agricultural uses, it is not expected to run-off or leach into surface waters.

In water, the two major pathways of dissipation are microbiological breakdown and binding to sediments (Giesy et al. 2000, World Health Organization International Program on Chemical Safety 1994). Glyphosate does not degrade rapidly in sterile water, but in the presence of microflora (bacteria and fungi) in water, glyphosate is broken down to AMPA (Figure 3) and eventually to carbon dioxide (Rueppel et al. 1977). Other metabolic pathways have been reported (Liu et al. 1991), including further degradation of AMPA to inorganic phosphate and CH_3-NH_3, and via sarcosine to glycine (Figure 3). None of these products are considered herbicidal and they would not be expected to be highly toxic to aquatic organisms at concentrations that would result from field use of glyphosate in aquatic systems. Photodegradation also may take place under field conditions where sufficient penetration of UV light occurs.

The dissipation of glyphosate from treated foliage and from leaf litter has also been characterized. As would be expected, most of the glyphosate sprayed on the plants penetrates into plant tissues after application, but some is available for washoff for several days after application (World Health Organization International Program on Chemical Safety 1994). If the plant dies as a result of this exposure, glyphosate would be present in the dead and decaying plant tissues. Glyphosate residues in leaf litter dissipate rapidly with a time to 50% disappearance (DT50) of 8-9 days under temperate forestry conditions (Feng and Thompson 1990). Similar rapid dissipation from fruits and lichen has also been observed (Stiltanen et al. 1981).

Dissipation under tropical conditions such as in Colombia will likely be more rapid than in temperate regions because of higher temperatures and moisture content which promote microbiological activity as well as chemical degradation of many pesticides. Large areas of Brazil, Colombia, Central America, most of Africa between the Sahara and Kalahari deserts, India, inland Indochina, and portions of Northern Australia share similar tropical conditions and some of those countries depend heavily on herbicides such as glyphosate (Racke et al. 1997). Glyphosate has been used in large areas of Brazil on no-tillage crops in general and, more recently, on transgenic soybeans. Comparing the fate of pesticides in tropical and temperate conditions, Racke et al. (1997) found no evidence of particular behavior of the pesticides in the tropics, they even concluded a greater rate of degradation under tropical conditions. The authors stated:

> *"Since soil microbial activities are strongly modulated by temperature, pesticide degradation would be expected to be greater in tropical soils, which experience higher year-round temperatures, than in temperate soils. This explanation would be consistent with observations of the elevated rates of soil organic matter turnover that characterize udic and ustic (rainy season) tropical environments. The few available studies which have directly compared pesticide fate in temperate and tropical soils held under identical conditions (i.e., laboratory) reveal no significant differences in either the kinetics or pathway of degradation. It appears that there are no inherent differences in pesticide fate due to soil properties uniquely possessed by tropical soils. Tropical soils themselves defy easy categorization, and their properties are as varied in nature as those from temperate zones. Pesticides appear to dissipate significantly more rapidly from soil under tropical conditions than under temperate conditions. The most prominent mechanisms for this acceleration in pesticide dissipation appear to be related to the effect of tropical climates, and would include increased volatility and enhanced chemical and microbial degradation rates on an annualized basis.*

2.1.2 Formulants and adjuvants

Formulants are substances that are added to a pesticide active ingredient at the time of manufacture to improve its efficacy and ease of use. These formulants serve many purposes and comprise a large range of substances, ranging from solvents to surfactants to modifiers of pH. The glyphosate formulation used in Colombia includes several formulants. Adjuvants are added to formulated pesticides at the time of application and, like formulants, increase efficacy, or ease of use in special situations where pests are difficult to control or where non-target effects need to be minimized. In the control program in Colombia, an adjuvant, Cosmo-Flux®, is added at the time of spraying.

The relatively great water solubility and the ionic nature of glyphosate retard penetration through plant cuticular waxes (Figure 5). For this reason, glyphosate is commonly formulated with surfactants which decrease the surface tension of the solution and increase penetration into the tissues of the plants (Giesy et al. 2000, World Health Organization International Program on Chemical Safety 1994).

2.1.2.1 Surfactants in the glyphosate formulation

The glyphosate formulation as used in eradication spraying in Colombia contains several formulants which are common to the commercial product as used in agricultural.

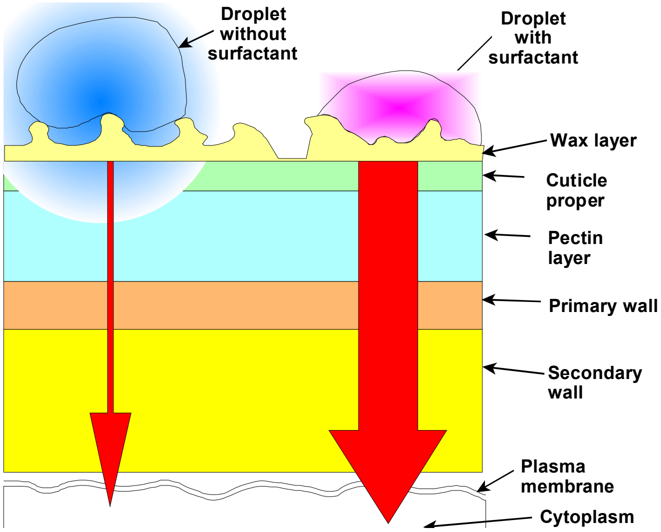


Figure 12 Penetration of an herbicide such as glyphosate through plant cuticular waxes in the absence (left) and presence of surfactants (right).

2.1.2.2 Cosmoflux 411F

As mentioned above, an adjuvant, Cosmo-Flux®, is added to the glyphosate at the time of spraying. Cosmo-Flux® is an agricultural adjuvant containing non-ionic surfactants (a mixture of linear and aryl polyethoxylates – 17% w/v) and isoparaffins (83% v/v) (Cosmoagro 2004). Adjuvants such as these are commonly added to pesticide formulations to improve efficacy through several mechanisms (Reeves 1992, Tadros 1994).

For example, surfactants such as the polyethoxylates in Cosmo-Flux®, increase efficacy through increasing target surface adherence, promoting better droplet spread, better dispersion, prevention of aggregation, and enhanced penetration of herbicides into target plant tissues through the reduction of surface tension on plants. Surfactants can also disrupt the water insoluble wax cuticle, thus increasing the penetration of herbicide active ingredient.

Base oils, such as the isoparaffins in Cosmo-Flux®, are another class of adjuvants used in pesticide formulations. They are used primarily to aid foliar absorption of the pesticide by disrupting the waxy cuticle on the outer surface of foliage which increases cell membrane permeability (Manthey and Nalewaja 1992).

2.1.3 Coca and poppy control programs

As discussed briefly above, the coca and poppy control programs make use of several procedures to identify, locate, map coca and poppy fields. The initial step in this process is the use of satellite images to locate the coca and poppy fields. These images are provided by North American and European governments to the Government of Colombia. The images are used to locate potential areas of coca and poppy production. Further visual observations are made using overflights with observers and/or photographs from a low-altitude aerial-photography plane, such as a Cessna Caravan, to verify the presence of the coca and poppy fields. The camera used for this purpose is multi spectral high-resolution. Maps are generated in a Geographic Information System (GIS) and are used to produce updated co-ordinates for the spray pilots as well as information for downloading into the aircraft navigation systems

(Figures 6 and 7). The field operation offices for the control program have computers and a satellite uplink for data transfer. The spray-planes, such as AT 65s, AT 802s, or OV 10s, are equipped with high resolution tracking equipment and Del Norte positional data recorders that display position, provide directional guidance, and store positional data on data cards for later analysis. Thus the locations of the fields, the flight-paths of the spray-planes, and the areas where spray is released are known to within a resolution of several meters.

Since 1994, the coca and, more recently, poppy fields have been identified and sprayed during the eradication program. Total areas of identified fields, and area sprayed in Colombia are shown in Figure 8. With increasing areas sprayed, the total area planted to coca has generally decreased since 2000.

2.1.3.1 Receiving environment

Colombia is located between about 4ºS and 12°N of the equator. The country presents very varied topography ranging from snow-capped peaks through high mountain plateaus to low-lying tropical regions. In general, coca tends to be grown at altitudes below 1,500 m and poppy at greater altitudes, usual 2,200 m. The biodiversity hotspot for the tropical Andean region includes significant areas of Colombia (Figure 9). The tropical Andes biodiversity region is estimated to contain 15-17 percent of the world's plant life in only 0.8 percent of its area. It has a area of 1,258,000 square kilometers, and extends from Western Venezuela to Northern Chile and Argentina and includes large portions of Colombia, Ecuador, Peru, and Bolivia (Centre for Biodiversity 2004).

Because the diversity hotspots are mainly associated with the Andean highlands and coca is mostly grown in lower altitudes, there is only some overlap between the areas of coca production and regions of high biodiversity. Poppy is grown at greater altitude and this overlaps with the biodiversity hotspot; however, the total areas grown at this time are small (Figure 8). E xact areas used for coca and poppy production within the diversity hotspot are not known, however, this information would be useful for assessing total impacts of production, especially for rare and endangered species of plants.

2.1.3.2 Method of application

All coca and poppy fields are sprayed by aerial application from fixed-wing aircraft. The procedure described below is based on observations recorded for the AT 65, AT 802, and OV 10 aircraft.

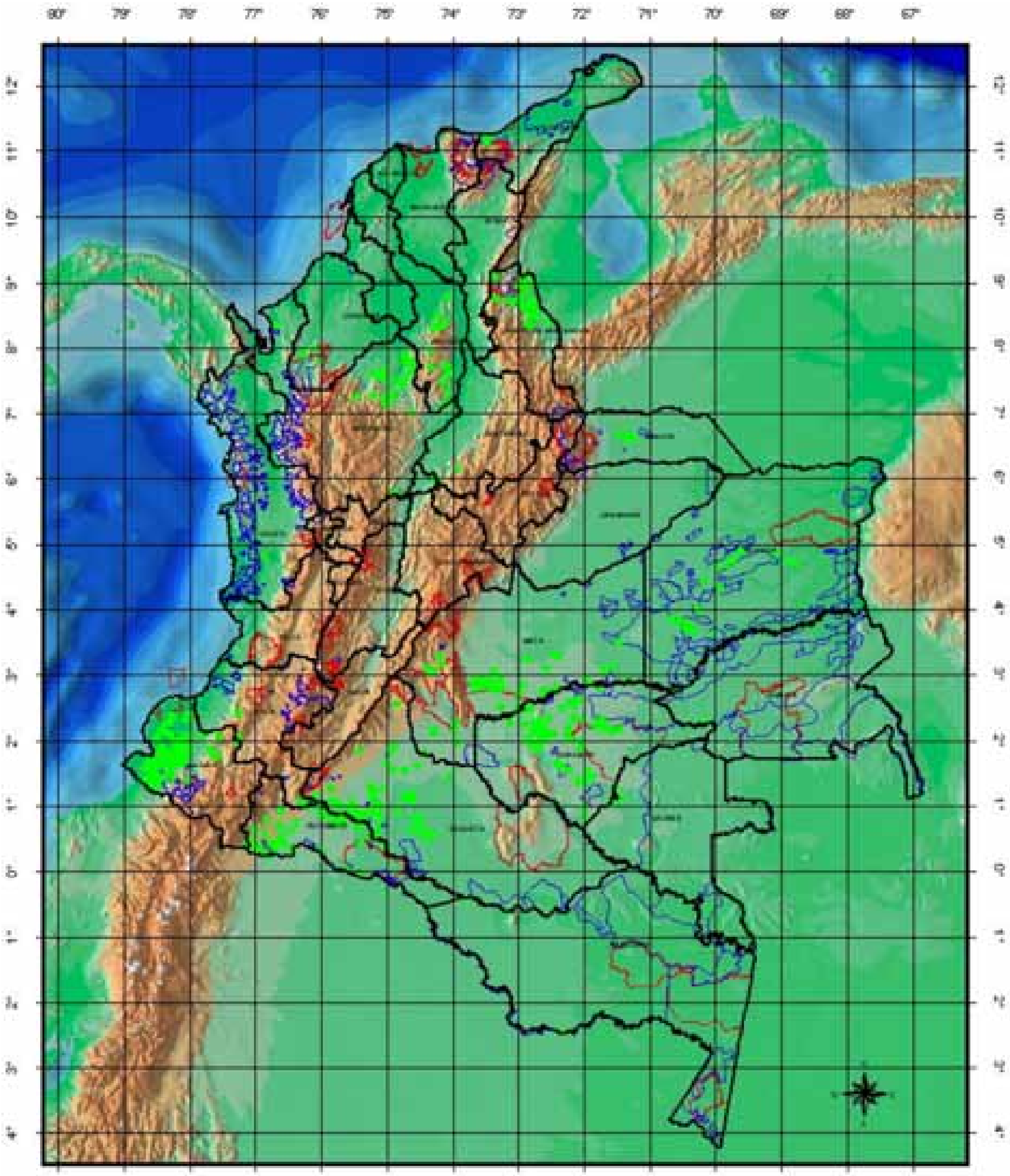


Figure 13 Map showing production of coca in Colombia in 2005. Bright green shows coca production. Blue boundaries indicate indigenous areas, red boundaries indicate national parks (Policia Nacional Direccion Antinarcoticos 2005).

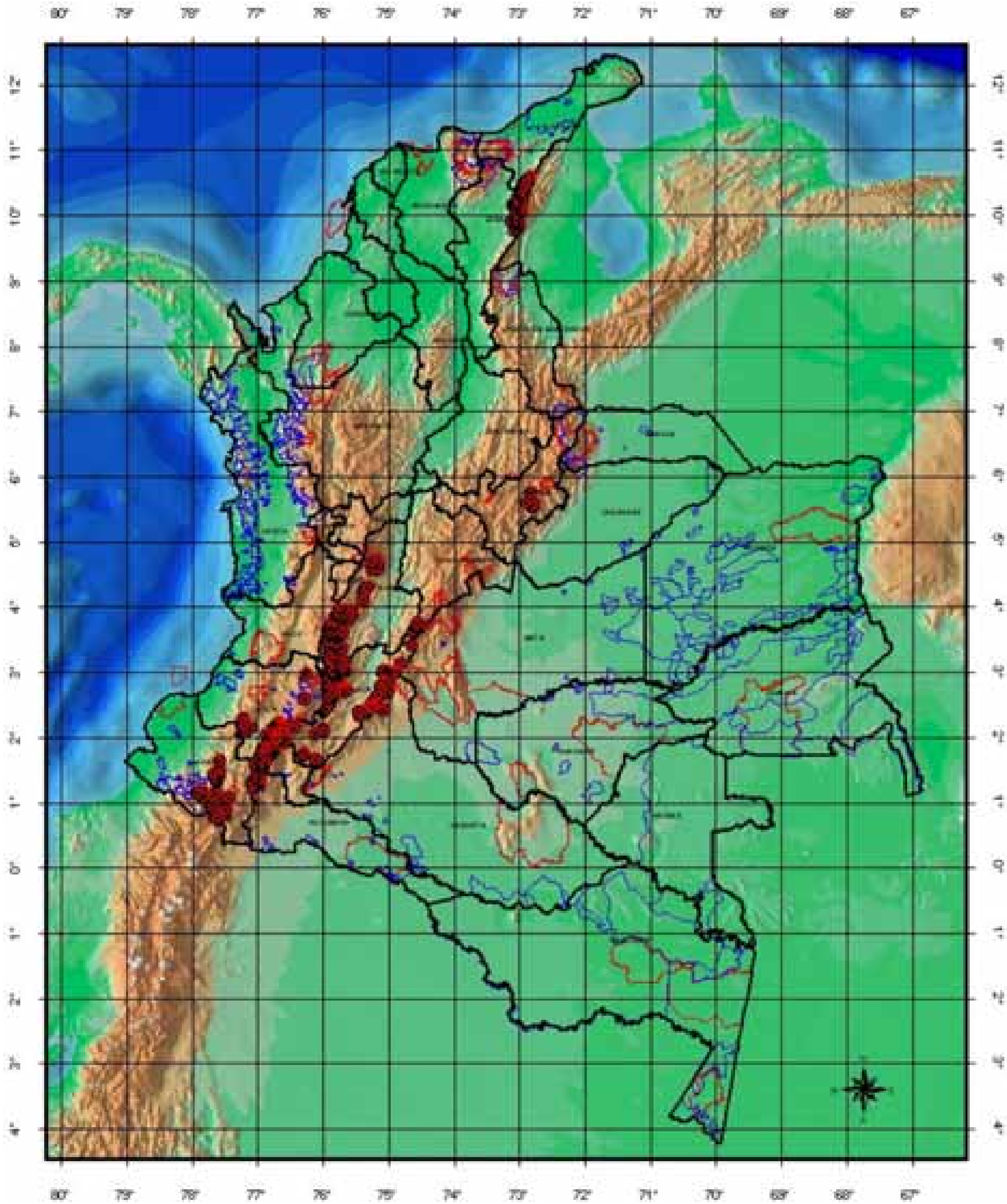


Figure 14 Map showing areas of poppy production in 2005. Bright red circles show poppy production. Blue boundaries indicate indigenous areas, red boundaries indicate national parks (Policia Nacional Direccion Antinarcoticos 2005).

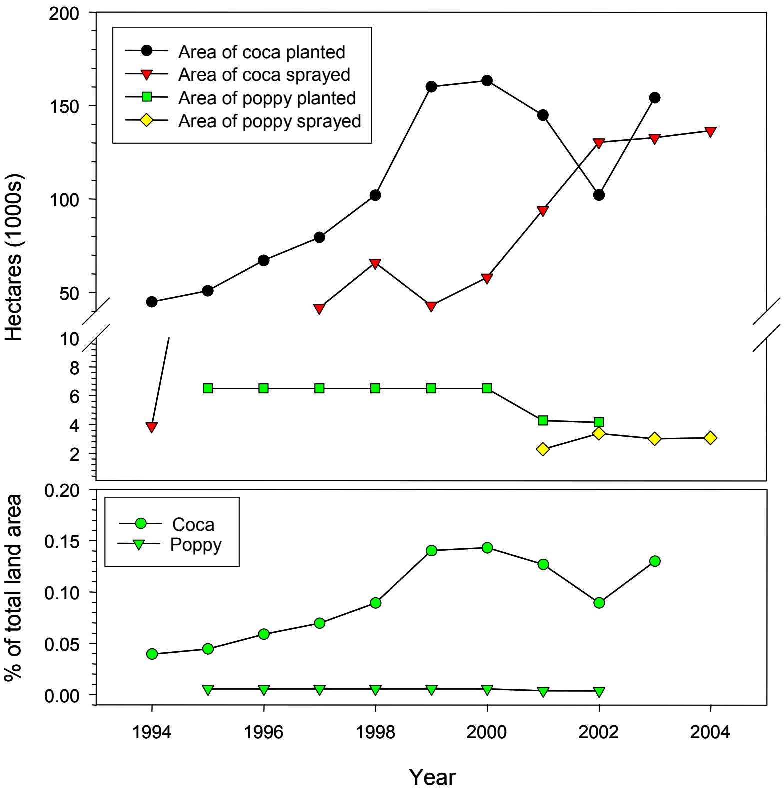


Figure 15 Areas planted with coca and poppy in Colombia from 1994 to 2002 as ha (above) and as a percent of the total land area of Colombia (below). From (Direccion Nacional de Estupefacientes 2002, Policia Nacional Direccion Antinarcoticos 2005)

The spray-planes are loaded in a special area of the tarmac at one of a number of bases throughout Colombia (Figure 10). Glyphosate and Cosmo-Flux® are stored in plastic containers in a tarp-lined area protected by a berm to contain accidental spills. The areas may be in the open or covered. The glyphosate is transferred from 200-L plastic barrels to a larger plastic storage tank (Figure 10-A). Cosmo-Flux® is transferred from 20-L plastic containers to a mixing tank. The required amounts of the components of the application mixture (glyphosate, Cosmo-Flux®, and water from a local source) are pumped through a metering pump (Figure 10-B) into the aircraft using a Table of Mixing Proportions to ensure the correct ratio of amounts are loaded. Appropriate protective equipment is used by the mixer-loaders who are trained in the loading procedures (Figure 10-C).

The spray boom (Figure 10-D) on the aircraft is equipped with rain-drop nozzles (Figure 10-E). These nozzles produce droplets with a volume mean diameter (VMD) between 300-1,500 μm and are similar to those used in forestry spraying for site preparation (Payne 1993). The aircraft spray systems are electronically calibrated to disperse a specified quantity of spray mix per hectare, compensating for variances in ground speed. These electronic spray controls are checked each day by technicians and also during the pilot's preflight inspection. During actual spray operations, the pilot monitors the spray system by observing the readings of the spray pressure and the spray flow rate gauges (U.S. Department of State 2002).

Figure 16 Map showing the region of Colombia identified as part of the Andean Biodiversity Region. (From Centre for Biodiversity 2004).

The same nozzles are used for both coca and poppy applications but twice as many are used for the poppy applications and different boom pressures are used. As a result, coca and poppy applications are done at separate times. The currently-used application rates are shown in Table 4.

Table 4. Application rates of glyphosate and Cosmo-Flux® for control of coca and poppy

	Litres/ha		Kg/ha	
	Coca	**Poppy**	**Coca**	**Poppy**
Glyphosate	10.4	2.5	4.992	1.2
Cosmo-Flux®	0.24	0.51		

From (Direccion Nacional de Estupefacientes 2002)

Each spray operation (Figure 10-F and G), which may consist of 2 or more spray-planes, is escorted by search-and-rescue (SAR) helicopter(s) in case of an accident or incident. Spraying is only conducted in daylight hours before mid-afternoon to ensure that conditions are appropriate for application. If rain is imminent, visibility is poor, or the wind speed is in excess of 7.5 km/h (4 knots), spraying is not carried out. Wind speed is checked during the operation by the SAR and other helicopters with the aid of smoke generated by the spray-planes. The spraying is done at about 30 m above ground and, although the flight path is determined from the GIS information and the Del Norte guidance system (Figure 10-H), the actual spraying is controlled by the pilots. In personal communications with five of the pilots, it was stated that, according to spraying guidelines, fields are not sprayed if people are seen to be present.

After a spray operation, the flight path of the spray-planes and the areas sprayed is downloaded from the Del Norte system (Figure 10-I) and processed by GIS to show the spray patterns and calculate the areas spayed (Figure 10-J). This information is transmitted to the DIRAN where records of the spray operations are retained and used for compilation of annual reports and statistics (Direccion Nacional de Estupefacientes 2002).

2.1.3.3 Frequency of application

The frequency of application varies with the local conditions and the actions taken by the growers after the coca or poppy is sprayed. When coca is sprayed, some growers will prune the bushes down to about 10 cm above ground in an attempt to prevent translocation of the herbicide to the roots. Sometimes, these plants will recover and resprout; however, they will not yield large amounts of coca leaves for several months. If the field is replanted to coca from seedlings, reasonable productivity may not be achieved 4-6 months. If the field is replanted from cuttings, productivity may be achieved sooner. Thus, spraying of a particular coca field may have a return frequency of about 6 to 12 months.

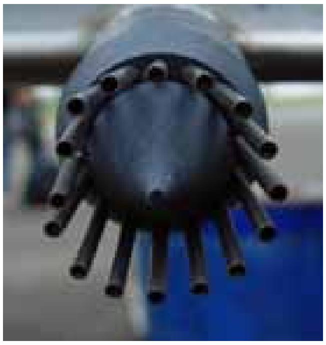
Being an annual, poppy is grown from seed. In the climatic conditions under which it is grown in Colombia, poppy fields would be harvested twice a year. If sprayed before reaching maturity and replanted immediately after spraying, they may be sprayed four times a year.


A) Mixing area for glyphosate and adjuvants


B) Mixer for glyphosate and adjuvant


C) Mixer-loader


D) Spray boom


E) Nozzle


F) AT-65 spray plane


G) OV10 Spray plane being loaded


H) Del Norte GPS system


I) Positional data


J) Spray locations

Figure 17 Photographs of aspects of the spray operation (photographs K R Solomon).

2.1.3.4 Exposure pathways in soil, air, water, and other media

In terms of the application, there are several pathways through which the glyphosate and adjuvants may come into contact with the environment (Figure 11).

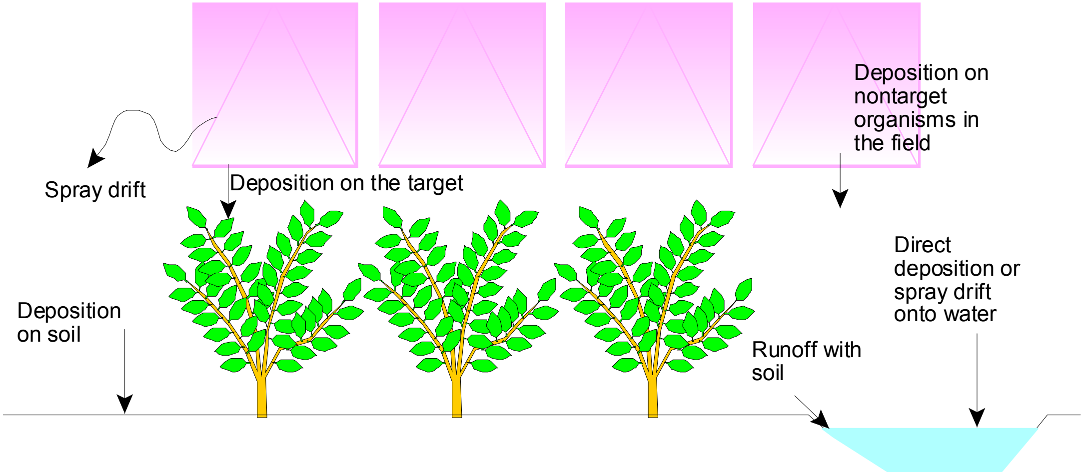


Figure 18 Diagram showing exposure routes for various environmental compartments when glyphosate is used for the control of illicit crops.

Deposition on the target crop (field) is the desired outcome of the operation; however, from the purposes of assessing risks in humans and the environment, exposures that result in movement and deposition off the field are important. Spray drift would result in movement off the target field and could result in adverse effects in nontarget plants and animals. Given the strong adsorption of glyphosate to soil, deposition on soil in the field will likely not result in significant effects on nontarget organisms, however, runoff of residues bound to soil particles may result in contamination of surface waters with sediment-bound residues. Direct deposition and spray drift may result in contamination of local surface waters with glyphosate if these are in the spray-swath or drift envelope of the application. Depending on the depth of the water, turbulence, flow, and suspended particles, this would result in exposures of aquatic organisms to both glyphosate and any adjuvants present in the spray mixture. Organisms present in the field during spraying would be exposed to the spray droplets and would receive a theoretical dose, depending on surface area exposed and body mass. Exposures that may occur via these routes are discussed in Section 3.1.4.

2.1.3.5 Off-target deposition

There are two types of off-target deposition. The first is related to incorrect application where the spray pilot initiates application too soon or turns off the spray too late, or the spray swath includes a non-target area on one or both sides of the target field. The second type of off-target deposition that may occur is spray drift. Experience with spray equipment of the type used in Colombia suggests that spray drift will be minimal (Payne et al. 1990). Estimates of accidental overspray have been made during assessments of the efficacy of the spray program (Helling 2003). Based on site-visits to 86 fields sprayed in 2002, and on observations of damaged plants beyond the boundary of the area cleared and planted with coca, 22 fields showed evidence of off-field deposition. Using the size of these areas, it was estimated that between 0.25 and 0.48% of the areas cleared for coca production were damaged by offsite spray deposition (Helling 2003). Applying this to the total area of coca sprayed (Figure 8) and calculating upper and lower intervals, the areas potentially affected are small when compared to the total area of Colombia (Table 5).

Table 5. Estimates of areas affected by off-target deposition of glyphosate in the spraying of coca in Colombia

Year	Ha sprayed	Area affected by off-target deposits (ha)		Upper interval as a % of the total area of Colombia
		Lower interval 0.25%	Upper interval 0.48%	
1994	3,871	9.7	18.6	0.0000002
1995	23,915	59.8	114.8	0.0000010
1997	41,861	104.7	200.9	0.0000018
1998	66,029	165.1	316.9	0.0000028
1999	43,111	107.8	206.9	0.0000018
2000	58,074	145.2	278.8	0.0000024
2001	94,152	235.4	451.9	0.0000040
2002	130,364	325.9	625.7	0.0000055
2003	132,817	332.0	637.5	0.0000056
2004	136,551	341.4	655.4	0.0000057

While the areas affected by off-target are estimated to be small, this estimate is based on visual observations of a relatively small number of fields. These data were only available for coca, not poppy, however, the total areas planted to poppy at this time are not large, and similar off-target deposition would be proportionately smaller than that associated with coca production. This is thus a source of uncertainty in the assessment. It is not logistically possible to visually inspect all sprayed fields, however, the routine monitoring of the areas planted to coca and poppy that is undertaken by satellite and low altitude imagery could be used to assess any off-target deposition which results in damage to plants. Changes in the size of sprayed fields over time could be used to extend these estimates over larger areas and increase their accuracy, although extension of the fields by growers may confound the data. The lower resolution of satellite imagery may preclude its use for this purpose; however, greater coverage by low-altitude images could facilitate this process.

2.2 Framework for risk assessment

The following sections outline the conceptual model and hypotheses for the assessment of the human health and environmental impact of coca and poppy production in Colombia. Although this document is focused on the risks associated with the coca and poppy eradication program, it is recognized that the eradication program is not conducted in isolation. There are a number of other activities associated with the process that result in risks to human health and the environment. While data are not available to quantify all these risks, some of them may be estimated on the basis of other knowledge and expert judgment. This was done using an adaptation of a risk prioritization scheme that has been used in ecological risk assessment (Harwell et al. 1992).

2.2.1 Context of the risks

2.2.1.1 Human health risks

Risks of the cycle of coca and poppy production were estimated as discussed above and are shown in Figure 12. For the purposes of this ranking process, the intensity score ranged from 0 to 5, with 5 being a severe effect such as a physical injury or toxicity. The recovery score also ranged from 0 to 5 and was based on the potential for complete recovery from the adverse effect. Frequency was based on an estimate of the proportion (%) of the total number of persons involved in coca and poppy cultivation, production, and the refinement of cocaine and heroin. The score for impact was the product of the individual scores and the percent impact is based on the sum of the impact scores. The scores for the risks associated with the eradication program were omitted from the ranking in this diagram but are discussed below in the conclusions to the risk assessment.

IMPACTS	INTENSITY SCORE	RECOVERY SCORE	FREQUENCY %	IMPACT SCORE	% IMPACT
Clear cutting and burning	5	3	3	45	**16.7**
Planting the coca or poppy	0	1	100	0	**0.0**
Fertilizer inputs	0	0.5	10	0	**0.0**
Pesticide inputs	5	3	10	150	**55.6**
Eradication spray	?	?	?	?	**?**
Processing and refining	5	3	5	75	**27.8**

Figure 19 Potential human health impacts of the cycle of coca or poppy production Scores for eradication spraying are specifically omitted.

2.2.1.2 Ecological risks

A similar procedure to that described above was used for ranking ecological risks associated with the cycle of coca and poppy production (Figure 13). The intensity score was ranked from 0 to 5, with 5 being most intense, such as the total destruction of the habitat by clear-cutting and burning when clearing a natural area. Intensity of effects in this case also included off-field effects such as on non-target animals and plants. Recovery time in this scheme is the estimated time for the impacted area to recover to a state similar to the initial condition. In the case of the clear cutting and burning, it is recognized that succession will begin immediately; however, full recovery to a mature and diverse tropical forest may take considerably more than the 60 years estimated here. Similarly, in the absence of cultivation, it was estimated that invasive and competitive species will displace coca and poppy in several years and an estimate of four years was used in this case. Given the need to apply fertilizer and pesticides frequently because of utilization of nutrients and resurgence of pests, the recovery time for these ecological impacts was judged to be small. The scores were multiplied to give the impact score and the percent impact was based on the sum of the impact scores.

Coca or poppy field developed in a natural area

IMPACTS	INTENSITY SCORE	RECOVERY TIME (Y)	IMPACT SCORE	% IMPACT
Clear cutting and burning	5	60	300	**97.6**
Planting the coca or poppy	1	4	4	**1.3**
Fertilizer inputs	1	0.5	0.5	**0.2**
Pesticide inputs	2	0.5	1	**0.3**
Eradication spray	?	?	?	**?**
Processing and refining	2	1	2	**0.7**

Figure 20 Potential environmental impacts of the cycle of coca or poppy production. Scores for eradication spraying are specifically omitted.

2.2.2 Conceptual model

For the purposes of the risk assessment of the use of glyphosate and adjuvants in the eradication of poppy and coca, the conceptual model applied was that normally applied to the agricultural application of pesticides where hazard and risk and directly related to the toxicity and exposure to the pesticide. Thus, for human health, toxicity data were compared to exposures estimated from worst-case data and also from more realistic data obtained in other uses of glyphosate, such as agriculture and forestry. Because of the low frequency of application of the sprays, exposure from this source is acute and resulting risks were compared to acute toxicity data. Toxicity data for the active ingredient, glyphosate, were obtained from the literature and from the results of acute laboratory-animal tests conducted with the mixture of glyphosate and Cosmo-Flux® as used in the spray program. It is recognized that glyphosate used in the eradication program may contribute to exposures via the food chain and drinking water; these were estimated and compared to toxicity data and exposure guidelines based on chronic toxicity for glyphosate. In addition, specific human health responses were assessed in epidemiological studies conducted specifically to address this issue in Colombia.

In assessing ecological risks, a similar agriculture-based approach was used. Similar to the above, exposures were estimated from worst-case models, from measurements made in other locations, and from measurements based on samples collected from the environment in Colombia. Because of the frequency of application in the eradication program (long periods between applications), ecological exposures resulting from the eradication spray operations were acute and were compared to acute toxicity data. Toxicity data were obtained from the literature and from laboratory-based tests on standard test organisms that were specifically conducted on the spray mixture as used in Colombia. The risk hypotheses are discussed below and the remainder of the document is focused on tests of these hypotheses.

2.2.3 Risk hypotheses

A large number of hypotheses were actually tested in this risk assessment; however, they were basically the same hypothesis with minor differences in the exposure and toxicity parameters. As is normal in the scientific method (Popper 1979), these hypotheses are stated as the null or negative hypothesis. Again, following the scientific method, we attempted to falsify or disprove these hypotheses through the use of appropriate data.

For human health, two main hypotheses were used:

- Exposures to glyphosate and adjuvants as used in the poppy and coca eradication programs do not cause acute adverse effects to humans exposed via a number of routes.
- The use of glyphosate and adjuvants in those locations where eradication of poppy and coca are conducted does not result in acute and chronic health outcomes that are different from other locations where glyphosate is not used or is used in other agricultural practices.

For ecological effects, one main hypothesis was used:

- Exposures to glyphosate and adjuvants as used in the poppy and coca eradication programs do not cause acute or chronic adverse outcomes on non-target organisms exposed via a number of routes

3 EXPOSURE CHARACTERIZATION

Exposure characterization is one of the key components to any risk assessment (NRC 1993, USEPA 1992, 1998). No measurements of farmer or pesticide applicator exposures have been made in Colombia. An assessment of pesticide use among farmers in the Amazon Basin of Ecuador has shown that paraquat and glyphosate are widely used. Risk behaviors were identified as frequent pesticide use, washing pesticide equipment in water sources used by humans, inadequate disposal of empty pesticide containers, eating and drinking during pesticide application, and using inadequate protective clothing (Hurtig et al. 2003). However, agricultural uses such as these are quite different from the aerial applications of glyphosate for eradication of coca and poppy in Colombia. In the following sections, the potential for exposures in humans and the environment to glyphosate as used in the eradication program of humans is discussed and characterized.

3.1.1 Human exposure groups

In the case of human exposures to pesticides in the agricultural setting there are usually two groups that are considered – applicators and bystanders. The group that experiences the greatest probability of exposure is the applicator group, which, in this case, includes the mixer-loaders, the spray-plane pilots, and the technicians who work on and service the aircraft. The second group is the made up of bystanders who may come into contact with the herbicide during application via direct deposition if they are within the spray swath, are directly exposed to spray drift, are exposed to deposits of spray when they reenter treated fields, or are exposed to the herbicide through the consumption of food items that have been sprayed, or drinking water that has been contaminated.

3.1.2 Applicator exposure

Risk to applicators was not a specific target of this assessment; however, exposure can be characterized for this group. Based on observations of the spray operations in several locations in Colombia, a number of measures are taken to reduce the potential for exposure of applicators (Table 6).

Table 6. Protective measures used to reduce exposure of applicators to glyphosate and formulants as used in poppy and coca eradication programs in Colombia.

Applicator subgroup	Mixer-loader	Spray pilot	Aircraft technician
Technology for handling of the formulation and spray mix.	Use of closed-loading systems and pumps to mix and transfer glyphosate and Cosmo-Flux® to the aircraft.	Not involved in mixing and loading.	Not normally involved in mixing and loading. Aircraft are washed down regularly so that exposure via contaminated surfaces in reduced.
Protective equipment worn.	Long pants, long sleeves, full rubber apron, rubber gloves, cloth hat or cap, particulate air filter and	None other than normal clothing, long sleeves, long pants, jacket, and boots.	Short or long sleeves, shorts or long pants, boots or sneakers, cloth cap or none.

Table 6. Protective measures used to reduce exposure of applicators to glyphosate and formulants as used in poppy and coca eradication programs in Colombia.

Applicator subgroup	Mixer-loader	Spray pilot	Aircraft technician
	dark glasses, leather military-style boots.		
Equipment used to remove contamination, should it occur.	Eye-wash station at all locations, clean water for washing hand and any contaminated surfaces, a shower in some locations.	Same as is available to the mixer loader.	Same as is available to the mixer loader.

No measures of exposure were available for mixer loaders in Colombia; however, they are likely to be similar to those of applicators in other situations. Based on observations on forestry and agricultural applicators (Acquavella et al. 2004, and summarized in Williams et al. 2000), exposures are generally small. From several studies, peak estimated exposure in applicators from all routes was 0.056 mg/kg body weight. The estimate of chronic exposure from all routes was 0.0085 mg/kg/day based on an 8 hour day and a 5 day work week. In the results of the recently published Farm Family Exposure Study, the greatest estimated systemic dose in a sample of 48 applicators was 0.004 mg/kg (Acquavella et al. 2004). In the spray program in Colombia, mixing and loading is done by one or two individuals who wear appropriate protective equipment. Pilots have limited opportunity for exposure and, as has been observed in other studies (Frank et al. 1985), will likely experience less exposure.

Exposures of mixer-loaders under the conditions of use in Colombia are likely to be similar to those observed in agricultural applications. Exposures for spray pilots and technicians will likely also be less than an agricultural applicator.

While most of the protective clothing worn by the mixer loaders is appropriate, the need for a respirator is questionable and the use of dark glasses in place of a full face shield is judged inappropriate. Dark glasses will not protect the eyes from a splash to the forehead that runs into the eyes, a vulnerable area in terms of glyphosate exposure during mixing and loading (Acquavella et al. 1999). A full face shield would offer better protection. As glyphosate is not volatile, nor atomized during mixing and loading, use of a respirator offers little reduction in potential exposure and complicates the use of a full face shield. The usefulness of a respirator is judged to be small.

3.1.3 Bystander exposure

Bystanders are the second group that can be exposed to glyphosate during application. Bystanders can be classified into several classes, depending on their route of exposure. These are discussed in the following sections.

3.1.3.1 Bystanders directly over-sprayed

Although it is unusual for people to be present in a coca field during application, it is possible that a person could be standing directly in the spray swath and would receive a direct application of the spray solution to the body. There are several scenarios that could occur (Figure 14 and Table 7).

The most likely scenario is the partially clothed human with a cross-sectional area of 0.25 m² exposed to the spray (bold text in Table 7). Given that glyphosate penetrates poorly through the skin with maximum penetration of about 2% (Williams et al. 2000), the body dose under a reasonable worst-case exposure will be approximately 0.08 mg/kg body weight.

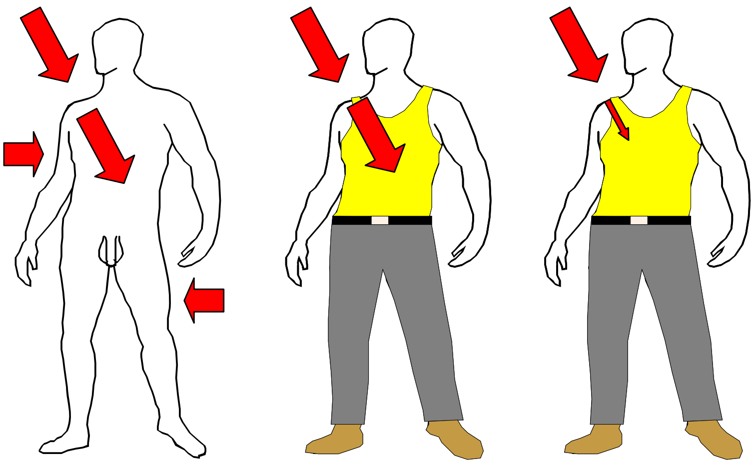


Figure 21 Illustration of human exposure scenarios

Table 7. Estimates of human exposure to glyphosate during a spray application

Scenario	Exposure in mg/kg body weight	
	Coca sprayed at 4.992 kg/ha	**Poppy sprayed at 1.2 kg/ha**
Naked human, total coverage of body, and complete penetration through skin.	14.2	3.4
Partially clothed human with cross sectional area of 0.25 m^2, complete penetration.	1.8	0.4
Partially clothed human with cross sectional area of 0.25 m^2, 2% penetration – most likely.	0.04	0.01
Assumptions: (human weighs 70 kg and has a body surface area of 2 m^2		

Bystander exposure to glyphosate was estimated as 0.0044 mg/kg/day for a child, 1-6 years of age (Williams et al. 2000). Exposures to glyphosate were measured in bystanders to farm applications (Acquavella et al. 2004). These studies were conducted in spouses and children who were not involved in applications and frequency of measurable exposure was small with 4 and 12% of the spouses and children respectively with detectable exposures based on urinary monitoring. The maximum systemic dose estimates for spouses and children were 0.00004 mg/kg and 0.0008 mg/kg, respectively (Acquavella et al. 2004). If bystanders are not directly sprayed nor reenter the field immediately after spraying, their exposures will likely be within a factor of 10 of farm bystanders. All of these measured exposures are considerably less than those estimated in Table 7. The values in Table 7 were thus considered to be reasonable worst-case values.

3.1.3.2 Re-entry

If a person was to reenter the sprayed field immediately after spraying and come into close contact with the treated foliage, such as when attempting to pick leaves from spayed coca plants, exposure to glyphosate could occur through the hands and arms. Given the area exposed, the small penetration, and the saturation of the transfer that would result once the hands were wet, total body dose is likely to be less than the reasonable worst-case scenario described in Table 7. The potential for re-entry exposure has been summarized by Williams et al. (2000). Re-entry exposures decreased with time after application and, on day-7 after application, were 3% of those estimated for day 1. Re-entry into areas of tall weeds (1.5 m) resulted in 10-fold greater exposures than in areas of short grass. Based on measurements in farm workers, estimates of re-entry exposure to glyphosate in adults ranged from 0.0000039 to 0.0026 mg/kg/h of reentry time. Maximum re-entry exposure for a 1-6 year-old child was estimated at 0.026 mg/kg for a 5 hour contact period. As these estimates are based on a spray application rate of 1 kg/ha, re-entry exposures under Colombian conditions are estimated to be somewhat greater (Table 8). These numbers are also greater than the direct overspray as the people involved may have repeated exposures if they reenter a field immediately after spraying.

Table 8. Estimates of human exposure to glyphosate during re-entry to treated fields

Scenario	**Exposure in mg/kg body weight**	
	Coca sprayed at 4.992 kg/ha	**Poppy sprayed at 1.2 kg/ha**
Maximum re-entry exposure estimated for an adult human with a 10 hour day.	0.013	0.003
Maximum re-entry exposure estimated for a 1-6 year-old child with a 10 hour day.	0.259	0.062

3.1.3.3 Inhalation

Because the vapor pressure of glyphosate (isopropylamonium) is small (2.1 x 10^{-3} mPa at 25°C) and it also has a small Henry's Law Constant (4.6 x 10^{-10} Pa m^3 mol^{-1}) (BCPC 2002-2003), it will not be present in air as a vapor at biologically relevant concentrations. The droplet sizes resulting from the spray application of glyphosate in Colombia are large with a mean droplet diameter of about 1000 µm and with very few droplets <500 µm. As such, they are unlikely to be inhaled and penetrate into the lungs. Based on measurements of glyphosate concentrations in air during applications, the maximum estimated daily dose (8 h) resulting from inhalation of spray droplets by applicators was 0.0062 mg/kg (Williams et al. 2000), a value that is judged to be applicable as a maximum exposure for bystanders to eradication spraying in Colombia.

3.1.3.4 Dietary and drinking water

As shown in Table 9, dietary and drinking water exposures to glyphosate have been estimated to be relatively small under conditions of use in N. America (Williams et al. 2000).

Table 9. Worst-case daily human exposure estimates for glyphosate (mg/kg/day)

Sources	**Female adult**		**Female child (1-6 years)**	
	Acute	**Chronic**	**Acute**	**Chronic**
Drinking water	0.000036	0.000002	0.000110	0.000004
Diet	0.024	0.024	0.052	0.052
Wild foods	0.045		0.045	
Total from diet and water	0.069	0.024	0.097	0.052
Values extrapolated from the above (Williams et al. 2000) to the greater application rate of 4.992 kg/ha used in control of coca				
Drinking water	0.000179	0.00001	0.00055	0.000018
Diet	0.119	0.119	0.259	0.259
Wild foods	0.224	0.224	0.224	0.489
Total from diet and water	0.343	0.293	0.483	0.747

The results of monitoring programs conducted by the Danish Veterinary and Food Administration from 1997 to 1999, reported on the content of glyphosate and several other pesticides in cereals produced in Denmark (Granby and Vahl 2001). Based on the residues of glyphosate in cereals, intake of glyphosate for a 60 kg adult was estimated at 0.007 mg/day.

Based on a study of 51 streams in nine Midwestern US States, the U.S. Geological Survey (USGS) reported the presence of glyphosate and a number of other herbicides in surface waters (Scribner et al. 2003). Of a total of 154 water samples collected during 2002, glyphosate was detected in 36 percent of the samples, and its degradation product, aminomethylphosphonic acid (AMPA) was detected in 69 percent of the samples. The highest measured concentration of glyphosate in any sample was 8.7 µg/L. The highest concentration of AMPA detected in the USGS study was 3.6 µg/L. Concentrations of glyphosate detected in surface waters in Colombia (see below) were, for the most part, less than 25 µg/L, the method detection limit. Exposures from drinking of untreated surface waters in areas where eradication spraying takes place are judged to be small and infrequent.

3.1.4 Environmental exposures

3.1.4.1 Air

As discussed above, the presence of glyphosate in air is unlikely as it, and the salt forms commonly used in glyphosate formulations, have essentially negligible vapor pressure. Spray droplets may, however, be present in air and are the likely reason for the detection of glyphosate, along with other pesticides, in rainwater in the European Union (EU) (Quaghebeur et al. 2004). During the period from 1997 to 2001, glyphosate was only detected in rainwater in Belgium in 2001 and then with a frequency of 10% and a maximum concentration of 6.2 µg/L.

3.1.4.2 Water

If water is directly over-sprayed during a spray operation, contamination of surface waters will result. Some coca fields are located near to ponds and lakes and some are near to streams and rivers (Helling 2003). While surface waters are not deliberately sprayed by the pilots, some over-spray of small watercourses and the edges of ponds, reservoirs, and lakes may occur. In the absence of measured concentrations immediately after spraying in surface waters located close to the fields, estimates of exposure were made using worst-case assumptions (Table 10) based on water depth assumptions used by the US EPA (Urban and Cook 1986) and the EU (Riley et al. 1991).

Table 10. Estimates of concentrations of glyphosate in surface water after a spray application

Scenario	**Exposure in µg/L (glyphosate[a])**	
	Coca sprayed at 4.992 kg/ha (3.69 kg AE/ha)	**Poppy sprayed at 1.2 kg/ha (0.89 kg AE/ha)**
Surface water, 2 m deep, rapid mixing and no absorption to sediments, no flow.	185	44
Surface water, 0.3 m deep, rapid mixing and no absorption to sediments, no flow.	1,229	296
Surface water, 0.15 m deep, rapid mixing and no absorption to sediments, no flow.	2,473	595
Surface water, 0.15 m deep, rapid mixing and 50% absorption to sediments, no flow.	1,237	297

[a] Note that the concentration is expressed as glyphosate acid to allow comparison to exposures used in environmental toxicity testing. In both these exposures and in the toxicity testing Cosmo-Flux®, proportional amounts are present and the exposure and toxicity values are thus directly comparable and can be used to assess the hazard of the mixture as applied in Colombia.

Glyphosate has been detected in surface waters (see above discussion on human exposures through drinking water) in a number of locations. Glyphosate residues have been reported in surface waters in Denmark as result of agricultural activities. These residues were observed as part of the Pesticide Leaching Assessment Program (PLAP), a project that was intended to study the leaching potential of pesticides to the groundwater (Kjaer et al. 2005, Kjaer et al. 2003). PLAP was focused on pesticides used in farming and monitored leaching at six agricultural test sites representative of Danish conditions. Water from special drilled wells and from normal tile drains was analyzed for glyphosate and aminomethylphosphonic acid (AMPA, a major degradate of glyphosate). It is not clear from the report if the samples were filtered prior to analysis. This is important as glyphosate binds strongly to organic matter in soils and can be transported in this form. The presence of macropores in the soil would facilitate transport to the tile drains.

In the samples from PLAP collected following glyphosate applications, there were no detections of glyphosate or its metabolite, AMPA, that exceeded 0.1 µg/L in any of the groundwater samples taken from the suction cells (1 and 2 m below ground surface), the vertical wells (about 1.5 – 5.5 m below ground surface), and the horizontal wells (about 3.5 m below ground surface).

Glyphosate residues were detected in water from tiles draining the field and were observed primarily in the autumn. The highest measured concentrations were 5.1 µg/L for glyphosate and 5.4 µg/L for AMPA. The calculated average annual concentrations of glyphosate and AMPA in drainage water were 0.54 and 0.17 µg/L, respectively, at one location, and 0.12 µg/L and 0.06 µg/L, respectively, at a second location. At a third location, glyphosate and AMPA were detected but average concentrations of both were below 0.1 µg/L. In other studies in Danish soils, degradation of glyphosate was shown to be slower in sandy soils than gravel but leaching was observed only in rounded gravel soils (Strange-Hansen et al. 2004) and leachate concentrations were less than 0.1 µg/L (Fomsgaard et al. 2003). Similarly, a recent study on fate of glyphosate in soils showed rapid dissipation with almost total dissipation one month after application (Veiga et al. 2001). Given the small organic content of gravel and the presence of macropores between the grains of gravel, movement through this matrix is not surprising. Complete degradation in other types of soil is as would be expected.

Other authors have reported glyphosate residues in surface waters in Europe (Skark et al. 1998, Skark et al. 2004) the frequency of detection was not large. The authors of these papers suggested that the contamination was from application to railroad beds, environments where gravel is used and where adsorption would be expected to be minimal. This conclusion is supported by other studies on the dissipation of herbicides applied to railroad beds (Ramwell et al. 2004) and highways (Huang et al. 2004, Ramwell et al. 2002). Application of glyphosate to hard surfaces in an urban context (road edges) can give peak run-off concentrations of 650 µg/L (Ramwell et al. 2002), but only 15 µg/L from a railway trackbed (Ramwell et al. 2004). In Germany, a study of two catchments found that non-agricultural pesticide use contributed more than two-thirds of the whole observed pesticide load in the tributaries and at least one-third in the River Ruhr (Skark et al. 2004). Most of the non-agricultural pesticides were derived from run-off from domestic, industrial and railway areas. Nevertheless, in Argentina, where glyphosate-tolerant soybean is now extensively grown and regularly treated, no residues have been observed in soil or water, either of glyphosate or its metabolite, AMPA (aminomethylphosphonic acid) (Arregui et al. 2004).

The USGS study on Midwestern US streams (Scribner et al. 2003), analyzed samples of water that were filtered through a 0.7 µm filter, thus the concentrations represent dissolved glyphosate and AMPA. Summary data from this study are shown in Table 11.

Table 11. Summary data on glyphosate concentration in Midwestern US streams

Herbicide	**Number of samples**	**Concentration in µg/L**	
		95^{th} centile	**Maximum**
Pre-emergence runoff samples			
Glyphosate	51	0.58	1.0
AMPA	51	0.55	1.8
Post-emergence runoff samples			
Glyphosate	52	1.5	4.5
AMPA	52	0.94	2.0
Harvest-season runoff samples			
Glyphosate	51	0.45	8.7
AMPA	51	1.3	3.6

Data from (Scribner et al. 2003)

Although the concentrations of glyphosate detected in surface waters in other areas where glyphosate is used in agricultural and other activities are relatively small, concentrations have not been measured in Colombia. To address this uncertainty, we conducted a monitoring study to measure concentrations of glyphosate, AMPA and other pesticides in surface waters.

The surface water monitoring study was conducted in five locations in Colombia representing areas where spraying of coca was planned to take place or where other agricultural activities were undertaken and were also close to where human health studies were being conducted. The sites were selected for safe access as well as ease of repeated sampling. These locations are summarized in Table 12 and further details as to temperatures, rainfall, and soil characteristics are provided in separate reports (PTG 2005a, b, c, d, e)

Table 12. Characteristics of sampling sites for glyphosate, AMPA and other pesticides in surface waters and sediments in regions of Colombia

Site name	Location	Altitude (m)	Major crop types	Known pesticide use
Valle del Cauca, Río Bolo	N 03º27.642' W 076º19.860'	1002	Sugar cane	Glyphosate and other pesticides
Boyacá, Quebrada Paunera	N 05º40.369' W 074º00.986'	557	Coca	Manual eradication, no aerial spraying of glyphosate
Sierra Nevada, Quebrada La Otra	N 11º13.991' W 074º01.588'	407	Organic coffee	None
Putumayo, Río Mansoya	N 00º43.259' W 076º05.634	329	Coca	Aerial eradication spraying
Nariño, Rio Sabaletas	N 01º27.915' W 078º38.975'	15	Coca	Aerial eradication spraying

To characterize concentrations of glyphosate and AMPA in surface waters, samples were taken at weekly intervals for a period or 24 weeks (CICAD/OAS 2004c). Samples, in plastic bottles, were frozen and held at -17C until shipped to Canada for analysis using standard methods (Thompson et al. 2004). The Method Detection Limit (MDL) for the analysis was 25 µg/L. Duplicate samples were taken and one sample held in Colombia until the duplicate had been analyzed. In addition, field-spiked samples and blanks were taken at bi-weekly intervals. In addition to water, sediment samples were taken at monthly intervals for analysis of glyphosate and AMPA if significant concentrations were detected in surface waters. Appropriate field spikes and blanks of sediment were also taken bi-monthly. Analytical quality control samples showed excellent recovery efficiency and precision of the analytical method with 98% recovery for glyphosate and 8.8% coefficient of variation (CV); 110% recovery efficiency for AMPA with 20% coefficient of variation. Blank field sample analyses show, on average, that no co-extractive interferences above the MDL for either glyphosate or AMPA at any of the sample sites. Field spike samples generally showed no significant degradation of glyphosate during sample handling and transport with overall average value of 90% of expected concentrations.

Results of these analyses are summarized in Table 13 (raw data are presented in Appendix 1). In all locations and on most occasions, residues of glyphosate and AMPA were present at concentrations below the MDL of 25 µg/L. On one occasion each in Valle del Cauca and Boyacá, concentrations of 30.1 and 25.5 µg/L, respectively, were found. These are sites where eradication spraying was not carried out and where the only use of glyphosate, if any, was in agriculture. These data suggest that little or no contamination of surface waters with glyphosate at significant concentrations has resulted from the use of glyphosate in either agricultural or eradication spraying in

Colombia. As concentrations in surface waters were mostly below the MDL, sediment analyses were not performed.

Table 13. Concentrations of glyphosate (AE) and AMPA in samples of surface water collected in Colombia between October 2004 and March 2005

Site name	**Total number of samples**	**Frequency of detection (n and %) for site**	
		Glyphosate	AMPA
Valle del Cauca, Río Bolo	17	1 (5.9%)	0 (0%)
Boyacá, Quebrada Paunera	18	1 (5.5%)	0 (0%)
Sierra Nevada, Quebrada La Otra	18	0 (0%)	0 (0%)
Putumayo, Río Mansoya[a]	16	0 (0%)	0 (0%)
Nariño, Rio Sabaletas[a, b]	17	0 (0%)	0 (0%)

[a] Locations where eradication operations were planned.

[b] Location where eradication spraying was carried out during the sampling period.

To characterize concentrations of other pesticides in surface waters and sediments, samples of water were taken in glass bottles every two weeks for a period of 22 weeks (CICAD/OAS 2004b). Samples were held at 4ºC until shipment to Canada for analysis. Analyses were conducted at the Laboratory Services Division of the University of Guelph using standard methods (LSD 2005). Duplicate samples were held in Colombia until analyses were completed. Field spikes and blanks were taken at 5-week intervals as were sediment samples. Sediment blanks and spikes were taken once during the study period.

The results of the analyses for other pesticides are summarized in Table 14 (raw data are presented in Appendix 2A-G). Blanks showed no contamination of samples during storage and shipping. Spiked samples showed variable recovery, particularly for carbaryl. Several pesticides were detected in surface waters. This is not unexpected as pesticides are widely used in agriculture in Colombia and, based on similar experience in other locations, some contamination of surface waters will occur. Of interest is the detection of endosulfan (I and II) and its breakdown product, endosulfan sulfate, in the samples taken at the Nariño site. Endosulfan is not registered for use in Colombia and its detection here likely is the result of illegal use. Whether this contamination resulted from regular agricultural activity or from use in the production of coca is unknown.

Table 14. Concentrations of other pesticides in samples of surface water and sediments taken in Colombia between October 2004 and March 2005

Site name	**Number of samples**	**Frequency of detection in surface water**	
		Number	Pesticides detected
Valle del Cauca, Río Bolo	10	3	2,4-D
Boyacá, Quebrada Paunera	8	0	0
Sierra Nevada, Quebrada La Otra	9	0	0
Putumayo, Río Mansoya	9	0	0
Nariño, Rio Sabaletas	8	1	endosulfan I, endosulfan II, endosulfan sulfate
	Number of samples	**Frequency of detection in sediment**	
		Number	Pesticides detected
Valle del Cauca, Río Bolo	3	0	0
Boyacá, Quebrada Paunera	3	0	0
Sierra Nevada, Quebrada La Otra	3	0	0
Putumayo, Río Mansoya	3	0	0
Nariño, Rio Sabaletas	2	0	0

3.1.4.3 Soil

Concentrations of glyphosate and AMPA in soils can be estimated from the application rates used in the eradication program (Table 15) and measurements could be made through the use of residue analysis, however, the more important question is the biological availability of the glyphosate, as this would determine its potential for biological effects.

Table 15. Estimates of glyphosate concentration in the top 25 mm of soil following a spray application

Scenario	Exposure in mg/kg	
	Coca sprayed at 4.992 kg/ha	Poppy sprayed at 1.2 kg/ha
Direct deposition on bare soil with a density of 1.5 kg/L.	13.3	3.2
Deposition on soil with a density of 1.5 kg/L under a canopy of foliage with an assumed interception of 50%.	6.7	1.6

While there are no direct measurements of glyphosate and AMPA concentrations available from treated coca and poppy fields in Colombia, the biological activity of any residues that may be present is judged to be small as the sprayed fields rapidly become colonized with invasive plants or are replanted to coca soon after spraying. From visual observations (Figure 15), from observation in other uses and other locations (Section 4.3.1), and from other reports (Helling 2003), this recolonization is rapid and there have been no adverse effects observed in terms of recolonization or replanting of the sprayed fields.

Figure 22 Photograph of coca plants near Caucasia, Colombia, replanted from cuttings in a field sprayed with glyphosate 56 days previously (Photo, K Solomon, 2004 06 09).

4 EFFECTS CHARACTERIZATION

4.1 GLYPHOSATE

The human-health and environmental effects of glyphosate have been extensively reviewed in the literature (Giesy et al. 2000, Solomon and Thompson 2003, Williams et al. 2000) and by regulatory agencies (NRA 1996, USEPA 1993a, 1997, 1999, World Health Organization International Program on Chemical Safety 1994) [1]. The following sections are primarily directed to a critical analysis of original articles published since 1999 or that were not included in the earlier reviews (Giesy et al. 2000, Solomon and Thompson 2003, Williams et al. 2000).

4.1.1 Effects of glyphosate on mammals

4.1.1.1 Laboratory toxicity studies

The toxicity of glyphosate and the formulation Roundup® were reviewed recently (Williams et al. 2000). Glyphosate and its isopropylamine salt have low acute toxicity by the oral, dermal, and subcutaneous routes of exposure (Table 16).

Table 16. Acute toxicity of glyphosate in selected mammals

Species	Route	Compound administered[a]	LD50 (mg/kg bw)
Mouse	Oral	Glyphosate	>10,000
		Glyphosate	1,538
	Subcutaneous	Glyphosate saline	6,250 (M)
		Glyphosate saline	7,810 (F)
	Intraperitoneal	Glyphosate saline	545 (M)
		Glyphosate saline	740 (F)
		Glyphosate	134
Rat	Oral	Glyphosate, Roundup, Glyphosate isopropylamine salt	>5,000
	Dermal	Roundup	>17,000
	Inhalation	Roundup, Glyphosate saline	LC50=3.18 mg/L (4 hours)
	Subcutaneous	Glyphosate saline	17,500
		Glyphosate saline	281 (M)
			467 (F)
	Intraperitoneal	Glyphosate	238
Rabbit	Oral	Glyphosate	3,800
	Dermal	Glyphosate, Roundup, Glyphosate isopropylamine salt.	>5,000
Goat	Oral	Glyphosate, Roundup, Glyphosate isopropylamine salt.	>3,500

Data from (Smith and Oehme 1992).

[1] It should be noted that several publications on glyphosate have appeared in the literature which focus on the adverse effects of glyphosate. A pamphlet/brochure by Post (1999) was produced on behalf of an activist organization. The pamphlet was very brief and was not peer-reviewed. In addition, an article purporting to be a scientific review was published in 1998 (Cox , 1998) in the "Journal of Pesticide Reform". It should be noted that the Journal of Pesticide Reform does not publish original articles, is not peer-reviewed, is produced by an activist group, and that the editor is often the author of the articles. Because of this, these articles were not used in this report.

Toxicity was greatest by intraperitoneal administration. When rats and mice were given glyphosate orally or intraperitoneally, several stress symptoms, increased respiration, elevated rectal temperatures, and occasional asphyxial convulsions were noted. Median lethal doses of 4,704 mg/kg to the rat and 1,581 mg/kg to the mouse orally were significantly higher than 235 and 130 mg/kg, respectively, median lethal doses obtained when glyphosate was given intraperitoneally. Lung hyperemia was the major lesion noted in the glyphosate poisoned animal (Bababurmi et al. 1978).

There is limited information on acute toxicity in dogs. However, there is a retrospective study conducted of 482 glyphosate calls recorded at the CNITV of France between 1991 and 1994. Only 31 cases were assessed as certain or highly probable and were linked with direct ingestion of glyphosate concentrates or spray in 25 dogs. The symptoms were most frequently described as vomiting, hypersalivation and diarrhea; prostration and paresis were not common. Symptomatic treatment resulted in rapid recovery without sequelae (Burgat et al. 1998). Campbell and Chapman (2000) described the onset of clinical effects in dogs observed in several cases of poisoning as usually between 30 minutes and 2 hours. Recovery usually occurs over 1-2 days. Salivation, vomiting, diarrhea, irritation, and swelling of lips are common early features. Tachycardia and excitability are often present in the early stages, with the animals subsequently becoming ataxic, depressed, and bradycardic. Inappetence, pharyngitis, pyrexia, twitching, shaking, and dilated pupils is noted occasionally. Rarely, jaundice, hepatic damage, and haematuria have been reported. Eye and skin irritation are also possible. Tachypnoea occurs in glyphosate poisoning in other animals but does not appear to be a feature of glyphosate toxicity in dogs.

Some recent studies have examined effects of chronic feeding of glyphosate to Wistar rats. A study was performed to measure the activity of some enzymes with a function in the pathways of NADPH generation, isocitrate dehydrogenase, glucose-6-phosphate dehydrogenase and malate dehydrogenase in liver, heart and brain of pregnant Wistar rats and their fetuses which were exposed to glyphosate solutions 0.5% and 1% at a dose of 0.2 and 0.4 ml/ml water during 21 days of pregnancy. Glyphosate affects these enzymes in the studied organs of the pregnant rats and their fetuses (Daruich et al. 2001).

Feeding Glyphosate-Biocarbo® formulation at rates of 4.87 mg/kg every two days for 75 days resulted in the leakage of hepatic intracellular enzymes, alanine aminotransferase (ALT) and aspartate aminotransferase (AST), suggesting irreversible damage in hepatocytes (Benedetti et al. 2004). The formulation used in this study was from Brazil and the nature of the formulants is unknown. In addition, the exposures extended over a long period of time and are inappropriate for assessing risks from acute and infrequent exposures such as may occur in eradication spraying.

The effect of glyphosate on several enzymes was studied *in vitro.* The enzymes were: serum acetylcholinesterase (AChE), lactate dehydrogenase (LDH), aspartate amino-transferase (AST), alanine aminotransferase (ALT, alkaline phosphatase (AP) and acid phosphatase (AcP). Results revealed that glyphosate inhibited all enzymes except AcP. IC50 values were 714.3, 750, 54.2, 270.8 and 71.4 mM for ACHE, LDH, AST, ALT, and AP, respectively (El-Demerdash et al. 2001). The most sensitive response, that of aspartate amino-transferase was observed at a concentration of 54.2 mM, which is equivalent to a concentration of 9,056 mg/L, a concentration that would not occur in vivo. These results of the studies discussed above do not suggest that glyphosate would have effects at concentrations lower than those previously observed.

Glyphosate has not been found to be genotoxic, mutagenic or carcinogenic. Glyphosate was not teratogenic or developmentally toxic (Williams et al. 2000) except at large exposures. Some studies were not reviewed by Williams et al. (2000) or were published after 2000. These are reviewed below.

In a study on Charles River CD-1 rats, test animals were given oral gavage doses (direct intubation into the stomach) of 0, 300, 1000 and 3,500 mg/kg body weight (bw)/day of glyphosate from day 6-19 of gestation. Control animals received 0.5% methocel. No internal or skeletal anomalies were seen at 300 and 1000 mg/kg bw/day, although maternal toxicity was apparent at 3,500 mg/kg bw/day with soft stools, diarrhea, red nasal discharge, reduced body weight, and death by gestation day 17 (6/25). In addition, mean fetal body weights were significantly reduced and early fetal resorption were significantly increased at this dose level (Rodwell 1980a). Female Dutch belted rabbits were given oral gavage doses of 0, 75, 175, and 350 mg/kg bw/day glyphosate from day 6-27 of gestation. Control animals received 0.5% methocel. No internal or skeletal abnormalities were seen (Rodwell 1980b). In a study from Brazil, examination of pregnant Wistar rats dosed orally with Roundup® from day 6 to 15 of pregnancy with rates of 0, 500, 750, or 1000 mg/kg of glyphosate showed skeletal alteration in fetuses (15.4, 33.1, 42.0, and 57.3%, respectively). There was 50% mortality of dams at 1000 mg/kg only (Dallegrave et al. 2003). The doses used in this study were large and considerably greater than those used in an earlier study (reviewed by Williams et al. 2000). In the earlier study, a No-Observed-Effect-Level (NOEL) of 15 mg/kg/day was described for fetal effects and 300 mg/kg/day for maternal effects. Given the very large doses used in the Dallegrave et al. study (2003), their results are not surprising and do not change the assessment of teratogenic potential. The Rodwell studies discussed above also showed responses at concentrations greater than those reviewed in Williams et al. (2000) and do not change the assessment of teratogenic potential.

A number of recent studies have been carried out in tissue culture systems. One of these assessed the affect of several formulated pesticides on the steroidogenesis pathway (StAR protein synthesis) in tissue cultures of mouse testicular Leydig tumor cells (Walsh et al. 2000). Exposure to the formulation at 25 mg/L in the cell culture medium did cause a reduction in steroidogenesis, but only for a period less than 24 hour during which there was recovery. In another study on tissue cultures, Lin and Garry reported results of bioassays carried out in cultures of the MCF-7 breast cancer cell (Lin and Garry 2000). The results presented by the authors indicated that, while some pesticides caused estrogen-like receptor mediated effects at high exposure concentrations, both glyphosate and the Roundup® formulation of glyphosate induced non-estrogen like proliferation, thereby supporting the view expressed by others (Williams et al. 2000) that neither glyphosate nor Roundup® are endocrine disruptors. The results of studies on cells in vitro are difficult to interpret as they exclude the normal pharmacokinetic and metabolic functions that would be present in whole animals. They should be compared to the multigenerational study used by regulatory agencies worldwide to assess reproductive/developmental toxicity, which is the most definitive study design for the evaluation of potential endocrine modulating substances in humans and other mammals. Comprehensive reproductive and developmental toxicology studies carried out in accordance with internationally accepted protocols have demonstrated that glyphosate is not a developmental or reproductive toxicant and is not an endocrine disruptor (Williams et al. 2000) (USEPA 1993a) (World Health Organization International Program on Chemical Safety 1994).

There was no evidence of neurotoxicity in a number of studies on glyphosate reviewed in Williams et al. (2000). Neurotoxicity was not observed in the large number of acute, subchronic, and chronic studies conducted in rodents nor was it observed in two specific neurotoxicity studies conducted in dogs. However, these studies did no assess potential effects on neurotransmitters and their metabolites in the brain and other parts of the nervous system –– measures of response used in current testing protocols for neurotoxicity.

Some reports on the immunotoxicity of glyphosate have appeared in the literature. Mice exposed to Roundup® at concentrations up to 1.05% in drinking water for 21 days showed no change in immune function (T-lymphocyte and macrophage-dependent antibody response) when, on day 21 of the herbicide exposure period, they were inoculated with sheep erythrocytes (Blakley 1997). In an in vitro study on cytokine production by human peripheral blood mononuclear cells, glyphosate had only a slight effect at the greatest concentration tested (1000 µM = 226,000 µg/L) (Nakashima et al. 2002). Results of both of these studies suggest that glyphosate does not affect immune response in mammals at realistic exposure concentrations. However, studies in fish suggest that that there may be some immunotoxic effects. Short exposures to Roundup® (10 minutes in a concentration of 100,000 µg/L) in carp (*Cyprinus carpio*) and European catfish (*Silurus glanis*) caused a decrease in metabolic and phagocytic activity as well as proliferative response (Terech-Majewska et al. 2004). In contrast to these effects at large concentrations, responses on splenic antibody plaque forming cells in the fish, *Tilapia nilotica*, were reported at concentrations of 1.65 x 10^{-2} µM (= 4.4 µg/L). As responses of the immune system are difficult to interpret in terms of survival of individuals or the population, they not formally used in assessment of pestcides by regulatory agencies.

The toxicokinetics of glyphosate were reviewed by Williams et al. (2000). Between 15 and 36% of ingested glyphosate is absorbed through the intestinal tract and only about 2% via the skin. Excretion of unabsorbed glyphosate is via the feces but the absorbed glyphosate is excreted via the urine with only a small amount of metabolism. Whole-body half-lives were biphasic, with an initial half-life of 6 hours and a terminal half-life of 79 to 337 hours in rats (Williams et al. 2000). Clearance from most tissues was rapid but it was cleared more slowly from the bone, possibly because of ionic binding to the calcium in the bones (Williams et al. 2000). Glyphosate is clearly not bioaccumulated and any absorbed dose is excreted in the urine relatively rapidly.

4.1.1.2 Cases of human poisoning

A number of anecdotal reports of human poisoning with glyphosate and formulations have been published in the literature. In some cases, these are reports of a single event and an observed response. In one such case toxic pneumonitis was observed after exposure to a glyphosate formulation (Pushnoy et al. 1998). However, no information was provided to demonstrate how airborne exposure could have occurred and the results are at odds with the known inhalation toxicity of the formulation (Williams et al. 2000) and tests done on the product as used in Colombia (Section 4.2.2).

In another case, a man accidentally sprayed himself with an unidentified formulation of glyphosate (Barbosa et al. 2001). He developed skin lesions 6 hours after the accident but these responded to routine treatment. However, one month later, the patient presented with a case of symmetrical Parkinsonism syndrome. This is an isolated case and it is impossible to conclude anything about causality as the disease may have already been present but asymptomatic. In a similar case, a woman of 78 years old presented with extensive chemical burns in legs and trunk caused by an accidental contact with a glyphosate formulation. These lesions disappeared, without consequences a month later (Amerio et al. 2004).

Acute intoxication information has been documented in two case-series studies, from Taiwan, China where glyphosate formulations were apparently used for attempted suicide (Chang et al. 1999, Lee et al. 2000). The first paper analyzed 15 intentional intoxications with glyphosate formulation and found that 68% of the patients presented esophageal, 72% gastric and 16% duodenal injuries. Esophageal injury was the most serious injury but was minor in comparison with strong acids. Lee et al. (2000) analyzed 131 suicide attempts in southern Taiwan. The most common symptoms were sore throat and nausea. Fatality rate was 8.4%. In this study 20.5% presented respiratory symptoms and more than half of them needed intubations. The authors propose that direct damage to the airway passage and mention that surfactant (POEA MON 0818) may be responsible for the toxicity. In many cases, the exact doses consumed by persons attempting suicide are not known and it is difficult to interpret these findings in the context of bystander and other accidental exposures which are usually many orders of magnitude less. It is, however, interesting to note the low fatality rate compared to what has been reported from other pesticides such as paraquat and the organophosphorus pesticides (Krieger 2001).

It is well known that the older formulations of glyphosate that contained the surfactant POEA (MON 0818) were eye irritants. Goldstein et al. (2002) analyzed 815 glyphosate related “calls” to the Pesticide Illness Surveillance Program (PISP), most of them involving eye irritation (399), skin (250), upper airway (7) and combinations of these. Of the 187 systemic cases, 22 (12%) had symptoms definitely related to exposure to formulations of glyphosate. Again, this is not surprising as the formulation of glyphosate is acidic (similar to strong vinegar) and the surfactant is an eye irritant. In other studies on eye and skin irritation reviewed in Williams et al. (2000), none of the reported exposures resulted in permanent change to the structure or function of the eye. Based on these findings, it was concluded that the potential for severe ocular effects in users of Roundup herbicides is extremely low. This observation is consistent with the minimal ocular and dermal effects observed with the formulation of glyphosate used in Colombia (Section 4.2.2).

4.1.1.3 Human epidemiology studies

A number of studies in the recent epidemiology literature have attempted to address the issue of glyphosate exposure and disease incidence in humans. Epidemiology studies on pesticides commonly suffer from two sources of error.

Possibly the most important of these is the error in assigning exposures. Exposures in the studied population are never measured directly and it is common to use surrogates for exposures such as areas treated with pesticides, number of applications made, and/or number of years of application. Recent studies have shown that these surrogates are susceptible to significant errors (Arbuckle et al. 2004), leading to the following quote from the authors of the paper:

> *"As the present analysis has shown, the consequences of this assumption could be a high false-positive rate in classification of exposure. The impact of this kind of error can be profound and has rarely been quantified. Until improvements are made in classifying pesticide exposure in epidemiologic studies, results on health effects will be subject to misclassification bias…."*

Similar conclusions have been put forward in other papers (Arbuckle et al. 2005, Harris et al. 2002, Solomon et al. 2005). A second possible source of error in these studies is the fact that the populations that are studied (farmers and professional applicators) typically use many pesticides. Thus, any substance-specific responses and causality are difficult to ascertain.

Cancer Studies. The work of Hardwell et al. (Hardell et al. 2002) presented a pooled analysis of two case-control studies, one on non-Hodgkin's Lymphoma (NHL) (Hardell and Eriksson 1999) and another one related to a Hairy Cell Leukemia (HCL), a rare subtype of NHL. In the 1999 study, the authors employed a case control type of study design for their investigation. Case control studies can suffer from poor exposure histories and recall bias in that study subjects will be required to recall exposures to a putative agent which may have occurred decades prior to the onset of the disease under study. In some cases, study subjects may be deceased (in this study, 192 of the 442 study subjects were deceased) requiring exposure information to be provided by next of kin, thereby further eroding confidence in data related to exposure histories. The study reported their results in terms of odds ratio (OR). An OR of >1.0 implies a greater disease rate for exposed individuals than for the unexposed, while an OR <1.0 suggests a decreased rate of disease in the exposed population. The data for the study were based on small numbers; only four cases and three controls, or less than 1% of the overall study subjects, reported the use of glyphosate. Furthermore, the confidence interval (CI) reported by the authors for exposure to glyphosate was 0.4-13, implying a lack of statistical confidence. In their pooled analysis (Hardell et al. 2002), they reported a positive association with use of glyphosate (OR 3.04, 95%CI of 1.08-8.52) when analyzed using univariate statistics with the highest risk for exposure during the latest decade before diagnosis. However, the OR was reduced when using multivariate statistics (OR 1.85, 95%CI of 0.55-6.20). In addition, the study was based on a small number of cases and controls (8/8) and lacked power to differentiate linkages.

De Roos et al. (2005) evaluated associations between glyphosate exposure and cancer incidence in the Agricultural Health Study (AHS), a prospective cohort study of 57,311 licensed pesticide applicators in Iowa and North Carolina. Among private and commercial applicators, 75.5% reported having ever used glyphosate, of which > 97% were men. In their analysis, glyphosate exposure was defined as a) ever personally mixed or applied products containing glyphosate; b) cumulative lifetime days of use, and c) intensity-weighted cumulative exposure. Glyphosate exposure was not associated with incidence of 12 common cancer types (the relative risk, RR, included 1 in all cases), however, the RR for multiple myeloma incidence was 2.6 (95% CI of 0.7–9.4 based on 32 cases in the total of 2,088 cancers), prompting the authors to suggest that this should be followed up in future studies.

Overall, there is no strong evidence to link glyphosate exposure to increased risk of cancer. Taken with the lack of any evidence of genotoxicity or carcinogenicity of glyphosate in laboratory studies (Williams et al. 2000), it is highly unlikely that glyphosate is carcinogenic in humans.

Neurological effects. A recent study on farmers in the Red River Valley in MN, USA, reported on the link between glyphosate and Attention Deficit Disorder and Attention Deficit Hyperactivity Disorder (ADD/ADHD) in children of farmers who applied it (Garry et al. 2002). They reported OR of 3.6 (95% CI, 1.3–9.6), however, the study suffered from several potential sources of error. The authors noted the lack of uniform diagnostic neurobehavioral information related to (ADD/ADHD) and that their study identified 14 cases of ADD/ADHD among 1,532 live births, a frequency that was actually considerably lower than background rates of ADD/ADHD that had previously been reported by researchers in Canada and the US. Notwithstanding, while Garry et al. (2002) concluded that their study showed a tentative association between ADD/ADHD and the use of glyphosate, they also noted that other experimental evidence did not support this conclusion, including that glyphosate was not genotoxic and that little, if any, evidence of neurotoxicity has been associated with exposure to glyphosate, except in cases of intentional oral overdose. Finally, the authors did express concern that their tentative conclusions could be explained by random chance alone, and stated the need for further detailed neurodevelopmental studies to resolve these outstanding issues. Overall, there appears to be little evidence to support a link between glyphosate exposure and neurobehavioral problems in children of exposed applicators.

Reproductive outcomes. Several papers have reported on the relation between adverse reproductive outcomes and the use of glyphosate. In a study in Ontario, Canada, Arbuckle et al. (2001) observed a moderate increase in the risk of late abortions associated with preconception exposure to glyphosate (OR = 1.7 95%CI,1.0-2.9). Another study in Ontario (part of the Ontario Farm Family Health Study) reported a positive association (decrease in fecundability of 20%, ratio range = 0.51-0.80) when both spouses participated in activities where they could be exposed to pesticides. This was observed for 6 of 13 pesticides categories, one of which was glyphosate (Curtis et al. 1999). The study was based on 2,012 planned pregnancies. There was no strong or consistent pattern of associations of pesticide exposure with time to pregnancy. For exposure intervals in which only the men participated in pesticide activities or in which neither men nor women participated in pesticide activities but pesticides had been used on the farm, conditional fecundability ratios ranged from 0.75 to 1.50, with no apparent consistency among pesticide classes, chemical families, or active ingredients. Again, while this study did suggest a linkage between pesticide exposure and fecundability, there is no evidence from laboratory studies that glyphosate is a reproductive toxicant at exposures that would be expected in humans (Williams et al. 2000).

Overall, there is little epidemiological evidence to link glyphosate to any specific diseases in humans. This conclusion is supported by laboratory toxicity studies. However, responses related to reproductive outcomes such as fecundability measured through time to pregnancy offer a useful measure of possible effects that can be applied in situations such as Colombia where other health data are difficult to gather. With this in mind, we designed a preliminary study to gather human epidemiological data in several regions in Colombia. These regions were the same as those selected for the surface-water sampling (Table 12). The design and results of the study are summarized in the following section. A detailed report is given in a separate document (Sanin 2005).

4.1.2 Human health epidemiology study in Colombia

The question that this study addressed was: Is glyphosate exposure associated with adverse reproductive effects? The specific objective was thus to elucidate possible effects on reproductive health from exposure to glyphosate by assessing fertility/fecundability among women resident in different areas of the country with different pesticide use patterns. The design was cross-sectional with retrospective collection of data and is equivalent to a retrospective cohort. The study population consisted of 600 women of reproductive age in each of five different areas (Table 17)

Table 17. Characteristics of the areas used in the epidemiology study

Site name	Focal crop	Known pesticide use
Valle del Cauca	Sugar cane	Glyphosate and other pesticides. Glyphosate applied by air.
Boyacá	Coca	Manual eradication, no aerial spraying of glyphosate. Use of other pesticides unknown.
Sierra Nevada	Organic coffee	No pesticide use and no coca known to be grown. Use of other pesticides unknown.
Putumayo	Coca	Aerial eradication spraying with lower intensity. Use of other pesticides unknown.
Nariño	Coca	Aerial eradication spraying with higher intensity. Use of other pesticides unknown.

The study protocol and questionnaire were approved through the Ethics Review Board of the Fundación Clínica Santa Fé de Bogotá, Colombia. All females of reproductive age in each area were informed about the objectives of the study and invited to participate if their first pregnancy (independent of the result of it) had occurred during the last 5 years, they had lived in the region at least for the same period, and they had not visited a physician for treatment of infertility nor used contraceptives during the year prior to getting pregnant. First pregnancies were the focus of the questionnaire. This reduced recall bias and other potential biases that are associated with subsequent pregnancies. Only one pregnancy was used to maintain outcome independence and minimize the effect of previous reproductive history.

Reproductive health was characterized through the following dependent variables (retrospectively) assessed by questionnaire:

Time to pregnancy (TTP): Number of months that it takes a couple to achieve a clinically detectable pregnancy without the use of contraceptives. A modified version of the key question from the questionnaire of Baird et al. (1991) was used to elicit TTP. Valid data on TTP can be derived retrospectively, with a recall time of 14 years or more (Joffe et al. 1995).

Fertility: Percentage of women who achieved pregnancy during the first year after intent.

The independent variable in the study was exposure to glyphosate for eradication of illicit crops. This was measured through use information from the region as indicated in Table 12. There were a number of possible confounders or independent predictors of the reproductive variables in study. These are listed below:

General Health and Nutrition Status	
Women and their partner	
Age	Complete years
Education	Highest grade achieved
Active smoking	Smoke or not; number of years number of cigarettes per day
Alcohol consumption	Number of drinks per month
Coffee consumption	Number of cups per day
Type of family	Nuclear or extended
Socioeconomic stratum	(Almost all all participants were stratum 1 – rural)
Only from Women:	
Body Mass Index	Weight (Kg) / (Height - m)
Reproductive history	Information on the father was also available

Techniques and procedures were as follows: In the five areas we started at the closest household to the location where water and sediment samples were taken from. Interviewers visited house by house to identify women who met inclusion criteria until the sample size (600 women in each zone) was completed. Those who met the inclusion criteria were informed about the project in a general way and were informed that there would no be reprisals for participation or non-participation and that the investigators guaranteed the privacy of the information collected. Each participant provided written informed consent.

Interviewers and supervisors were trained on the objectives of the project and the questionnaire for two days. All interviewers lived in the study area and were supervised by local epidemiologists who knew the study area and who were well known by the population. These local epidemiologists were supervised by PTG team. All the information collected was submitted to a quality control procedure. The data were captured in Microsoft Excel (Microsoft Corporation 2003) and processed with the STATA 7.0. (Stata Corporation, College Station, Texas) with macros developed by Dinno (2002). The modified version of the key question from the questionnaire of Baird et al. (1991) was used to elicit TTP was, “How many months were you having sexual intercourse before you became pregnant for the first time?" TTP was defined as duration in months, not divided by menstrual cycle duration in days, because women are more able to recall time in months than in cycles (Joffe 1997). For analysis purposes, if TTP was reported as zero months, the answer was interpreted as one month. Cutoff points for categorization of continuous variables were set as follows:

Age at time of interview - 25;

Age when started to try to get pregnant and age when first got pregnant - 20.

Of a total of 3005 women interviewed, 413 exclusions were made. These included: 233 women without TTP data and 21 with TTP values greater than 60 months and 159 women who consulted to physician about infertility. Hence, 2592 (86.3%) were included in the analyses reported here.

For each exposure and potential determinant variable, non-parametric ANOVAs of TTP were conducted. In the fecundability predictor models, censoring of TTP was introduced, in order to reduce the effect of other medical causes on TTP. If a woman took more than 12 months to conceive, a value of "null" for a separate censor variable was included with a value equal to 0 if TTP was 12 months or less and 1 if TTP was greater than 12 months.

Each month was classified according to the ecological exposure and determinant variables and an indicator variable was generated for every month giving information on whether the cycle under this exposure resulted in a pregnancy or not. Fecundability odds ratios (fOR) were calculated with 95% confidence intervals (95% CI) using a discrete time analogue of Cox's proportional hazard model (Baird et al. 1986, Curtis et al. 1999, Zhou and Weinberg 1999). This process generate a fOR for which values below unity indicate sub-fertility.

The initial saturated multivariate model included all variables significant on bivariate analysis ($p<0.10$) and variables of prime biological importance (age at time of trying to get pregnant). Variables were eliminated one by one according to the p values (>0.05) and effects of elimination on the coefficients of other variables in the model assessed. Several goodness of fit statistics for logistic regression were checked (Hosmer and Lemeshow 1989). The final model consisted of only those variables that contributed to the explanatory value of the model (coefficient of determination). Co-linearity was tested with VIF (Variance Inflation Factor). The assumption that the fOR was constant across time (Weinberg and Wilcox 1998) was tested graphically and by including an interaction term between cycle (time) and exposure or determinant variables in the final model. The latter were not significant, implying that the proportional assumption was not violated. Finally, to evaluate a possible selection bias based on willingness to participate, the analyses were repeated excluding the pregnancies occurring by the first month (Weinberg et al. 1994). No significant changes in the final model were observed.

The distribution of pregnancies in relation TTP (Figure 16) was different between the five regions. In previous work in Colombia (Idrovo et al. 2005), the percentage for first month was about 30% - low compared with data from developed countries. In this case, Valle del Cauca had very low initial percentage and Boyacá had high values for the first and twelfth months (Figure 1). The mean for 12 months in developed countries is 85-90%.

Participating women were generally young (mean and median age 21 years old) and had completed at least some secondary education. The vast majority had regular menstrual cycles (96.7%); a substantial proportion had irregular partner relationships. Most experienced their first pregnancy at young ages (73.6% at < 20 years). During the year before first pregnancy, most were free of illness (84%), had not had x-rays (95.4%), and did not smoke tobacco (95.1%). Alcohol and coffee consumption were 51.8% and 80.3% respectively. The majority of women were housekeepers at the time of first pregnancy.

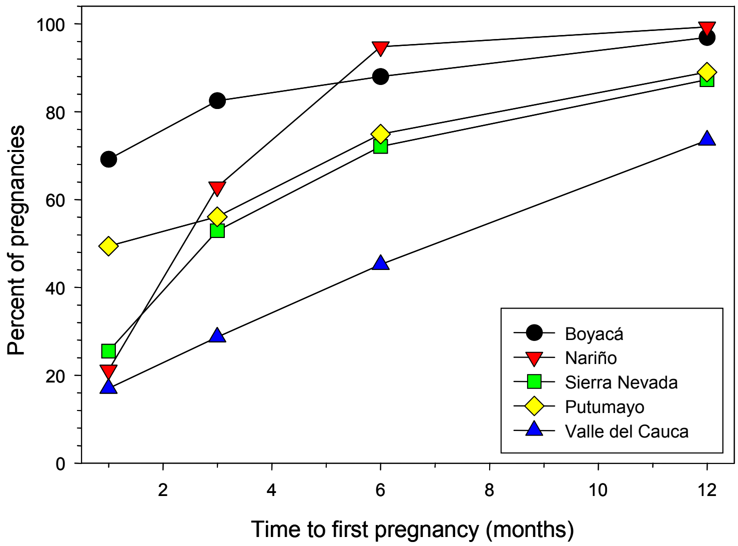


Figure 23 Summary of the results of the time to pregnancy study

In the crude analyses, longer TTP was associated with a number of factors such as, region, older maternal age, ethnic group, irregular menstrual cycles, and irregular partner relationship. Previously visit to physician for problems related with fertility, x-rays taken in the year before pregnancy (YBP), and coffee consumption in the YBP also were associated with longer TTP. Coffee consumption had a significant test for trend. Maternal overweight was associated with a longer TTP. A tendency to longer TTP was observed among those engaged in some waged work and with higher education. Paternal unemployment or self work, were associated with longer TTP. No other paternal data were related with the TTP.

After adjustment of the model for region, several associations were identified (Table 18). Although non-significant in the adjusted model (p< 0.1), coffee intake and self perception about bad quality of water was associated with longer TTP and all sources of water presented greater risk of longer TTP when they were compared with pure water ("nacimiento"), except for a few cases which use carried water ("carro-tanque").

Table 18. Causes of fecundability adjusted [a] for the relationship between time to preganacy (TTP) and region [b] based on an alternative model.

Variable	fRMa [c]	SE [d]	95% CI [e]	*p*
Region [f]				
Nariño	0.56	0.048	0.47, 0.66	<0.01
Sierra Nevada	0.36	0.031	0.31, 0.43	<0.01
Putumayo	0.35	0.029	0.29, 0.41	<0.01
Valle del Cauca	0.15	0.014	0.13, 0.18	<0.01
Age at first preganacy > 20 years [g]	0.81	0.048	0.73, 0.91	<0.01
Irregular relationship [h]	0.76	0.041	0.68, 0.84	<0.01
Consumption of coffee [i]				
Medium (1-3 cups per day)	0.91	0.059	0.81, 1.04	0.15
High (4 and more cups per day)	0.84	0.083	0.69, 1.02	0.08
Perception of contamination of water [j]	0.91	0.51	0.81, 1.01	0.08

n = 2592 mothers 11,270 cycles.

[a] Proportional risk model of Cox, modified after Dinno (2002) Modelo de Riesgos proporcionales de Cox, modificado (Dinno, 2000). [b] Restricted to those mothers who did not consult a physician regarding problems in conceiving. [c] **fRMa** Adjusted cause of fecundability. [d] Standard Error. [e] 95% confidence interval. [f] Compared to Boyacá as reference. [g] Compared to ≤20 years as reference. [h] Compared to regular relationship as reference. [i] Compared to no consumption as reference. [j] Compared to no contamination as reference and based on self-perception and source of water normally consumed.

In the final multivariate model, the main predictor of TTP was the region adjusted by irregular relationship with partner and maternal age at first pregnancy. Boyacá had the minimal risk and was the reference region. Nariño, Sierra Nevada, and Putumayo, had slightly higher risk. The greatest risk was in the Valle del Cauca region. There was no association between TTP and use of herbicides in the eradication of illicit crops in the regions studied. The reason(s) for the increased risk for longer TTP in the Valle del Cauca region where sugar cane is grown is not known. In this study, the increased risk in Valle del Cauca cannot be attributed to exposure to pesticides alone since Sierra Nevada, where organic crops are grown, also showed a statistically significant difference from the reference location (Boyacá). This study was designed to test hypotheses related to the use of glyphosate in eradication spraying and the data cannot be used to identify causality associated with other risk factors. To test this question in Valle del Cauca or any other region, a new study would have to be designed and conducted. Some of the factors associated with higher TTP that were identified in our study should be included in any future studies that may be conducted.

4.1.3 Effects of glyphosate in non-target organisms in the environment.

The mechanism of action of glyphosate is via the disruption of the shikimate metabolic pathway that leads to the synthesis of aromatic compounds in numerous microorganisms and plants. Glyphosate inhibits the shikimate pathway by blocking 5-enolpyruvyl-shikimate-3-phosphate synthase (EPSPS). This reduces the synthesis of aromatic amino acids and causes accumulation of high concentrations of shikimic acid and its derivatives. Glyphosate translocates to active growing tissues, particularly effective in most plants because its degradation is slow. Thus, the herbicide moves throughout the plant before symptoms are noticed. The shikimate pathway is absent from mammals (Eschenburg et al. 2003, Roberts et al. 2002, Roberts et al. 1998). However, toxic effects of the compound on, for example, non-mammalian aquatic organisms, have been observed at large concentrations. These effects are discussed in more detail below.

A common question in conducting risk assessments in tropical regions and other non-temperate regions is the paucity of toxicity data for "tropical species". It is true that most of the test species used in toxicity testing, particularly of pesticides, are "temperate species" largely because of the location of testing laboratories that are able to conduct guideline toxicity tests under Good Laboratory Practice (GLP). Except for a few substances with defined mechanisms of action, there is no reason to believe that organisms from tropical regions are inherently more or less sensitive than organisms from temperate regions. It is well known that DDT and some related pesticides become more toxic at lower temperatures (Dyer et al. 1997); however the mechanisms here are well understood. Comparison of responses of tropical and temperate organisms to a number of pesticides other than DDT has shown that there are not significant differences in sensitivity (Maltby et al. 2005). With this in mind, we used the rich data set of toxicity values that has accumulated in the literature for glyphosate and its formulations.

4.1.3.1 Effects in non-target terrestrial animals

The potential environmental effects of glyphosate and Roundup® were extensively reviewed in 1999 (Giesy et al. 2000). Some additional papers have appeared since that time. Glyphosate is not considered directly toxic to terrestrial organisms.

Soil invertebrates. The effects of glyphosate on earthworms have been reviewed (Giesy et al. 2000) and risks were judged to be essentially negligible. A recent study on the earthworm *Eisenia fetida* reported that, although a commercial formulation of glyphosate was not directly toxic to the earthworms, it did cause effects on locomotory activity that may be detrimental to the earthworms (Verrell and Van Buskirk 2004). The formulation used in the study was Ortho Groundclear Total Vegetation Killer which contains 5% by volume of glyphosate as the isopropylamine salt (IPA). In this study, the authors applied 82 ml of a 1:4 solution of Groundclear to 2 L of soil in a plastic box. This amount of glyphosate is much greater than would be applied under normal agricultural uses or in the control of illicit crops. Assuming that the boxes of soil were cubes, the area of the surface would be 12.6 x 12.6 cm or 159 cm^2. This being so, the application rate used by the authors was equivalent to 518 kg glyphosate/ha, a totally unrealistic application rate and 100 times more than that used in the control of coca. This study was obviously seriously flawed and the results are not applicable to any use of glyphosate. This study has no relevance to the use of glyphosate for the control of illicit crops in Colombia.

Soil microorganisms. Glyphosate has little effect on soil microorganisms (Giesy et al. 2000). Since the symbiotic soil and root-associated microorganisms may be partially dependent on the plant for nutrients, the death or injury of the plant will result in effects on the organisms associated with it. Similarly, death of the plants would release organic matter and nutrients into the soil and this would affect soil microorganisms in a similar way to the application of compost or fertilizer. This effect was reported for glyphosate and its effects on grass (Tenuta and Beuchamp 1995). This would also occur with other herbicides and with mechanical control of plants. Effects have been demonstrated in hydroponically grown plants exposed through the watering solution, however, this route of exposure is not relevant to field conditions where glyphosate would bind strongly to soil particles and not be biologically available. Effects on symbiotic microbiota have also been demonstrated in glyphosate tolerant plants treated at 10 times the normal field application rates but these are not relevant exposures as the studies were done in vitro and in the absence of soil (Mårtensson 1992). Some effects on metabolism of phenolic substances in symbiotic bacteria in glyphosate-tolerant soybeans have been shown; however, these changes did not alter nitrogenase activity (Hernandez et al. 1999). Microbial systems in soil are complex and considerable variation can be expected among tests and among soil types. More recent studies on the effects of glyphosate on microbiological activity in soils have shown an increase in microbiological activity, mainly in fungi, which are likely using the glyphosate as a source of carbon, nitrogen, and phosphorus (Araujo et al. 2003, Haney et al. 2002, Laatikainen and Heinonen-Tanski 2002). These changes in microbiological activity are not judged to be deleterious.

The effects of several fungicides and herbicides on the growth of the ectomycorrhizal fungi *Lactarius deliciosus,* strain LDF5, and *Pisolithus tinctorius*, strains 30AM, 3SR and Mx, in pure culture have been studied. Glyphosate at concentrations of 0, 1, 10, 100, and 1000 mg/Kg had no effect (Diaz et al. 2003). Some 64 strains of ectomycorhizal fungi were tested against the most common pesticides used in forestry in Finland. Glyphosate did not produce strong inhibition in any of the strains, most were unaffected, and some were stimulated by 1 mg/L Roundup Bio® in agar (Laatikainen and Heinonen-Tanski 2002). Laboratory tests on four species of entomopathogenic fungi have shown that technical glyphosate has no effect, but a range of formulated products did have fungicidal properties, especially RoundUp Ready-To-Use® (Morjan and Pedigo 2002). In fact, as fungi and bacteria have the shikimate pathway, this suggests the potential use of shikimate pathway inhibitors for the beneficial control of fungal pathogens and apicomplexan parasites, such as *Toxoplasma gondii*, *Plasmodium falciparum*, and *Cryptosporidium parvum* (Roberts et al. 2002, Roberts et al. 1998).

Analysis of all lines of evidence for effects of glyphosate on soil microorganisms indicates that adverse effects would be unlikely as a result of application at normal field rates. Any minor effects to communities, such as described above, would be expected to disappear rapidly (Giesy et al. 2000, World Health Organization International Program on Chemical Safety 1994). After reviewing several studies conducted in many climates, different soils over the past 10 years and under various cropping systems, Motavalli et al. (2004) have concluded that so far no conclusive evidence shows that glyphosate has any relevant effect on nutrient transformations by microbes. However, they point out that this topic needs further study, as not every situation has been adequately researched. Further, because of lack of bioavailability on soils, adverse effects on beneficial soil fungi and bacteria are unlikely to occur under field conditions of use. Glyphosate binds strongly to soil particles and would not be available for uptake by these microorganisms, many of which are actually inside the tissues of the plants. The fact that seeds will readily germinate in soils soon after treatment with glyphosate and that nitrogen-fixing Roundup Ready® soybeans grow and develop high yields despite treatment with glyphosate demonstrates the practical insignificance of these effects under actual conditions of use.

Terrestrial invertebrates. As glyphosate is a non-selective herbicide, it will cause habitat alteration. Habitat alteration also results from a number of human activities in the production of food and fiber. The most important of these is the clearing of land for agricultural production. Whether this is through slash and burn processes such as are used in the initial preparation of coca and poppy fields in Colombia or the application of a herbicides such as glyphosate and paraquat, also used in coca production, the effects on non-target species are the same. Use of cultural, mechanical controls, or herbicides, to alter habitat (remove plants) will have effects on organisms that normally use these plants for food or shelter.

After applying glyphosate at double the recommended application rates, no effects were observed in microarthropods in soil (Gomez and Sagardoy 1985). As weed species compositions and densities are directly affected by the glyphosate, indirect effects are more likely to occur. Jackson and Pitre (2004a) found that populations of adult *Cerotoma trifurcata*, adult *Spissistilus festinus*, larvae of *Plathypena scabra*, and the caterpillar of *Anticarsia gemmatalis* were unaffected by glyphosate but, populations of adult *Geocoris punctipes*, a Hompoteran insect predator, were decreased by the herbicide. The authors concluded that this effect was due to reduced weed densities after glyphosate treatment. Populations of green cloverworm (*Hypena scabra*) were evaluated on soybean glyphosate-resistant varieties, with and without exposure to glyphosate and no differences among treatments were detected on developmental time and survivorship (Morjan and Pedigo 2002). Weed management systems, more than glyphosate, that allowed more weeds to grow generally had higher insect population densities (Buckelew et al. 2000).

Effects of glyphosate and associated cultural practices can affect arthopods indirectly. In studies conducted in the United Kingdom, indirect effects of glyphosate were observed in the spider *Lepthyphantes tenuis.* These were a result of habitat alteration and were related to death of plants and decreasing height of vegetation. Glyphosate applications only had a within-season indirect habitat effect on *L. tenuis* as field margins sampled 16 months after an application of 360 g glyphosate/ha showed no detrimental effects (Bell et al. 2002, Haughton et al. 2001). Tests of the fecundity and mortality of *Geocoris punctipes* (Say), exposed to glyphosate as Roundup® on soybean found no effects over a 10-d post-treatment period. Exposure of *G. punctipes* eggs to glyphosate spray had no effect on egg hatch (Jackson and Pitre 2004b). Some reductions in numbers of this species 3 weeks after treatment probably reflect weed removal, i.e. habitat alteration (Jackson and Pitre 2004a).

Similarly, studies on populations of leaf litter invertebrates in areas of Australia where glyphosate was spayed at 1 to 1.4 kg/ha for the control of an invasive weed, showed no significant effects four months after spraying (Lindsay and French 2004). The authors pointed out that variability in treated and untreated areas was large and suggested that the nature of the vegetative community and its structure and the post-spray weather may also be important. In agriculture, these effects are part of the risk assessment related to integrated pest management (IPM) and potential effects on beneficial organisms are weighed in the risk benefit equation. In conclusion, there is little evidence of any direct effect of glyphosate on insects in the field or in natural environments.

Terrestrial vertebrates. Technical glyphosate, formulated glyphosate, and glyphosate mixed with Cosmo-Flux® are not acutely toxic to mammals via several routes of exposures (reviewed in this report). Although wild mammals have not been specifically tested with the mixture as used in Colombia, the data from these laboratory studies suggest that they would be insensitive and not directly affected by a direct overspray.

Birds are not susceptible to glyphosate. In studies on Bobwhite quail, *Colinus virginianus* and Mallard duck, *Anas platyrhynchos*, acute oral LD50 values of >4,640 and >4,640 mg/kg bw have been reported (USEPA 2001). Again, direct effects of formulated glyphosate or glyphosate plus Cosmo-Flux® are judged to very unlikely.

Indirect effects on terrestrial wildlife have been reported to be associated with the use of glyphosate in agriculture and forestry uses. Alteration of habitat is more of an issue in semi-wild areas such as forests where herbicides may be used to control competing vegetation and allows conifers to grow and mature more rapidly. In these cases, short-term effects on birds and other wildlife do occur, however, these populations usually recover in 2-3 years (Kimball and Hunter 1990, Santillo et al. 1989a, Santillo et al. 1989b) and even the vegetation will recover in less than ten years (BC Ministry of Forests 2000, Boateng et al. 2000). Normally, in these uses, the actual areas treated with herbicides are relatively small and are surrounded by or adjacent to untreated areas that can act as refugia or sites for repopulation by animals that have moved away because of the changes in habitat. As new vegetation develops to replace that controlled by the herbicide, the habitat will again become usable to these animals (Giesy et al. 2000, World Health Organization International Program on Chemical Safety 1994).

Glyphosate is widely used for vegetation management, including in the restoration of native plant communities where exotic or invasive species are controlled, (e.g. Hartman and McCarthy 2004). The use of glyphosate for “conifer release” from competition has minimal effects on wildlife and can be used to enhance biodiversity if used for spot and patch treatments, (e.g. Sullivan and Sullivan 2003). A review of management of northern US forests, including the use of herbicides including glyphosate, indicated no adverse ecological effects (Lautenschlager and Sullivan 2002). However, the impacts of vegetation removal by manual clearance and glyphosate application in conifer plantations has effects on bird communities in British Colombia, mediated by the removal of deciduous plants. Where the herbicide was used, number of bird species declined, total number of individuals increased, and common species dominated. Populations of residents, short-distance migrants, ground gleaners, and conifer nesters increased significantly after herbicide treatment. Deciduous nesters and foliage gleaners increased in abundance (nonsignificantly) in control and manually thinned areas. Warbling Vireos (*Vireo gilvus*), which are deciduous specialists, declined in areas treated with herbicide and may be particularly susceptible to the indirect effects of glyphosate application on plant removal (Easton and Martin 1998, Easton and Martin 2002).

Nevertheless, control of *Cirsium arvense* (Canada thistle) using wick application of glyphosate in wildfowl areas can enhance plant diversity that is of benefit to water birds (Krueger-Mangold et al. 2002). However, the broad spectrum activity of glyphosate means that accidental overspray of rare non-target plant species during control of invasive plants will cause damage (Matarczyk et al. 2002).

Beneficial insects. Glyphosate is not considered toxic to honeybees, with a reported LD50 of >100 µg/bee (USEPA 2001), however, the formulation, with the adjuvant Cosmo-Flux®, as used in Colombia may have different toxicity because of the surfactants added to the mixture. To test this hypothesis, toxicity testing of a mixture of a commercial formulation of glyphosate and the surfactant Cosmo-Flux® 411F, was conducted to determine the acute contact toxicity to honey bees (*Apis mellifera* L.) (Stantec 2005a). This was done in accordance with the testing methods and guidelines developed by the Organization for Economic Cooperation and Development (OECD) Method #214, "Honeybees, Acute Contact Toxicity Test" (OECD 1998a) and the United States Environmental Protection Agency (U.S. EPA) Office of Prevention, Pesticides and Toxic Substances (OPPTS) Ecological Effects Test Guideline 850.3020, "Honey Bee Acute Contact Toxicity" (USEPA 1996a). The results of this study showed that the mixture of glyphosate and Cosmo-Flux® 411F is acutely nontoxic via contact exposure to honey bees (i.e., did not cause mortality or stress effects in bees within 48-hours of treatment) at concentrations equal to or less than 56.8 mg AE/bee. These results are similar to those for glyphosate and formulations from the US EPA ECOTOX data base (USEPA 2001) and show that the formulated product as used in Colombia is not hazardous to bees and, by extrapolation, to other beneficial insects.

4.1.3.2 Effects in aquatic animals

Several extensive reviews of the effects of glyphosate on aquatic organisms have concluded that glyphosate presents an essentially negligible risk to aquatic organisms (Giesy et al. 2000, Solomon and Thompson 2003, World Health Organization International Program on Chemical Safety 1994). Several recent publications have reported on the effects of glyphosate and several of its formulations in frogs. The acute toxicity of technical-grade glyphosate acid, glyphosate isopropylamine and three glyphosate formulations to Australian frogs was measured (Mann and Bidwell 1999). The authors reported the acute toxicity for adults of one species and tadpoles of four species of southwestern Australian frogs in 48-h static/renewal tests. The 48-h LC50 values for Roundup® Herbicide (MON 2139) tested against tadpoles of *Crinia insignifera*, *Heleioporus eyrei, Limnodynastes dorsalis*, and *Litoria moorei* ranged between 8,100 and 32,200 µg/L (2,900 and 11,600 µg/L glyphosate acid equivalent

[AE], while the 48-h LC50 values for Roundup® Herbicide tested against adult and newly metamorphosed *C. insignifera* ranged from 137,000-144,000 µg/L (49,400-51,800 µg/L AE). These values were different, depending on the type of dilution water (lake or tap water). For the purposes of this risk assessment, the most sensitive stage was used.

Touchdown® Herbicide (4 LC-E) tested against tadpoles of *C. insignifera, H. eyrei, L. dorsalis*, and *L. moorei* was slightly less toxic than Roundup® with 48-h LC50 values ranging between 27,300 and 48,700 µg/L (9,000 and 16,100 µg/L AE). Roundup® Biactive (MON 77920) was practically nontoxic to tadpoles of the same four species producing 48-h LC50 values of 911,000 µg/L (328,000 µg/L AE) for *L. moorei* and >1,000,000 µg/L (>360,000 µg/L AE) for *C. insignifera*, *H. eyrei*, and *L. dorsalis*. Technical glyphosate isopropylamine salt was practically nontoxic, producing no mortality among tadpoles of any of the four species over 48 h, at concentrations between 503,000 and 684,000 µg/L (343,000 and 466,000 µg/L AE). The toxicity of technical-grade glyphosate acid (48-h LC50, 81,200 -121,000 µg/L) is likely to be due to acid intolerance. Slight differences in species sensitivity were evident, with *L. moorei* tadpoles showing greater sensitivity than tadpoles of the other four species. Adult and newly emergent metamorphs were less sensitive than tadpoles.

A series of studies on frogs were conducted with several formulations of glyphosate in relation to its use in forestry in Canada (Chen et al. 2004, Edginton et al. 2004, Thompson et al. 2004, Wojtaszek et al. 2004). Using a formulation of glyphosate (Vision®) containing glyphosate and ethoxylated tallowamine surfactant - POEA, LC50 values as low as 880 µg/L (as glyphosate) were reported for tadpoles of *Xenopus laevis*, *Bufo americanus*, *Rana clamitans*, *Rana pipiens* (Edginton et al. 2004). Embryo stages were less sensitive than older larvae and toxicity was affected by the pH of the exposure medium, although not in a consistent manner. For the purposes of this assessment, values obtained at the most sensitive pH and for the most sensitive stage were used.

In a related study on the toxicity of the Vision® formulation of glyphosate to the zooplankton organism, *Simocephalus vetulus*, and tadpoles (Gosner stage 25) of *Rana pipiens,* interactions between pH and food availability were reported (Chen et al. 2004). Both high pH (7.5 vs. 6.5) and food deprivation increased the toxicity of this formulation. As only two concentrations were tested (750 and 1,500 µg/L), LC50 values could not be determined.

Field studies conducted on larvae of *Rana clamitans* and *Rana pipiens* with the Vision® formulation of glyphosate showed that, in the presence of natural factors such as sediment and environmentally relevant pH, the toxicity of the formulation was reduced as compared to laboratory observations (Wojtaszek et al. 2004). The authors reported 96-h median lethal concentration (LC50) values ranging from 2,700 to 11,500 µg/L (as glyphosate) (Wojtaszek et al. 2004). Although the authors used a formulation of glyphosate containing the more toxic surfactant POEA, the results confirm that, in the presence of sediments, reduction in the bioavailability of glyphosate (and formulants) occurs and this further reduces risks, a conclusion reached for this forestry use (Thompson et al. 2004) but which is equally relevant to the use of glyphosate in Colombia.

In another study on amphibians, the toxicity of a number of glyphosate formulations to frogs (*Rana clamitans, R. pipiens, R. sylvatica*, and *Bufo americanus*) was reported (Howe et al. 2004). The formulations included Roundup Original®, glyphosate technical, the POEA surfactan used in some glyphosate-based herbicides, and five newer glyphosate formulations of glyphosate. As expected, the most toxic of the materials was the POEA surfactant, followed by Roundup Original®, Roundup Transorb®, and Glyfos AU®. No significant acute toxicity was observed with glyphosate technical material (96-h LC50 >17,900 µg/L). LC50 values for Roundup Original® in *R. clamitans, R. pipiens,* and *R. sylvatica* were 2,200, 2,900, and 5,100 µg/L (AE), respectively. These values were used in this risk assessment. Several other formulations of glyphosate were also tested in *R. clamitans* and these (Roundup Biactive®, Touchdown®, and Glyfos BIO®) were essentially non-toxic with LC50 values of >57,000 µg/L.

In a study carried out with several commercial pesticide formulations in leopard frogs (*Rana pipiens*), green frogs (*R. clamitans*), bullfrogs (*R. catesbeiana*), the American toad (*Bufo americanus*), and gray tree frogs (*Hyla versicolor*), effects of Roundup® and interactions with other pesticides were reported (Relyea 2004). The formulation of Roundup® used in this study contained the more toxic POEA surfactant. Survival and growth over a 16 day period were not significantly affected by the glyphosate formulation at 1,000 µg/L (glyphosate AE) but some species were affected at 2,000 µg/L. Some interactions were observed between the glyphosate formulation and other pesticides such as the insecticides diazinon, carbaryl, and malathion. A recent paper reported that a glyphosate formulation containing POEA was highly toxic to tadpoles of several species of frogs exposed under realistic conditions in small (1000-L) field microcosms (Relyea 2005). The tadpoles (Wood frog, *Rana sylvatica*; leopard frog, *Rana pipiens*; American toad, Bufo americanus; gray tree frog, Hyla versicolor; and the spring peeper, Pseudacris crucifer) were exposed to a concentration of 3,800 µg/L (AE) of glyphosate formulation applied as a commercial formulation (unspecified) directly to the surface of the water. The rate of application was equivalent to 16 kg/ha, a value that is unrealistic and probably the result of an error in the methods. At this concentration, glyphosate formulated with POEA would be expected to be lethal to tadpoles. The discussion in the paper that suggests that use of glyphosate may be having adverse effects on frogs thus based on a flawed study design and is not supported by other data, much of which is discussed above.

Effects on other non-target aquatic organisms have also been recently reported in the literature. In studies on the toxicity of glyphosate to several aquatic algae and zooplankton, Tsui and Chu (2003) showed that technical glyphosate was considerably less toxic than the product Roundup®, which is formulated with the POEA surfactant. LC and EC50 values for technical glyphosate ranged from 5,890 to 415,000 µg/L. In tests conducted in the presence of sediment (Tsui and Chu 2004), these same authors showed that biological availability of glyphosate was significantly reduced by binding to sediment. The reduction in porewater concentration that resulted from the presence of sediments was proportional to the amount of organic carbon in the sediments.

Tests on the fish *Oreochromis niloticus* (Nile tilapia) exposed for 3 months to sublethal concentrations (5,000 and 15,000 µg/L) of glyphosate as Roundup® caused significant damage to gill, liver, and kidney tissue. The structural damages could be correlated to the significant increase ($p \leq 0.05$) in aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase activities in the second and third months of exposure. The results indicated that long-term exposure to Roundup® at large, although sublethal concentrations had caused histopathological and biochemical alterations of the fish (Jiraungkoorskul et al. 2003). Because technical glyphosate was not tested and the contribution of the surfactants to this response cannot be judged.

In studies on the freshwater mussel *Utterbackia imbecillis*, a commercial formulation of Roundup® was reported to have low toxicity (24-h LC50 of 18,300 µg/L and a No Observed Effect Concentration (NOEC) of 10,040 µg/L – 7,442 µg/L AE) to larval mussels (Conners and Black 2004). In studies on genotoxicity in these mussels, there was no significant difference in response between the control and mussel larvae treated at ¼ the NOEC, ≈ 2,500 µg/L (1,850 AE).

Response of total free amino acids profiles of snails to glyphosate exposures has been studied (Tate et al. 2000). These authors showed that exposure of the aquatic snails (*Pseudosuccinae columella*) to technical glyphosate at nominal concentrations of 1000-10,000 µg/L lead to increased egg-laying and increased amino acid concentrations in the tissues. Technical glyphosate was not particularly toxic with a 24-LC50 of 98,900 µg/L. The effect on egg-laying and amino acid concentrations was stimulative rather than adverse but the authors speculate that it could lead to increases in incidence of diseases for which the snails are intermediate hosts. Increases in parasites may affect organisms in the environment. Similar stimulation was observed in the rotifer *Brachionus calyciflorus* where growth rates and sexual and asexual reproduction were stimulated in the presence of glyphosate (formulated, but formulation unknown) at concentration of ≥4,000 µg/L (growth) and ≥2,000 µg/L for reproduction and resting egg production (Xi and Feng 2004). Again, although stimulatory and not "adverse" the authors point out that the increases in one species may affect other species indirectly.

In a study on grazing of the alga, *Scenedesmus spp*. by the aquatic crustacean, *Daphnia pulex*, technical glyphosate was shown to have no adverse effect, although it appeared to stimulate the growth of the algae (Bengtsson et al. 2004). Stimulation of algal growth was suggested to be due to release of nitrogen and phosphorus from the metabolism of glyphosate by the *Daphnia*. Similar stimulation was also seen in the effects of glyphosate (Rodeo®, a formulation without any surfactants) on the primary productivity of a natural phytoplankton algal assemblage dominated by species of diatoms and a dinoflagelate (Schaffer and Sebetich 2004). A 60% increase in productivity as measured by assimilation of $^{14}CO_2$ was observed at concentrations of glyphosate of 125, 1,250, and 12,500 µg/L, with no apparent concentration-response. The authors speculate that the increase was caused by the release of nitrogen and phosphorus from the breakdown of glyphosate.

The effects of glyphosate on fish and other aquatic organisms are clearly related to the surfactant in the formulation rather than the glyphosate itself. Surfactants can disrupt cell membranes and this type of response would be expected. For this reason, the glyphosate formulation and the surfactant (Cosmo-Flux®-411) as used in Colombia for the eradication of coca and poppy were tested for toxicity to the aquatic organisms, algae, crustacea, and fish (Section 4.2.2). The protocols used are described below and results are summarized in Table 19.

Algal tests. The testing of a mixture of a commercial formulation of glyphosate and the surfactant Cosmo-Flux® 411F, was conducted to determine growth inhibition of the freshwater green alga, *Selenastrum capricornutum* Printz, according to the Organization for Economic Co-operation and Development (OECD) Method # 201, "Alga, Growth Inhibition Test" (OECD 1984b) and in general accordance with OPPTS Method 850.5400, "Algal Toxicity, Tiers I and II" (USEPA 1996b).

Water Flea. Tests were conducted to determine the acute toxicity of a commercial formulation of glyphosate and the surfactant Cosmo-Flux® 411F to *Daphnia magna* according to OECD Method #202, "*Daphnia sp*., Acute Immobilization Test and Reproduction Test" (OECD 1984a), however, the reproduction component of the test was not conducted.

Rainbow Trout and Fathead Minnow. Tests were conducted to determine the acute toxicity of a commercial formulation of glyphosate and the surfactant Cosmo-Flux® 411F to *Oncorhynchus mykiss* and *Pimephales promelas* according to OECD Method #203, "Fish, Acute Toxicity Test" (OECD 1992). In all of these tests, OECD Principles of GLP (OECD 1998b) were followed.

Table 19. Toxicity values obtained from toxicity tests conducted on a mixture of glyphosate and Cosmo-Flux®.

Test species	Common name	96 hour LC/EC50 in µg/L (as glyphosate AE)	Reference
Selenastrum	Algae	2,278-5,727[a]	(Stantec 2005b)
Daphnia magna	Water flea	4,240 (3,230-5,720)[b]	(Stantec 2005e)
Onchorynchus mykiss	Rainbow trout	1,850 (1,410-2,420)[b]	(Stantec 2005c)
Pimephales promelas	Fathead minnow	4,600 (1,810-1,173)[b]	(Stantec 2005d)

[a] Lowest and highest effect measures in the study
[b] LC/EC50 and 95% Confidence Interval

The acute toxicity data for formulated glyphosate in aquatic animals from Solomon and Thompson (2003) were combined with some of the new data for amphibians described above and are displayed graphically as a point of reference for characterizing the toxicity of glyphosate plus Cosmo-Flux® as used in Colombia (Figure 17). The graph is presented as a cumulative frequency distribution in a manner similar to that used in probabilistic risk assessments for pesticides (Solomon and Takacs 2002). These data show that the combination of formulated glyphosate and Cosmo-Flux®, as used in Colombia, is more toxic to the aquatic organisms tested than formulations without the addition of surfactants and adjuvants. This is not altogether surprising. It has been shown that the toxicity of glyphosate itself to aquatic organisms is very small (Solomon and Thompson 2003) but, when mixed with some surfactants and adjuvants, this toxicity can be increased. The toxicity of Cosmo-Flux® was not tested on its own; however, from experience with other adjuvants, it is clearly the cause of the increased toxicity of the mixture.

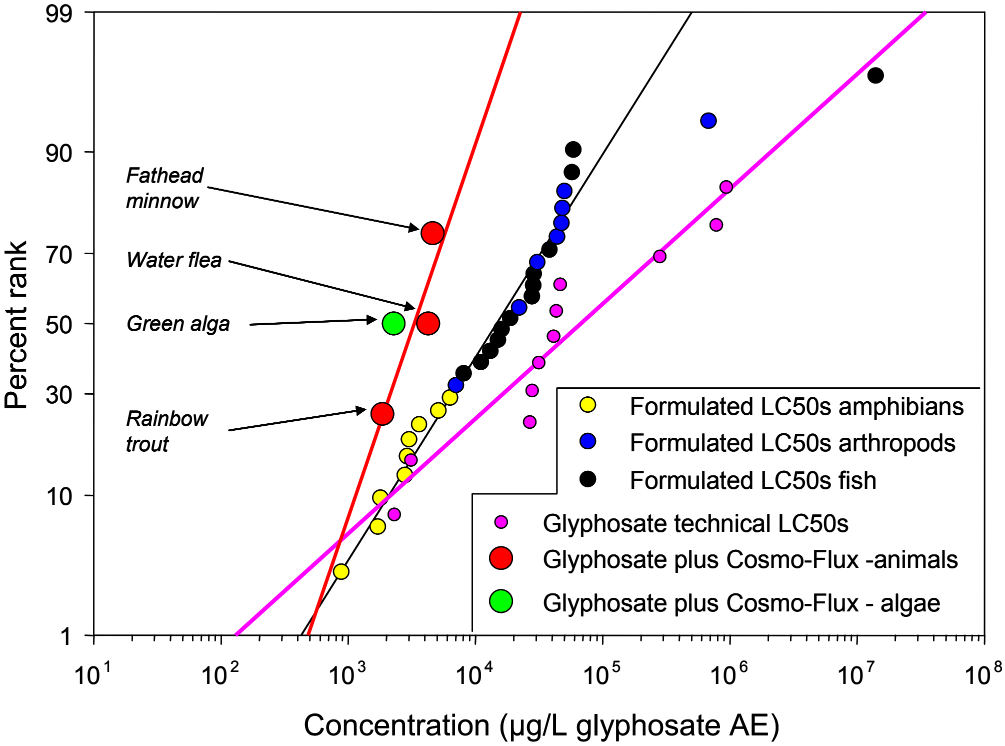


Figure 24 Distribution of toxicity values for glyphosate technical, formulated glyphosate (Roundup®) in all aquatic organisms and in fish and the glyphosate and Cosmo-Flux® 411 mixture as used in Colombia

It is interesting to note that larval amphibians appear to be more susceptible to glyphosate formulation than are other aquatic animals. The reason for this is likely the surfactants in the formulation of Roundup®; as discussed above, other formulations of glyphosate are less toxic to amphibians (Howe et al. 2004).

4.1.3.3 Effects of glyphosate on plants

There are differences in glyphosate uptake between different coca species and between young and mature plants of *Erythroxylum coca* and *E. novogranatense* (Ferreira and Reddy 2000). Leaf absorption is greater in young plants of both species and greater in *E. novogranatense*. Earlier studies showed that control of regrowth was better in *E. novogranatense* for equivalent dose of glyphosate (Ferreira et al. 1997). This study also indicated that defoliation of *E. coca* 24 hours prior to application resulted in no significant effect of glyphosate (applied up to 6.7 Kg/ha) on regrowth. This confirms that, as for other plants, uptake via the leaves is the major route of penetration into the plant.

A study on the control of the perennial weed pepperweed (*Lepidium latifolium*) has shown better control with glyphosate following mowing. The mechanism is via the better movement of glyphosate to roots from leaves lower in the canopy. Following mowing, the leaf distribution and the spray deposition is closer to the ground, giving better basipetal translocation to roots and better subsequent control (Renz and DiTomaso 2004). In forestry situations with an aerial application, spray deposition is typically much greater higher in the canopy, (e.g. Thompson et al. 1997). Studies of glyphosate efficacy on annual weeds have indicated that application during the day (09:00 and 18:00h) gives best control (Martinson et al. 2002, Miller et al. 2003).

Resistance to glyphosate is known for an increasing number of species, including *Conyza canadensis* (Mueller et al. 2003), Illinois waterhemp (*Amaranthus rudis* and *A. tuberculatus*) (Patzoldt et al. 2002), *Eleusine indica* (Baerson et al. 2002), *Lolium multiflorum* (Perez and Kogan 2003) and *Lolium rigidum* (Neve et al. 2003a, b). Rates of evolution of resistance in the latter species are dependent on herbicide use patterns as part of crop production.

Non-target impacts of glyphosate on seed germination and growth characteristics of the F1 generation of treated wild plant species have been reported. Blackburn and Boutin (2003) noted effects on seven out of 11 species tested with 1%, 10% or 100% of a 0.89 Kg a.i./ha label rate of glyphosate formulated as Roundup® solution sprayed near seed maturity. Effects of glyphosate drift on rice seed germination were reported by (Ellis et al. 2003) and (May et al. 2003) noted reduced seed production in alfalfa in the year following applications of glyphosate at 1.760 Kg a.i./ha for *Cirsium arvense* control. Nevertheless, applications of glyphosate at 0.420 kg AE/ha on susceptible soybean had adverse effects on sprayed plants, but not on progeny (Norsworthy 2004). Subtle adverse effects of glyphosate on pollen viability and seed set in glyphosate-resistant cotton were noted by (Pline et al. 2003). Pollen viability of glyphosate-resistant corn was also significantly reduced by glyphosate applied at 1.12 kg AI/ha, but yield and seed set is not significantly affected (Thomas et al. 2004). These data indicate that drift might cause subtle ecological changes to plant communities associated with changes in plant recruitment. However, this would be significant only for communities largely made up of monocarpic plant species (that flower once and die, especially annuals) dependent on seeds for recruitment.

4.2 SURFACTANTS

There are a number of formulations of glyphosate on the market and these may contain a number of surfactants (Giesy et al. 2000, Solomon and Thompson 2003, Williams et al. 2000). Normally, this would not be an issue in the risk assessment of a pesticide, however, in the case of glyphosate; the active ingredient is of very low toxicity to non-target organisms, thus making the surfactant toxicity more important in the risk assessment process. For example, tests on Ca^{2+}-activated ATPase and cholinesterase (ChE) activities in the nervous system of the slug *Phyllocaulis soleiformis* showed no effects of pure glyphosate. An effect noted with the formulation Gliz 480CS® was caused by non-glyphosate components of the formulation (da Silva et al. 2003). Technical grade glyphosate at concentrations of 52 mM (870 mg/L) did not affect the protozoans *Tetrahymena thermophila* or the parasite *Ichthyophthirius multifiliis*. However, the commercial formulation Glyphosate® was up to 100 times more toxic, reflecting data for fish species and other aquatic invertebrates and caused by surfactants in the formulation (Everett and Dickerson 2003).

Because the spray solution as used in the eradication of coca and poppy in Colombia contains surfactants as part of the formulation as well as additional surfactants (Cosmo-Flux®) added to the spray mix, the toxicity of the formulants and the adjuvants may interact to change the toxicity of the mixture. This was the reason why standardized toxicity tests for mammals and environmental non-target organisms were conducted with the spray mixture itself. These are discussed below.

4.2.1 Effects on glyphosate and Cosmo-Flux® on non-target aquatic organisms

A base set of toxicity data is required for all pesticide registrations. For freshwater environments, the set normally makes use of a coldwater fish such as rainbow trout fingerlings (*Onchorynchus mykiss*), a warmwater fish such as fathead minnows (*Pimephales promelas*), an invertebrate such as the water flea (*Daphnia magna*), and an alga such as *Selanastrum capricornutum*. These are standard test organisms, have been used for testing glyphosate itself and several other formulations, and thus are useful for comparison purposes. To reduce the requirement for animals in the testing, one combination of glyphosate and Cosmo-Flux®, the combination for poppy (Table 4), was selected. This mixture contains more Cosmo-Flux® than used for coca and thus represents a worst-case exposure. These data are summarized in Table 19 and Figure 17, above.

4.2.2 Effects of glyphosate and Cosmo-Flux® on mammals

Two series of mammalian toxicity tests on the formulation of glyphosate and Cosmo-Flux® as used for eradication of coca in Colombia were conducted. One set of these studies was conducted in the USA under good laboratory practices (GLP) and using the quality control assurance as appropriate for regulatory decision making. The other studies were conducted in Colombia, also in compliance with GLP and according to US EPA guidelines.

4.2.2.1 Analysis of the formulation

The objective of this study was to assess the concentration(s) of glyphosate (active ingredient) in the formulation (Springborn 2003a). Three 500 mL samples of each mixture were collected from the top/middle/bottom of Air Tractor N8513Q PNC 4003 (Test Article Mixtures 1 and 3), Air Tractor N8514G PNC 4005 (Test Article Mixtures 2 and 4), and Air Tractor N8513V PNC 4004 (Test Article Mixture 5). Test Article Mixtures 1 and 2 were prepared as follows:

Ingredient	**Amount Added (gallons)**
Herbicide: glyphosate	131.7
Surfactant: Cosmo Flux-411F	3.0
Lake Water	165.3
Mixing Time: Test Article Mixture 1 - 13 minutes; Test Article Mixture 2 - 12 minutes.	

Test Article Mixtures 3, 4 and 5 were prepared as follows:

Ingredient	Amount Added (gallons)
Herbicide: glyphosate	110.0
Surfactant: Cosmo Flux-411F	2.5
Lake Water	137.5
Mixing Time: Test Article Mixture 3 - 12 minutes; Test Article Mixture 4 - 11 minutes; Test Article Mixture 5 - 13 minutes.	

The test article mixtures were prepared on December 5, 2002. The overall concentration of the formulation was 16.53 [in terms of % glyphosate (AE)] before use at SLI and 15.20 [in terms of % glyphosate (AE)] after use at testing laboratory, indicating that the test material was stable during the period of testing. The overall result (16.53% glyphosate AE) was higher than the anticipated 14.80% glyphosate (AE) value but within acceptable error of mixing conditions in the field. Since the results of the analysis were appropriate and would provide conservative results for toxicity, irritation and sensitization because they were slightly higher than expected, the five test article mixes were pooled into a single container for use in the remaining studies.

4.2.2.2 Acute oral toxicity

The single-dose oral toxicity of glyphosate and Cosmo-Flux® was carried out in Sprague Dawley rats (Springborn 2003b). A limit test was carried out in which one group of 10 young adult rats (5 male and 5 female) weighed 325-356 g and 190-208 g respectively and received the test article at a single dose of 5,000 mg/kg body weight (bw). Following dosing, the rats were observed daily and weighed weekly. All animals were humanely killed 14-days post-exposure and subjected to a gross pathology examination. No mortality occurred during the study. Clinical abnormalities observed during the study included transient incidences of soft stools, fecal staining, rough coat, congested breathing, rales (wet, crackly lung noises heard on inspiration which indicate fluid in the air sacs of the lungs), and dark material around the facial area. Body weight gain was noted for all animals during the test period. No significant macroscopic findings were observed at necropsy on study day 14. The oral LD50 for test article in rats was estimated to be greater than 5,000 mg/kg.

Other rat oral acute studies were performed on a mixture of glyphosate (44%), Cosmo-Flux® (1%), and water (55%) (Immunopharmos 2002a) and a mixture of glyphosate (5%), Cosmo-Flux® (1%), and water (95%) (Immunopharmos 2002b).

Both studies were performed according to using EPA guidelines 870-1100. In the first, groups of 5 male and 5 female Wistar rats, approx. 135 g bw, were treated with the test substance by *gavage* at concentrations of 1,250, 2,500 and 5,000 mg/kg bw (Immunopharmos 2002a). The test substance was dissolved in distilled water. The animals were observed for 5 hours during the first day and later on all days during the 14 day post-dosing period. During the study, the animals did not show any adverse effects. The Reed and Muench test was used for the calculation of LD50. The LD50 value of test substance was greater than 5,000 mg/kg bw for males and females.

In the second study (Immunopharmos 2002b), groups of 10 Wistar rats (5 male and 5 female), ranging from 116 to 138 g bw, were treated with the test substance by *gavage* at concentrations of 1,250, 2,500 and 5,000 mg/kg bw. The test substance was dissolved in distilled water. The animals were observed as above. During the study, the animals showed no adverse effects. The Reed and Muench test was used for the calculation of LD50. The LD50 value of test substance was greater than 5,000 mg/kg bw for males and females.

4.2.2.3 Acute Inhalation toxicity

A limit test was performed in 10 young adult Sprague Dawley rats (5 male and 5 female) weighing 248-275 g and 201-212 g respectively received a 4-hour nose-only inhalation exposure at an aerosol concentration of 2.60 mg/L (Springborn 2003c). The mass median aerodynamic diameter and geometric standard deviation of the sampled particles were 2.9 µm ± 2.17. The percentage of particles ≤ 4.0 µm was determined to be 66%. After exposure, the rats were observed daily and weighed weekly. All animals were humanely killed at 14-days post-exposure and subjected to a gross pathology examination on day 14. There was no mortality during the study. The clinical abnormalities observed during the study included breathing abnormalities, no/decreased defecation, urine staining, rough hair coat, dark material around the facial area and decreased food consumption. Body weight loss was noted in 2 males and 1 female during days 0 to 7. Body weight gain was noted for all other animals during the test period. At study termination, the animals had exceeded/maintained their initial body weight. No macroscopic findings were observed at necropsy (day 14). The inhalation LC50 of test material was estimated to be greater than 2.60 mg/L but exposures greater than or equal to this value may be harmful.

Other rat acute inhalation toxicity studies were performed on a mixture of glyphosate (44%), Cosmo-Flux® (1%), and water (55%) (Immunopharmos 2002a) and a mixture of glyphosate (5%), Cosmo-Flux® (1%), and water (95%) (Immunopharmos 2002b).

Both studies were performed under EPA guideline 870-1300. In the first, ten Wistar rats (5 male and 5 female) were used for each concentration (Immunopharmos 2002c). The test substance was dissolved in sterile water to achieve concentrations of 5, 10, and 20 mg/L air/hour during 4 hours of exposure. After the exposure period, the animals were kept for a 14-day observation period. The mass median aerodynamic diameter and geometric standard deviation of the sampled particles were not indicated. There were no deaths during exposure period and no signs of systemic toxicity were observed at the three concentrations tested. All animals were humanely killed at 14 days post-exposure and subjected to a gross pathology and histopathology examinations and no abnormalities were observed. The LC50 value of the test substance was higher than 20 mg/L of air. Therefore, the test substance is not considered as harmful at concentrations less than 20 mg/L.

In the second study (Immunopharmos 2002d), ten Wistar rats (5 male and 5 female) were used for each concentration. The test substance was dissolved in sterile water to achieve concentrations of 5, 10, and 20 mg/L air/hour during 4 hours of exposure. After the exposure period, the animals were kept for a 14-day observation period. The mass median aerodynamic diameter and geometric standard deviation of the sampled particles were not indicated. There were no deaths during the exposure period and no signs of systemic toxicity at the three concentrations tested. All animals were humanely killed 14 days post-exposure and subjected to a gross pathology and histopathology examinations. At necropsy the surviving animals showed petechial lung (3/10) while the remaining organs were normal. The LC50 value of the test substance was higher than 20 mg/L of air.

4.2.2.4 Acute dermal toxicity

A limit test was performed in 10 Sprague Dawley rats (5 male and 5 female) receiving a single dermal administration of the test article at a dose of 5,000 mg/kg bw (Springborn 2003d). Following dosing, the rats were observed daily and weighed weekly. All animals were humanely killed after 14-days exposure and subjected to a gross pathology examination. No mortality occurred during the study. Clinical abnormalities observed during the study included transient incidences of dark material around the facial area and decreased defecation. Dermal irritation was noted at the site of test article application. Body weight loss was noted in 1 male and 2 females during the study (day 7 to 14). Body weight gain was noted for all other animals during the test period. At necropsy (day 14), no significant macroscopic findings were observed. The acute dermal LD50 of test article was estimated to be greater than 5,000 mg/kg in the rat.

4.2.2.5 Skin irritation

A potential irritation of the test material was evaluated on the skin of New Zealand White rabbits (Springborn 2003e). Each of 3 rabbits (13 weeks of age and weighed 2.5-2.8 kg prior to dosing) received a 0.5 ml dose of the test article as a single dermal application. The dose was held in contact with the skin under a semi-occlusive binder for an exposure period of 4 hours. Following the exposure period, the binder was removed and the remaining test article was wiped from the skin using gauze moistened with deionized water followed by dry gauze. Test sites were subsequently examined and scored for dermal irritation for up to 72 hours following patch application. Exposure to the test article produced very slight erythema on 3/3 test sites at the 1-hour scoring interval. The dermal irritation resolved completely on all test sites by 24-hour. The test article was considered to be a slight irritant to the skin of the rabbit. The calculated Primary Irritation Index for the test article was 0.25.

Other skin irritation studies were performed on a mixture of glyphosate (44%), Cosmo-Flux® (1%), and water (55%) (Immunopharmos 2002g) and a mixture of glyphosate (5%), Cosmo-Flux® (1%), and water (95%) (Immunopharmos 2002h). Both studies were performed using EPA guidance 870-2500.

In the first, 0.5 ml of test substance was applied to the clipped and abraded skin of 3 male and 3 female New Zealand White rabbits (2.3-2.4 kg bw) (Immunopharmos 2002g). The application site of the test substance was covered with three occlusive dressings for 15 minutes, 1 hour, and 4 hours, after which the site was washed. Skin reactions were measured for erythema and edema using a modified Draize test. The readings were made at 24, 48, and 72 hours after treatment. Body weight was not measured. There were no signs of irritation at the application site or systemic toxicity. In the second study, 0.5 ml of test substance was applied to the clipped and abraded skin of 3 male and 3 female New Zealand White rabbits (2.3-2.4 kg bw) (Immunopharmos 2002h). The application site of the test substance was covered with three occlusive dressings for 15 minutes, 1 hour, and 4 hours, after which the site was washed. Skin reactions were measured for erythema and edema using a modified Draize test. The readings were made at 24, 48, and 72 hours after treatment. Bodyweight was not measured. There were no signs of irritation and/or edema on the shaved skin.

4.2.2.6 Eye irritation

The eye irritation for the test article was evaluated in rabbits (Springborn 2003f). Each of 3 New Zealand White rabbits received a 0.1 mL dose of the test article in the conjunctival sac of the right eye. The left eye of each untreated animal served as a negative control. Test and control eyes were examined for signs of irritation for up to 7 days after dosing. Exposure to the test article produced iritis (3/3 test eyes) at the 1-hour scoring interval which resolved completely in all eyes by 24-hour. Conjunctivitis (redness, swelling and discharge) was noted in 3/3 test eyes at the 1-hour. The conjunctival irritation resolved completely in all treated eyes by day 7. An additional ocular finding of slight dulling of normal luster of the cornea was noted in 1/3 test eyes. Based on these results, the test material is considered to be a moderate irritant to the eye.

Other eye irritation studies were performed on a mixture of glyphosate (44%), Cosmo-Flux® (1%), and water (55%) (Immunopharmos 2002e) and a mixture of glyphosate (5%), Cosmo-Flux® (1%), and water (95%) (Immunopharmos 2002f). Both studies were performed using EPA guidance 870-2400.

In the first, 18 New Zealand White rabbits were used (Immunopharmos 2002e). The test substance (0.1 ml) was placed into the conjunctival sacs of rabbits. The left eye of each untreated animal served as negative control. The eyes of 3 rabbits of each sex were rinsed for 30 second after the test substance application. A further 6 rabbits were left with unrinsed eyes. The eyes were examined for irritation at 1, 24, 48, 72, 96 hours, and 7 days after instillation. The animals showed the following signs: opacity (5/12, from grade 1 to 3); corneal damage (4/12 neovascularization on cornea); iritis (5/12 grade 1, disappearing 4 days latter); conjunctivitis (12/12 from grade 1 to 3); chemosis (10/12 from grade 1 to 3); discharge (4/12 animals presented discharge the first days of the study).

The eyes of the 6 animals rinsed 30 seconds after application of the test substance presented as follows: opacity (6/6 did not present corneal opacity); corneal damage (6/6, with no damage); iritis (6/6 with no iritis); conjunctivitis (6/6 animals presented from grade 1 to 3, which was diminishing which disappeared at the end of the study, 7 days); chemosis (3/6 animals presented grade 1 which disappeared in 24 hours); discharge (6/6 animals presented discharge the first two days of the study). In conclusion, the test substance caused slight to moderate irritation in the eyes from animal that were treated and then not rinsed. This irritation was observable between days 1 and 7. In contrast, the test substance did not produce irritation in animals, the eyes of which were treated and then rinsed for 30 seconds after the application of test substance.

In the second study, 18 New Zealand White rabbits were used (Immunopharmos 2002). Again, 0.1 ml of the test substance was placed into the conjunctival sacs of rabbits. The left eye of each untreated animal served as negative control. The eyes of 3 rabbits of each sex were rinsed for 30 seconds after the test substance application. A further 6 rabbits were left with unrinsed eyes. The eyes were examined for irritation at 1, 24, 48, 72, 96 hours after instillation. The test substance did not cause irritation in the eyes from animals treated and not rinsed (observed between days 1 and 4). The test substance did not produce irritation in the eyes of animals treated and rinsed 30 seconds after the application of test substance and then observed for 4 days.

4.2.2.7 Skin sensitization

The dermal sensitization potential of test substance was evaluated in guinea pigs (Springborn 2003g). Twenty Hartley albino guinea pigs (10 male and 10 female) were topically treated with 100% test substance, once per week, during three weeks. Following a 2-week rest period, a challenge was performed [20 animals treated and 10 animals untreated (challenge control)] were topically treated with 100% test substance. A positive control group was given hexylcinnamaldehyde (HCA). Based on the results of this study, test substance was not considered to be a sensitizer.

Other skin sensitization studies were performed on a mixture of glyphosate (44%), Cosmo-Flux® (1%), and water (55%) (Immunopharmos 2002j) and a mixture of glyphosate (5%), Cosmo-Flux® (1%), and water (95%) (Immunopharmos 2002i). Both studies were performed according to EPA guideline 870-2600. In the first, 30 Hartley guinea-pigs (300-350 g bw), were divided into 6 groups; 2 groups of males with 5 animals and 2 groups of females with 5 animals for the study, and 2 groups of 5 animals of both sexes that serves as control. The test substance (0.5 ml) was applied to the skin of albino guinea-pigs three times with an interval between each exposure of 1 week (0, 7, and 14 days) and for a duration of 6 hours in each application. The animals were inspected at 24, 48, and 72 hours after applications. The control group (5 male and 5 female) received sterile distilled water. A positive sensitization study was conducted every 6 month using a sensitizing agent (data not given). The test material caused no dermal adverse reactions even after several applications (Buehler test). It was noted that the test material was not a sensitizer for the skin

In the second study (Immunopharmos 2002i), 30 Hartley guinea-pigs (300-350 g of weight), were divided in 6 groups; 2 groups of males with 5 animals and 2 groups of females with 5 animals for the study, and 2 groups of 5 animals of both sexes that served as a control. The test substance (0.5 ml) was applied to the skin of albino guinea-pigs, three times with an interval for each exposure of 1 week (0, 7, and 14 days) and 6 hours for each application (Buehler test). A total of 0.5 ml was applied over the exposed skin. The animals were inspected at 24, 48, and 72 hours after application. The control group (5 male and 5 female) received sterile distilled water. The positive sensitization study was conducted in the laboratory every 6 months using a sensitizing agent (data not given). The test material caused no adverse dermal reactions even after several applications (Buehler test). It was concluded that the test material was not a sensitizer for the skin.

4.2.2.8 General conclusions on the mammalian acute toxicity of glyphosate and Cosmo-Flux®

Based on the results of these studies undertaken with the mixture glyphosate and Cosmo-Flux®, the following conclusions can be drawn:

- The acute oral and dermal LD50 value was estimated to be greater than 5,000 mg/kg bw in the rat. Therefore, this formulation is considered as practically non-toxic by the oral route.
- The acute inhalation LC50 value was estimated to be greater than 2.60 mg/L in the rat. In one study the rats showed breathing abnormalities after exposures at 2.6 mg/L for 4 hours. This value for the test substance is considered as potentially harmful for durations of exposure of the order of 4 hours. In two other studies, the mixture was shown to not be harmful at exposures up to 20 mg/L for 4 hours. Exposures via the inhalation route in these animal studies were via small droplets. Exposures via inhalation under field conditions will be smaller as the droplets are larger and less easily inhaled.
- The formulation is considered to be a slight and moderate irritant to the skin and eyes of the rabbit. The calculated Primary Irritation Index for the test article was 0.25.

Based on these observations, the hazard to the humans via application or bystander exposures are considered small and are limited to slight to moderate skin and eye irritation. These responses will be reduced if the affected areas are rinsed shortly after exposure to remove contamination. It was also concluded that the addition of the adjuvant Cosmo-Flux® to the glyphosate did not change its toxicological properties to mammals.

4.3 EFFECTS IN THE FIELD

4.3.1 Duration of effects in the field

In tropical forest situations, similar to some of the locations of the coca eradication programs, there are limited data on vegetation recovery following glyphosate application. Nevertheless, there are a number of studies of successional patterns following land clearance and for tree gaps. Forest clearance has been a historical feature of the development of agriculture from across the globe, (e.g. Boahene 1998, Matlack 1997). In Central America, agricultural intensification and forest clearance in Mayan and other cultures has been determined from the pollen record, (e.g. Clement and Horn 2001, Curtis et al. 1998, Goman and Byrne 1998). Patterns of successional change (recovery) in Neotropical forests have been reviewed by (Gauriguata and Ostertag 2001). The authors note:

> "*the consensus of these analyses is that the regenerative power of Neotropical forest vegetation is high, if propagule sources are close by and land use intensity before abandonment has not been severe. Nevertheless, the recovery of biophysical properties and vegetation is heavily dependent on the interactions between site-specific factors and*

land use, which makes it extremely difficult to predict successional trajectories in anthropogenic settings."

In relation to the eradication program, patterns of vegetation recovery will be dependent on size of plot, location of plot in relation to surrounding vegetation types and local anthropogenic management, i.e., subsequent cultivation activities.

A study of tree regeneration in dry and humid selectively-logged Bolivian tropical forests indicated that tree release with glyphosate in logging gaps had no significant impact on target tree species growth (Pariona et al. 2003). While glyphosate controlled vegetation for a limited period, there were problems with the recruitment of commercial trees in logging gaps, suggesting a silvicultural need for site preparation treatments and more judicious seed tree retention.

Glyphosate has been widely used for controlling deciduous understorey vegetation in managed northern forests, so-called conifer-release treatments, (e.g. Lautenschlager and Sullivan 2002). Recovery of the deciduous herb and shrub layers occurs over a period of 2-3 years in general and the tree layer over 10 years (See Section 4.3.2.3). Often, total structural diversity is unaffected by glyphosate treatments after one year.

4.3.1.1 Forest clearance and soils

The impacts of forest clearance on soil fertility are generally well-understood. Typically, tropical forest soils are fragile, being nutrient-poor and subject to leaching. Tree clearance can quickly result in loss of nutrients, change in pH, and therefore change in element availability to plants (McAlister et al. 1998). Such conditions often allow only shifting cultivation under subsistence production, so-called slash-and-burn agriculture. Studies in Jamaican forests have shown that cultivations result in large amounts of soil erosion compared with secondary forest. An agroforestry treatment with *Calliandra calothyrsus* contour hedges reduced erosion and increased rainfall infiltration within the hedges (McDonald et al. 2002). As coca is a shrub, typically grown in rows, it might be argued that soil and water changes associated with forest clearance may be less than for annual crops such as maize, but clearly both have significant adverse effects on primary forest sites.

Whilst vegetation recovery may be rapid, in eastern North America, research has led to the surprising conclusion that 19th century agricultural practices decreased forest floor nutrient content and C:N and C:P ratios and increased nitrifier populations and net nitrate production, for approximately a century after abandonment (Compton and Boone 2000). The level of agricultural intensity, in terms of cultivation and fertilizer use, may have significant long-term impact on soils.

4.3.1.2 Effects on associated fauna

In an area of highly disturbed tropical dry forest in Cordoba Department, northern Colombia, small mammals were censused by live-trapping, running from secondary growth forest into agricultural areas (Adler et al. 1997). The results suggest that the disturbed habitat supports a small mammal fauna of low diversity. However, several of the species appear to have benefited from forest clearance and agricultural activities and may occasionally reach extremely high numbers, though populations were not stable. A similar effect on reduced diversity of termites with increasing disturbance has been shown in dry forest in Uganda (Okwakol 2000). Changes in bird populations of a eucalypt forest in Australia following clear-felling indicate that full recovery may take up to 70 years (Williams et al. 2001).

Whilst some species are adapted to disturbed conditions and can utilize agricultural land and secondary forest, there are many species associated with primary forest only, for example the Great Argus pheasant in Indonesian tropical forests (Nijman 1998). With much of Colombia associated with extremely high biodiversity, there are very many endemic plant and animal species associated with National Parks and indeed with eradication areas.

Studies on the impacts of vegetation change caused by glyphosate use on associated fauna in northern environments are available for some species. For example, following the application of glyphosate in clear-cut forest areas in Maine, USA, the use by moose (*Alces alces*) of treated and untreated areas was compared 1-2 years and 7-11 years post application (Eschenburg et al. 2003, Eschholz et al. 1996). At 1 and 2 years post-treatment, tracks of foraging moose were 57 and 75% less abundant on treated than untreated clear-cuts (P = 0.013). However, at 7-11 years post-treatment, tracks of foraging moose (P = 0.05) and moose beds (P = 0.06) were greater on treated than untreated clear-cuts. Less foraging activity at 1-2 years post-treatment appeared to be the result of reduced browse availability, because conifer cover for bedding was similar on treated and untreated clear-cuts. The authors hypothesized that greater counts of tracks of foraging moose on older treated clear-cuts was due to increased foraging activity on sites with more abundant conifer cover (Eschholz et al. 1996, Raymond et al. 1996), i.e. tree cover had returned sufficiently after 10 years. Studies of small mammal responses to glyphosate vegetation control in similar environments (Sullivan et al. 1998) have indicated that vegetation recovery 2-3 years after treatment was sufficient to return population dynamics to expected ranges.

Spot applications of glyphosate to reduce invasive ground flora in forests can have the beneficial effect of opening up the ground layer and encouraging spring ephemeral species to establish larger populations. Carlson (2004) reported this effect when controlling *Alliaria peteolata*, an invasive biennial plant. The impact of glyphosate on the target species was only for a single season.

4.3.1.3 Interactions with surfactants

Surfactants significantly improve coca control with glyphosate (Collins and Helling 2002) and control of *Salvinia molesta*, an aquatic fern (Fairchild et al. 2002). Nevertheless, the behavior of surfactants is complex (Liu 2004). Spray droplet size affects retention on the target plant, but also the absorption into the plant. Smaller droplets are better retained on the plant, but absorption through the leaf is better from larger “coarse” droplets (Feng et al. 2003). A study of volume rate effects of glyphosate on grasses has shown that reduced application volumes give better control, partly affected by the concentration of surfactants in formulated products (Ramsdale et al. 2003).

Studies of biodegradable non-phytotoxic rapeseed oil derivatives (triglyceride ethoxylates; Agnique RSO(R) series containing an average of 5, 10, 30 and 60 units of ethylene oxide) indicate that these adjuvants gave similar or better control of *Phaseolus* *vulgaris* L. compared with 0.36 Kg AE/L SL Roundup Ultra®. In these studies Agnique RSO 60 generally was most effective (Haefs et al. 2002). Tests with a range of surfactants and different herbicides on several plant species indicate that the optimum surfactant structure is both herbicide and plant species dependent (Johnson et al. 2002).

Studies of synergism between amino acid biosynthesis-inhibiting herbicides indicate that, in most cases associated with glyphosate, the lack of effects with technical herbicide confirm that surfactants are important components of formulated products (Kudsk and Mathiassen 2004).

4.3.2 Recovery from effects

4.3.2.1 Principles

Glyphosate, as a well-translocated herbicide, affects most plant species, if sufficient herbicide can penetrate plant tissues, particularly leaves. Effects typically result in plant death over a period of 2 to 3 weeks, though species with extensive storage organs, e.g. long rhizomes, large size, or particularly impenetrable leaf surfaces, may survive. A low dose of glyphosate can result in growth abnormalities in plants, most typically localized accelerated branching. If the dose of herbicide is insufficient to cause death, it has been proposed that plant fitness may also be reduced, such that if there is competition with other plants, death may result indirectly, though there is little published evidence for this.

The effect of glyphosate is limited to the plants that receive spray at the time of application, as the herbicide is rapidly adsorbed onto soil and root uptake does not occur. The broad spectrum of plant species controlled and the pattern of foliar uptake, together with the safety of the compound, have led to widespread use of the herbicide for total vegetation control, pre-harvest weed control in annual crops and for the eradication of perennial plants.

Recovery of treated areas is dependent on the initial level of control, the quantities of material (and the methods used) for plant regeneration and the environmental conditions of the site. Plants have a variety of adaptations for regenerating, with some life forms showing a range of methods, while others have only a single strategy. Monocarpic species, typically annuals, have seeds for recruitment of the next generation. Polycarpic species may also produce seeds, but many also have a variety of vegetative means of regenerating, such as rhizomes, bulbs, corms and runners. Patterns of secondary succession, the resultant plant communities over time, reflect the plant-environment interactions and the opportunities for regeneration provided by the local species pool. Seeds in the soil or that can reach a site from the surroundings, together with vegetative fragments, will establish initially. Continued agricultural operations, such as cutting or soil disturbance, will have a major influence on the species that survive. In most situations, vegetation recovery is rapid, with ruderal and pioneer plant species establishing within weeks of application.

4.3.2.2 Tropical situations

In tropical forests, similar to some of the locations of the coca eradication programs, there is limited published data on vegetation recovery following glyphosate application. Nevertheless, there are a number of studies of successional patterns following land clearance and for tree gaps. Secondary succession (forest recovery) has become more common in some forest areas, for example in Puerto Rico (Chinea 2002). Forest recovery is generally fairly rapid, but recovery of the full complement of forest species can take many years (>30 y) and the effects of bulldozing for initial clearance can reduce diversity of native species and enhance establishment of non-native species. Comparisons of different aged plots (2-40 y) in the Bolivian Amazon forests have contributed to the knowledge of secondary succession (Pena-Claros 2003). Not surprisingly, it takes longer for the forest canopy to achieve similar diversity to mature forest, compared with the understory and subcanopy communities.

In relation to the eradication program, patterns of vegetation recovery will be dependent on size of plot, location of plot in relation to surrounding vegetation types and local anthropogenic management, i.e., subsequent cultivation activities. Nevertheless, it should be noted that naturally occurring tree gaps (20-460 m^2) are an important component of overall forest diversity, providing opportunities for understory and subcanopy species and regeneration of canopy species in the modified light climate (Martins et al. 2004, Martins and Rodrigues 2002). In Brazilian varzea (white-water) forests, natural patterns of succession are affected by both light and local flooding (Wittmann et al. 2004). The patch scale of eradication applications of glyphosate may or may not be at the scale of natural gap dynamics; this deserves further scientific study.

In the high Andes alpine paramo habitats, patterns of succession were described (Sarmiento et al. 2003). Following cultivation, usually for potato, patterns of secondary succession were such that after 12 years, the species diversity of the undisturbed paramo had still not been attained. The characteristic paramo life forms, sclerophilous shrubs (e.g. *Baccharis prunifolia*, *Hypericum laricifolium*) and giant rosettes (e.g., *Espeletia schultzii*), appear very early and gradually increase in abundance during succession (Sarmiento et al. 2003).

In situations of agricultural expansion over large areas in Europe and North America, there is evidence that, where the proportion of remaining ancient habitat is low, subsequent forest recovery on abandoned agricultural land can be extended over long time periods (Vellend 2003). It is unlikely that habitat fragmentation and intensity of agriculture will combine to provide such a scenario in the coca eradication program areas.

4.3.2.3 Temperate situations

Glyphosate has been widely used for controlling deciduous understorey vegetation in managed northern forests, so-called conifer-release treatments, (e.g. Lautenschlager and Sullivan 2002). Effects on the successional patterns of vegetation in such temperate and boreal situations are that woody and herbaceous species are most reduced by glyphosate, (e.g. Bell et al. 1997). In a study in British Colombia, species richness, diversity, and turnover of the herb, shrub, and tree layers were not significantly ($p>0.10$) different between mechanical and glyphosate spray cut stump treatments and a control. Similarly, the structural diversity of herb, shrub, and tree layers were also not significantly ($p>0.10$) different between treatments and control. By opening the canopy and decreasing the dominance of the deciduous tree layer, both manual and cut-stump treatments showed greater total structural diversity (herb, shrub, and tree layers combined) relative to the control. However, differences in total structural diversity between treatments and control were, for the most part, not significant ($p>0.10$). Therefore, these vegetation management treatments affected only the volume of the targeted deciduous tree layer and did not adversely affect the species richness, diversity, turnover, or structural diversity of the plant community. The authors note that the results may be applicable to other temperate forest ecosystems where conifer release is practiced in young plantations (Lindgren and Sullivan 2001). Herb biomass and cover usually recover to untreated values within 2-3 years of conifer release treatment (Sullivan 1994). Meanwhile, the reduced competition on target conifers allows enhanced growth with little adverse effect on plant diversity (Sullivan et al. 1996, Sullivan et al. 1998). Nevertheless, some plant groups may take longer to recover from glyphosate application. For example, cryptogams (ferns) may take longer than 5 years to recover in boreal forest situations (Newmaster and Bell 2002), probably reflecting longer generation times and poor dispersal. Spot applications of glyphosate to reduce invasive ground flora in forests can have the beneficial effect of opening up the ground layer and encouraging spring ephemeral species to establish larger populations. Carlson and Gorchov (2004) reported this effect when controlling *Alliaria peteolata*, an invasive biennial plant. The impact of glyphosate on the target species was only for a single season. Reviewing the effects of glyphosate use in forestry, (Sullivan and Sullivan 2003) noted that:

> "…*the magnitude of observed changes in mean species richness and diversity of vascular plants, birds, and small mammals, from the effects of herbicide treatment, were within the mean values of natural fluctuations of these variables. The biological significance of this impact is limited to shifts in species composition based on changes in floral composition and structure of habitats. Management for a mosaic of habitats within forest and agricultural landscapes, which provide a range of conditions for plant and animal species, should help ameliorate the short-term changes in species composition accompanying vegetation management with glyphosate*".

Single applications of glyphosate control much of the vegetation that receives spray, but recovery is generally rapid and within the range of natural disturbances.

4.3.2.4 Conclusions

The experience of glyphosate use in northern temperate forests is such that vegetation and fauna recover over a period of 2 to 3 years, following a single conifer-release treatment. With generally rapid plant growth under tropical conditions, available data confirm this scenario for Colombian conditions. In comparison, land clearance for agriculture (or coca production) is a much more environmentally damaging operation, impacting adversely on soils in particular. Land clearance for illicit crops is already a threat to the conservation of bird species diversity in Colombia (Álvarez 2002). Whilst there are legitimate scientific questions as to the effects of a) the spatial scale of individual glyphosate applications and b) the return frequency of eradication treatments, field operational factors set these parameters. Spray areas reflect the patch scale of coca and poppy growing, averaging 1-2 ha each in a total of ~150,000 ha. Re-application frequencies are generally greater than 6 months for coca and greater than 3 months for poppy and, bearing in mind the molecule is biologically unavailable in the soil and soil-bound residues have a half life of between 14 and 32 days, the environmental impacts are no greater than single applications.

5 RISK ASSESSMENT

The risk assessment was conducted by comparing estimated exposures to effect values for glyphosate from specific toxicity studies, from the literature, and from regulatory guidelines such as those established by the US EPA (1993b). The estimated exposures used were those calculated for the use of glyphosate for eradication spraying in Colombia. This was done for human and environmental risks and is outlined above.

5.1 HUMAN HEALTH

From an assessment of the results of toxicity testing of the formulation of glyphosate and Cosmo-Flux® as used in Colombia (Section 4.2.2), it was concluded that the addition of Cosmo-Flux® to the spray mixture did not affect the toxicity of the glyphosate to mammals. For this reason, it was possible to compare the toxicity of glyphosate and its formulations to exposures estimated under conditions of use in Colombia.

Exposures for the assessment were taken from Tables 7-9. The greatest values were taken as reasonable worst-case for a hazard assessment. These results are shown in Table 20 and illustrated graphically in Figure 18. In comparing the exposure and effect concentrations a margin of exposure approach was used. Thus a number greater than 1 (Table 20) means that the exposure was less than the exposure or dose that caused the response in the toxicology study.

From the data in Table 20, it is clear that potential exposures to glyphosate and Cosmo-Flux® as used for the eradication of coca and poppy in Colombia do not present a risk to human bystanders. In all cases, the margin of exposure for the most sensitive endpoint in laboratory animal studies with glyphosate was greater than 100 – a conservative value often used to account for uncertainty in risk assessments of this type. As well, estimated worst- case exposures were below the Reference Dose (RfD) established for glyphosate by the US EPA. The toxicity values used in both of these approaches were derived from chronic exposures where the animals were dosed over extended time periods. They are thus additionally protective of short and infrequent exposures that would occur during the use of glyphosate in the eradication spray program. Some exposure values were close to the inhalation toxicity value but, but as discussed above, droplet size is large and inhalation will be less than in the laboratory animal studies as well as the droplet size used in agricultural uses, from which the potential inhalation exposure was derived.

Table 20. Summary of reasonable worst-case estimated exposures of humans to glyphosate resulting from use in the eradication of coca and poppy in Colombia and margins of exposure.

Source of exposure	**Exposure value in mg/kg**		**Margin of exposure compared to the most sensitive NOEL(175 mg/kg)**	
	Coca	Poppy	Coca	Poppy
Direct overspray	0.04	0.01	4,918	20,417
Reentry	0.26	0.06	676	2,804
Inhalation	0.01	0.01	28,226	28,226
Diet and water	0.75	0.18	234	972
Worst case total exposure from all sources	1.05	0.26	167	680
Source of exposure	Exposure value in mg/kg		Margin of exposure for the US EPA RfD (2 mg/kg/day)	
	Coca	Poppy	Coca	Poppy
Direct overspray	0.04	0.01	56	233
Reentry	0.26	0.06	8	32
Inhalation	0.01	0.01	323	323
Diet and water	0.75	0.18	2.7	11.1
Worst case total exposure from all sources	1.05	0.26	1.9	7.8

5.2 ENVIRONMENT

Assessment of the environmental risks of glyphosate and Cosmo-Flux® to aquatic organisms was based on data from the literature and from studies conducted on the mixture of formulated glyphosate and Cosmo-Flux® as used in Colombia. As discussed in Section 4.1.2, the toxicity of the mixture of glyphosate and Cosmo-Flux® was greater than that reported for formulated glyphosate itself. When the toxicity values for the mixture as used in Colombia are compared to the range of estimated exposures that would result from a direct overspray of surface waters (Table 10), it is clear that aquatic animals and algae in some shallow water bodies may be at risk (Figure 19).

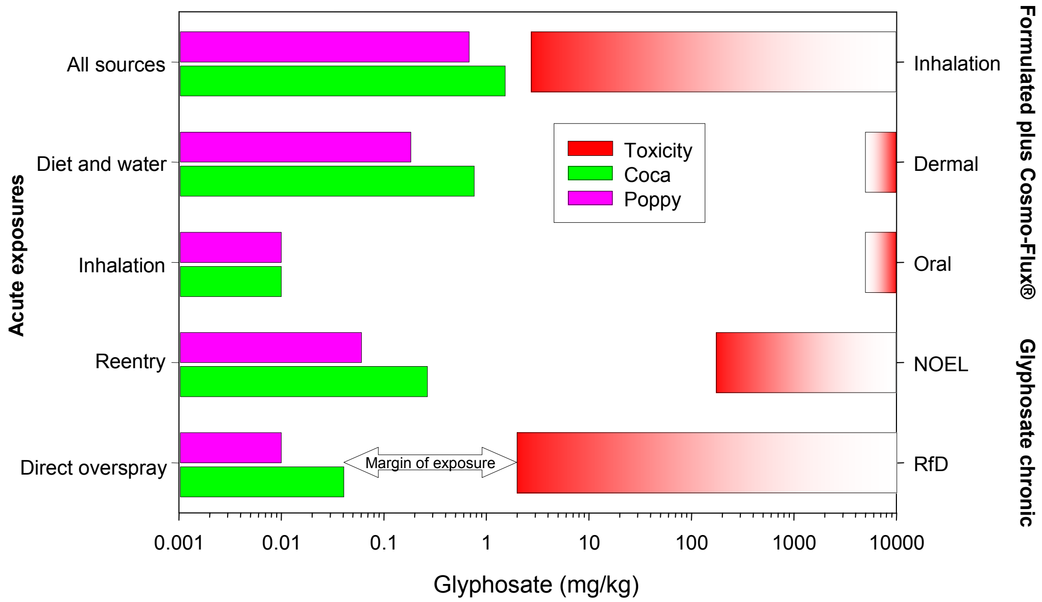


Figure 25 Illustration of acute toxicity values in laboratory mammals for glyphosate plus Cosmo-Flux®, the NOEL from the most sensitive chronic study in laboratory animals, and the RfD (glyphosate) and the estimated worst-case acute exposures that may be experiences under conditions of use in Colombia.

While the overlap of the range of estimated exposure concentrations with the toxicity values for the green alga and rainbow trout suggests that there may be increased risk in situations where an accidental overspray will occur, this would have to be in a location where a shallow water body is in close enough proximity to the coca field that it is accidentally over-sprayed, that it is less than 30 cm deep, and that it is not flowing. Because flow of the water would likely result in rapid hydraulic dilution to concentrations to below the threshold of biological activity, organisms in flowing water would not be at risk. It was not possible to determine the actual frequency of these risks as data on proximity of surface water to coca fields is not available at this time. Based on the toxicity data with formulated Roundup® in amphibians, this group of organisms may be at risk, however, specific testing in amphibians has not yet been conducted on the mixture of glyphosate plus Cosmo-Flux® as used in Colombia.

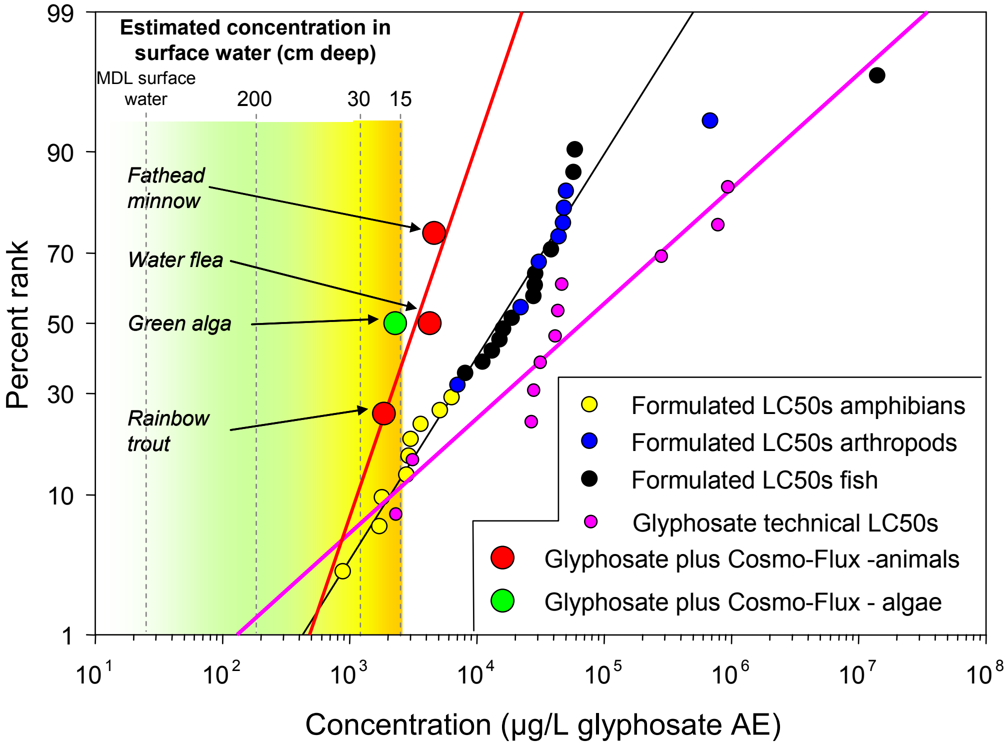


Figure 26 Distribution of toxicity values for glyphosate technical, formulated glyphosate (Roundup®) in all aquatic organisms and in fish and the toxicity values in four aquatic species for glyphosate and Cosmo-Flux® 411 mixture as used in Colombia. The yellow rectangle shows the range of predicted worst-case exposures resulting from direct overspray of surface waters ranging from 15 to >200 cm in depth. Lines are the regressions through the log-probability transformed data.

Based on the toxicity data for honeybees (Section 4.1.2.1), the mixture of glyphosate and Cosmo-Flux® 411F is not acutely toxic via contact exposure to honey bees. It did not cause mortality or stress effects in bees in the normal 48 hour period after treatment at concentrations equal to or less than 56.8 mg AE/bee. These results show that the formulated product is not directly hazardous to bees and, by extrapolation, to other beneficial insects.

Although no acute or chronic data are available on wild animals, extrapolation of the mammalian data discussed above (Sections 4.1.2 and 4.2.2) and from reports in the literature support the conclusion that glyphosate and Cosmo-Flux®, as used in the eradication program in Colombia, will not have adverse direct effects on wild mammals or birds. Indirect effects through habitat alteration are possible. However, it is unlikely that the coca and poppy fields are significant habitats for wildlife. Human activities related to cultivation and harvesting the crop will be more disruptive to wildlife and death of the coca bushes or the poppy plants as a result of spraying with glyphosate will not add an additional stressor. In fact, if the sprayed area is not replanted and allowed to naturalize, this new successional habitat may be more attractive to birds and mammals than an old-growth forest. Given that coca and poppy fields are usually located in remote areas and are often surrounded by natural habitats, sources for recolonization or alternate habitats will be close by. Some habitat alteration will result from accidental over-sprays that affect non-target vegetation, however, as discussed above (Section 2.1.3.5), these areas are small in relation to the sprayed fields < 0.48%), represent a very small proportion of the total habitat available << 0.001%, and will undergo rapid recolonization and succession to habitats suitable for wildlife.

6 CONCLUSIONS

Because of differences in the approaches to human and ecological risk assessment, the conclusions of this report are discussed separately in the following sections. In these discussions, the risks associated with the use of glyphosate and Cosmo-Flux® in the coca and poppy eradication program in Colombia are related to the total impacts of coca and poppy production as discussed in the Problem Formulation (Section 2.2.1).

6.1 HUMAN HEALTH RELEVANCE

Based on all of the evidence and information presented above, the Panel concluded that the risks to humans and human health from the use of glyphosate and Cosmo-Flux® in the eradication of coca and poppy in Colombia were minimal (Figure 20). The acute toxicity of the formulated product and Cosmo-Flux® to laboratory animals was very low, the likely exposures were low, and the frequency of exposures was low. When these risks are compared to other risks associated with clearing of land, the uncontrolled and unmonitored use of other pesticides to protect the coca and poppy, and exposures to substances used in the refining of the raw product into cocaine and heroin, they are essentially negligible.

IMPACTS	INTENSITY SCORE	RECOVERY SCORE	FREQUENCY %	IMPACT SCORE	% IMPACT
Clear cutting and burning	5	3	3	45	**16.7**
Planting the coca or poppy	0	1	100	0	**0.0**
Fertilizer inputs	0	0.5	10	0	**0.0**
Pesticide inputs	5	3	10	150	**55.5**
Eradication spray	**<0.1**	**0**	**1**	**<0.1**	**<0.1**
Processing and refining	5	3	5	75	**27.8**

Figure 27 Potential human health impacts of the cycle of coca or poppy production and the spray eradication program.

6.2 ECOLOGICAL RELEVANCE

Based on the evidence and data discussed above and the results of a number of specific studies conducted specifically for this assessment, the Panel concluded that the risks to the environment from the use of glyphosate and Cosmo-Flux® in the eradication of coca and poppy in Colombia were small in most circumstances (Figure 21). Risks of direct effects in terrestrial wildlife such as mammals and birds were judged to be negligible as were those to beneficial insects such as bees. Moderate risks to some aquatic wildlife may exist in some locations where shallow and static water bodies are located in close proximity to coca fields and are accidentally over-sprayed. However, when taken in the context of the environmental risks from other activities associated with the production of coca and poppy, in particular, the uncontrolled and unplanned clearing of pristine lands in ecologically important areas for the purposes of planting the crop, the added risks associated with the spray program are small.

IMPACTS	INTENSITY SCORE	RECOVERY TIME (Y)	IMPACT SCORE	% IMPACT
Clear cutting and burning	5	60	300	**97.6**
Planting the coca or poppy	1	4	4	**1.3**
Fertilizer inputs	1	0.5	0.5	**0.2**
Pesticide inputs	2	0.5	1	**0.3**
Eradication spray	**1**	**0.5**	**0.5**	**0.2**
Processing and refining	2	1	2	**0.7**

Figure 28 Potential environmental impacts of the cycle of coca or poppy production and the spray eradication program.

6.3 STRENGTHS AND UNCERTAINTIES IN THE ASSESSMENT

This assessment has both strengths and uncertainties. These are discussed in the following sections. These strengths and uncertainties lie in the exposure and effects characterizations and, because these are used in the risk characterization, are also reflected in the risk assessment. Uncertainties are inherent in all risk assessments and, in some cases, can be easily addressed though additional data collection or specific studies. Recommendations for additional studies and data collection are addressed in the final section of this report.

6.3.1 Exposures

6.3.1.1 Environmental exposures

Applications of glyphosate are well characterized. State of the art equipment is used. The locations of application and the areas sprayed are well documented and measured with resolutions only equaled in some applications in forestry in other jurisdictions. The mixing and application rates are well characterized and the probability of application of amounts of glyphosate and Cosmo-Flux® greater than those specified are judged to be small. The resultant concentrations in soil and water that may result from an accidental overspray also have high certainty. The environmental behavior of glyphosate is well characterized and, under the conditions of use in the eradication program in Colombia, will not persist, accumulate, or biomagnify in the environment. Analyses of surface waters and sediments in one watershed where eradication spraying was carried out did not reveal the presence of significant concentrations of glyphosate, confirming the conclusion based on its properties that it is not mobile in the environments where it is applied. Residues of glyphosate were not frequently detected in areas where eradication spraying was not conducted but where glyphosate use was known to occur in agriculture. Given that considerably more glyphosate is used in agriculture and other non-eradication uses (~85%), this further confirms that glyphosate is not sufficiently mobile to result in significant contamination of surface waters in Colombia, regardless of the use pattern.

Uncertainties in the exposure characterization lie in lack of precise measurements of the proximity of sprayed fields to surface waters and the proportion of treated areas that are in close proximity to these surface waters. The sampling of the surface waters only took place for a period of 24 weeks and only 5 locations were sampled in this way. Although two of these were scheduled to be sprayed, only one location was treated during the sampling period. For logistical reasons, it was also not possible to sample close to the application sites. If sampling had been conducted at more sites closer to the sprayed fields and over a longer time period, residues may have been detected more frequently.

6.3.1.2 Human exposures

Human exposures to glyphosate were estimated from extensive and well documented studies in other jurisdictions and are judged to be accurate with respect to bystanders who are directly over-sprayed. Exposures were judged to be small and, in all cases, considerably below thresholds of concern.

Application rates of glyphosate used for coca eradication are greater than those used in conventional agriculture suggesting that experience and exposures measured under these conditions may not be applicable to bystander exposures in eradication spraying in Colombia. While this may be true, the margins between exposures doses at which chronic effects may occur are great enough to provide a wide margin of safety to bystanders. Less information is available regarding the likelihood of exposure upon reentry to coca fields immediately after spraying. This relates to the anecdotal evidence that picking of leaves or pruning of plants immediately after they are sprayed with glyphosate will “save” the plants. Exposures under these conditions are unmeasured, but are estimated to be considerably below the US EPA reference dose.

6.3.2 Effects

6.3.2.1 Environmental effects

The environmental toxicology database for glyphosate is relatively large and its effects in non-target organisms are well known or can be extrapolated. Glyphosate itself is of low toxicity to non-target organisms, however, there are a number of formulations of glyphosate that exist in the marketplace and these may contain many different surfactants and/or adjuvants. It is also known that it is the surfactants that determine the toxicity of the formulation as many are more toxic than technical glyphosate itself. Because of this, the Panel had several toxicity tests conducted with the formulated product of glyphosate plus Cosmo-Flux® as used in the eradication program in Colombia. This reduced uncertainty with respect to toxicity to beneficial insects such as the honeybee and to aquatic organisms. Recent studies have reported that amphibians, such as frogs, are amongst the more sensitive aquatic organisms with respect to formulations of glyphosate such as Roundup® and Vision®. We did not conduct toxicity studies in amphibians with the mixture of glyphosate plus Cosmo-Flux® and this is a source of some uncertainty for ecological risks for frogs.

6.3.2.2 Effects in humans

The database of effect data for glyphosate is large and its risks to humans and the environment have extensively reviewed and assessed in a number of national and international jurisdictions as well as in the open scientific literature. In all cases, glyphosate has been judged to be of low risk. However, some of the studies on which these assessments are based were conducted prior to the refinement of testing guidelines and the availability of new and more sensitive methods of analysis and effect characterization, such as those based on alteration in the concentrations of neurotransmitters and their metabolites in the central nervous system. In the process of reassessment and re-registration, older studies will be replaced with newer tests conducted according to current guidelines. Given the large and expanding use of glyphosate in agriculture, the priorities for updating the database will likely be high. Changes in the regulatory status of glyphosate should be monitored and any newly identified risks included in an updated risk assessment.

There is considerable literature on the epidemiology of pesticides and possible effects on human health. As a result of recent work, it is clear that many epidemiology studies are confounded by the use of poor and inaccurate surrogates for exposures to pesticides. The Panel also conducted a preliminary epidemiological study to assess possible linkages between the use of glyphosate and adverse human-health outcomes and recognizes that, for clear logistical reasons, no measures of exposure were available for the various groups enrolled in the study other than the use of glyphosate for eradication spraying in the region. The results of this study do not suggest that there is an association between the use of glyphosate in the eradication program and time to pregnancy (TTP) as a reproductive outcome. A somewhat greater risk for longer TTP was observed in one region (Valle del Cauca) where eradication spraying is not conducted but it was not possible to identify any specific factors that may have been responsible for this observation.

6.3.3 Confounding risks

Through the Tier-1 and Tier-2 hazard assessments of the other substances used in the production and refining of cocaine and heroin, the Panel recognizes that some of these substances present a significantly greater hazard to both humans and the environment than does the mixture of glyphosate and Cosmo-Flux® used in the eradication program in Colombia. Exacerbating these hazards is the lack of information about the conditions of use of these substances. Because of the lack of specific data on use and exposure, it was not possible to conduct detailed risk assessments for these substances. From anecdotal evidence and observations in other locations, it is clear that, in most cases, these substances are used without adequate safety training, without adequate protective equipment, without suitable disposal methods, and without supervision. This represents a significant and serious potential risk to humans and the environment.

6.4 RECOMMENDATIONS

The Panel has identified a number of uncertainties in its review of the data and from these makes the following recommendations. These recommendations are grouped into two classes, recommendations to retain current practices that were judged to be essential or useful (Table 21) and recommendations related to new activities or data collection that will address key uncertainties identified in our study (Table 22).

Table 21. Recommendations for the continuance of current practices in the coca and poppy eradication program in Colombia

Practice	Benefit of continuance	Ranking of importance (5 = most important)
Mixer-loader, worker, and environmental protection in the storage, mixing, and loading operations.	Protection of the humans and the environment from excessive exposures.	5
Use of state of art application technology.	Accurate records of location and areas sprayed.	5
Replace the respirator worn by the mixer-loader with a full face shield to reduce the potential for splashed material to run down the face into the eyes.	This recommendation is modification of current procedures that will reduce the risk of splashes of concentrated formulation into the eyes.	5
Use of glyphosate in the eradication program.	The risk of this product to humans and the environment is judged to be lower than any currently-available alternatives. However, if new candidate products become available, their use should only be considered after an appropriate risk assessment has been conducted.	4

Table 22. Recommendations for the collection of new data and information in the coca and poppy eradication program in Colombia

Recommendation	Benefit of new data	Ranking of importance (5 = most important)
Conduct a study to identify risk factors associated with time to pregnancy (TTP).	This is a recommendation resulting from the observation of increased risk of longer TTP in one region of Colombia (Valle del Cauca) where eradication spraying was not carried out. The study should be considered for prioritization in the general human health research programs conducted in Colombia.	3
Including proximity to surface waters in (geographic Information System (GIS) analysis of locations and areas of coca and poppy fields.	Better indication of likely frequency of contamination of these habitats. This would help to better quantify the risks to aquatic organisms in shallow-water non-flowing habitats.	2
Identify mixtures of glyphosate and adjuvants that are less toxic to aquatic organisms than the currently used mixture. The priority of this recommendation would depend on the results of the GIS analysis.	Reduction in possible environmental impacts to non-target organisms in shallow surface water environments.	2
Testing of the glyphosate-Cosmo-Flux® formulation for toxicity to amphibians.	Decrease in uncertainty regarding the toxicity to amphibians.	2
Use of GIS to quantify areas of coca and poppy production in biodiversity hotspots.	Better quantification of proportion of regions identified as important sources of biodiversity that are being adversely impacted because of clear-cutting and planting of coca and poppy.	2
Use of GIS to quantify size of fields planted to coca and poppy and track these over time to judge extent of environmental impact as well as recovery.	Allow more accurate quantification of potentially impacted areas as well as recovery when these fields are abandoned.	2
Review the regulatory status of glyphosate on a regular basis.	Ensure that new testing and toxicity data on glyphosate are included in the risk assessment of	2

Table 22. Recommendations for the collection of new data and information in the coca and poppy eradication program in Colombia

Recommendation	Benefit of new data	Ranking of importance (5 = most important)
	its use in eradication spraying in Colombia.	
Measurement of exposures to glyphosate in bystanders to sprays and reentry into sprayed fields. This recommendation would follow selection of new formulations and mixtures of adjuvants that have lower environmental toxicity.	Better characterization of exposures under conditions of use in Colombia.	1

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8 GLOSSARY

Absorption: The movement of a substance across an exposed surface (e.g., skin, respiratory / digestive mucous) and into the circulation to be distributed throughout the body. This will vary depending on a compound's inherent ability to cross a particular barrier.

AE - Acid Equivalent: The concentration of a substance (glyphosate) expressed in terms of the amount of glyphosate acid, rather than the salt.

A.I. - Active Ingredient: The component of a mixture / formulation which is ultimately responsible for the physiological effects.

Acute toxicity: The potential of a compound to cause injury or illness when given in a single dose or in multiple doses over a short period of time (e.g. 24 h). These effects are based on mechanisms of chemical action where perceptible physiological alterations can be appreciated shortly after administration (e.g. death).

ADI - Acceptable daily intake: This is an estimate of the maximum amount of a compound (often in food) which can be ingested daily over a lifetime without any appreciable detrimental health effects. This parameter has been developed primarily by the WHO and FAO.

Adjuvant: Ingredient added to a particular formulation in order to enhance the availability and efficacy of the active ingredient. These often act by increasing the spreading or uptake of the active ingredient(s).

Adsorption: The process by which a compound is held or bound to a surface by chemical or physical attraction.

Anthropogenic: Chemicals artificially developed by man.

Aromatic: Organic compound in which constituent atoms form a ring (s). These ring structures may grant a compound its characteristic properties such as solubility in lipids.

Bioaccumulation: The accumulation of a particular compound in certain body tissues. This occurs when rate of uptake exceeds that of metabolism and/or excretion. Over time this results in a higher concentration of the substance in the organism than in its environment. Important factors governing the extent of this process include the lipid solubility of the compound as well as how readily it is metabolized.

Bioactivation: The process by which a chemical becomes more reactive due to alterations in its structure and hence chemical properties. This can occur in the environment or within a biological system.

Bioconcentration Factor (BCF): Measure of the tendency of a substance in water to accumulate within the tissues of fish or other organisms. The concentration in the organism can be roughly calculated by multiplying the concentration in the water by the bioconcentration factor. The value determined is useful in helping to determine the possible human consumption level.

CAS No.: Chemical Abstract System registry number. Pertains to a database providing chemical substance information.

Carcinogenic: Any chemical that can cause the formation of cancerous lesions. Often this is achieved through the formation of genetic mutations within a cell(s) resulting in the loss in ability to regulate proliferation.

Chlorosis: A disease in plants, causing the flowers to turn green or the leaves to lose their normal green color.

Chronic toxicity: The nature of adverse effects over a prolonged period of chemical exposure. Such effect measures can include the development of cancer or decrease in growth.

Dermatitis: Inflammation of the skin.

Dose-response: The change in the intensity of physiological effect with dosage. The relationship of response to dose will vary depending on the mechanism through which the compound is acting.

EC50: Median effective concentration. The concentration of a substance in a medium (such as water) which produces an defined effect in 50% of test organisms.

Ecosystem: A collection of populations (microorganisms, plants, and animals) that occur in the same place at the same time and that can therefore potentially interact with each other as well as their physical and chemical environment and thus form a functional entity.

Emulsification: The mixture of two immiscible (non-mixable) liquids by the dispersion of one into the other in the form of tiny droplets.

Environmental fate: The movement, accumulation, and disappearance of chemicals in the environment after their release.

EPA: Environmental Protection Agency (and in the U.S. EPA).

Epidemiological study: The study of the distribution and determinants of health-related states and events within populations. The prevalence of a particular disease as well as various risk factors for its development are studied.

Exposure: Amount of a chemical which comes into contact with a body surface (skin, respiratory tract, digestive tract) from which it can be absorbed into the body. Exposure does not include any chemical that is nearby but not in contact or which is intercepted by clothing or protective equipment.

Exposure route: The means by which a compound comes into contact an absorptive interface such as dermal or inhalation.

Formulant: A substance normally added to a pesticide to increase its ease of use, penetration into the target organism, or to facilitate its application.

Genotoxic: Describes any substance capable of damaging DNA resulting in mutations or the development of cancer.

Half-life: The time for the concentration of a particular chemical or drug to decrease by half of its initial concentration. This will vary depending on its rate of degradation, metabolism, and/or elimination.

Hazard quotient: The ratio of exposure concentration to a reference (threshold) value. If this value is above acceptable concentration, an adverse effect is possible.

Inert ingredients: All components of a mixture not classified as the primary active ingredient. See, Formulant.

Intraperitoneal: Within the peritoneal cavity, the area that contains the abdominal organs.

Intravenous: The injection or entry of a substance directly into a vein and hence into general circulation.

K_{OW} (Log): The octanol-water partition coefficient (K_{OW}) is a ratio of the concentration of the chemical in n-octanol and water at equilibrium. Chemicals with a K_{OW} greater than 1 preferentially partition into octanol. May be expressed as a $\log_{10}$. The value obtained from this determination gives an indication of the potential for the substance to bioconcentrate into organisms.

LC50 - Lethal Concentration 50: The concentration that is lethal to 50% of test organisms. This value is usually used when referring to the toxicity of a substance to organisms exposed via a matrix such as water.

LD50 – Lethal Dose 50: The dose that is lethal to 50% of test animals. This value is used when referring to the toxicity of a substance to organisms that exposed to a specific amount of substance such as via the oral or the injection route.

Leaching: The movement of a substance through the soil.

LOAEL - Lowest Observed Adverse Effect Level: The lowest dose of a toxin at which an adverse effect can be noted in a particular test species. This value will vary depending on the species being utilized.

Matrix: The medium through which an organism may be exposed to a substance. Water for aquatic organisms, soil for soil organisms, air, etc.

Mechanism of action: The process by which a substance produces its characteristic effects. It is often used interchangeably with "toxic mode of action" however it is usually a more specific term. This is a description of the physiological processes that are altered and the consequences of such changes.

Metabolite: A product of natural metabolic processes.

MRL-Maximum Residue Limit: The maximum amount of a substance permissible on food products as well as animal feeds. This value is recommended by the Codex Alimentarius Commission. This takes into account various safety factors as does the ADI.

MTD-Maximum Tolerated Dose): The dose at which significant toxic effects occur without resulting in death.

Mutagen: Any substance or agent that is capable of creating changes in DNA that are subsequently passed on to future cells. These changes may sometimes lead to the development of cancer or changes in organism characteristics.

NOAEL-No Observable Adverse Effects Level: The highest dose that results in no adverse effects being noted in test organisms.

Oxidation: An alteration of chemical structure by the removal of an electron. This is accomplished by any compound that is capable of achieving this (oxidant).

Percutaneous: Pertaining to any agent than can traverse or is administered through the skin.

Persistence: The resistance of a substance to metabolism or environmental degradation. A chemical deemed as persistent will have a long half-life and will remain in the environment for an extended period of time.

PPB-Parts Per Billion: A measure of concentration where the proportion is such that one part of solute exists per one billion parts of solvent or matrix.

PPM-Parts Per Million: A measure of concentration where the proportion is such that one part of solute exists per one million parts of solvent or matrix.

RfD-Reference Dose: A numerical estimate of a daily oral exposure to humans of a substance. This dose level considered unlikely to cause harmful effects during a lifetime. This value takes into account sensitive subgroups whom can be exposed to this agent.

Safety factor: The difference between the NOAEL and the dose allowed in routine exposure. This value is calculated by using the NOAEL for the most sensitive species and dividing it by various uncertainty factors depending on the readily available scientific data. For example if a value is being extrapolated to man from animals, the NOAEL will be divided by a factor of 10. Such numerical factors will vary depending on the size of the uncertainty (i.e. more related species extrapolation will utilize a smaller safety factor).

Sensitizer: A chemical that is capable of causing the development of an allergic response upon subsequent exposure.

Solubility: The relative ability of a certain substance to be dissolved in a particular solvent. For example, compounds that are very readily dissolved in water may be only minimally dissolved in a more lipid-like solvent such as organic solvents (e.g. octanol).

Sub-chronic: Refers to a period of repeated exposure which is usually about 10% of an organism's expected life-span.

Synergism: The process by which two or more substances interact via a biological mechanism to produce a greater than additive response.

Teratogenesis: The development of a deformed offspring after exposure of the fetus to a certain chemical insult. The various developmental stages at which this exposure occurs will result in different abnormalities.

Toxicity test: The determination of the toxic potential of a particular substance on a group of selected organisms under defined conditions.

Toxicodynamics: The mechanism through which a toxic compound exerts its physiological effect. This includes the relationship between the structure of a compound and the means by which it acts.

Toxicokinetics: The movement of chemicals through the body. This includes rate/extent of absorption, distribution, metabolism and elimination.

TWA-Time Weighted Average: The average exposure concentration over an 8-hour work shift.

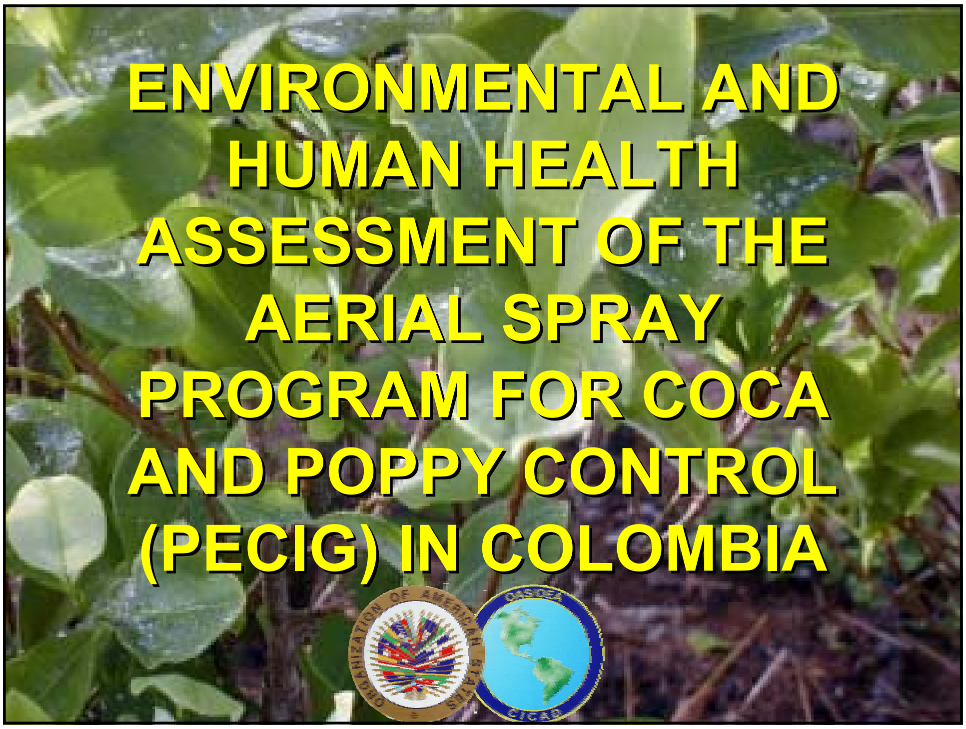
Volatility: The ability of a compound to evaporate and partition into the air.

Xenobiotic: Any substance to which an organism is exposed which is not produced internally in that organism at that time.

Annex 117

37TH REGULAR SESSION OF CICAD, SANTO DOMINGO, DOMINICAN REPUBLIC, 26-29 APRIL 2005, DOCUMENT 1421

(Available at: http://www.cicad.oas.org/apps/Document.aspx?Id=265 (last visited 7 March 2010))



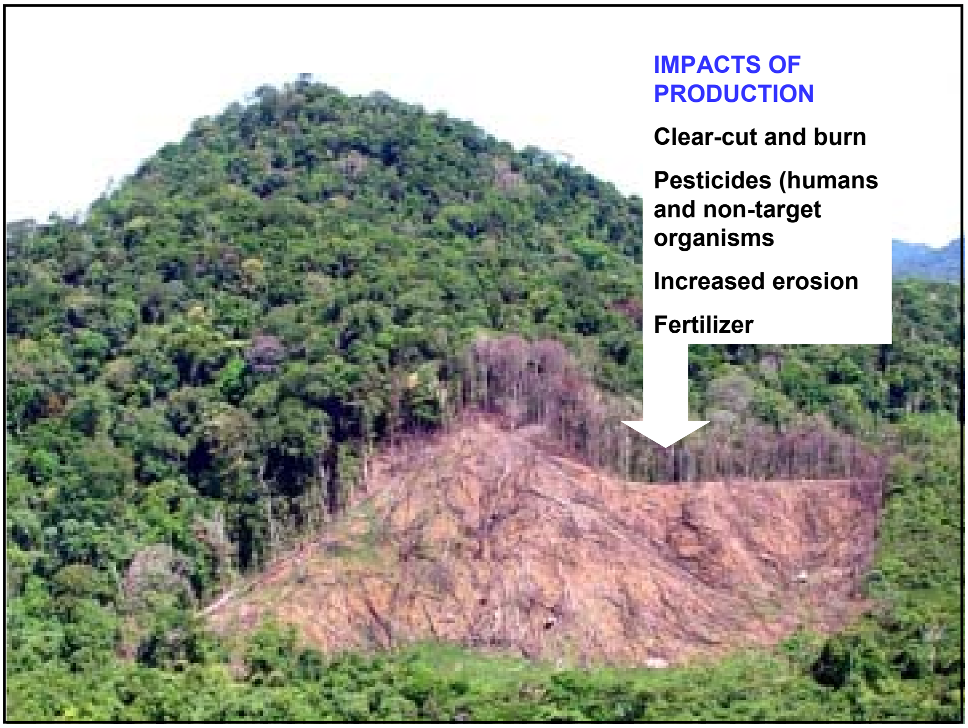
Report prepared for the Comisión Interamericana para el Control del Abuso de Drogas (CICAD)
Organization of American States (OAS)
37th session

Santo Domingo, April 26, 2005

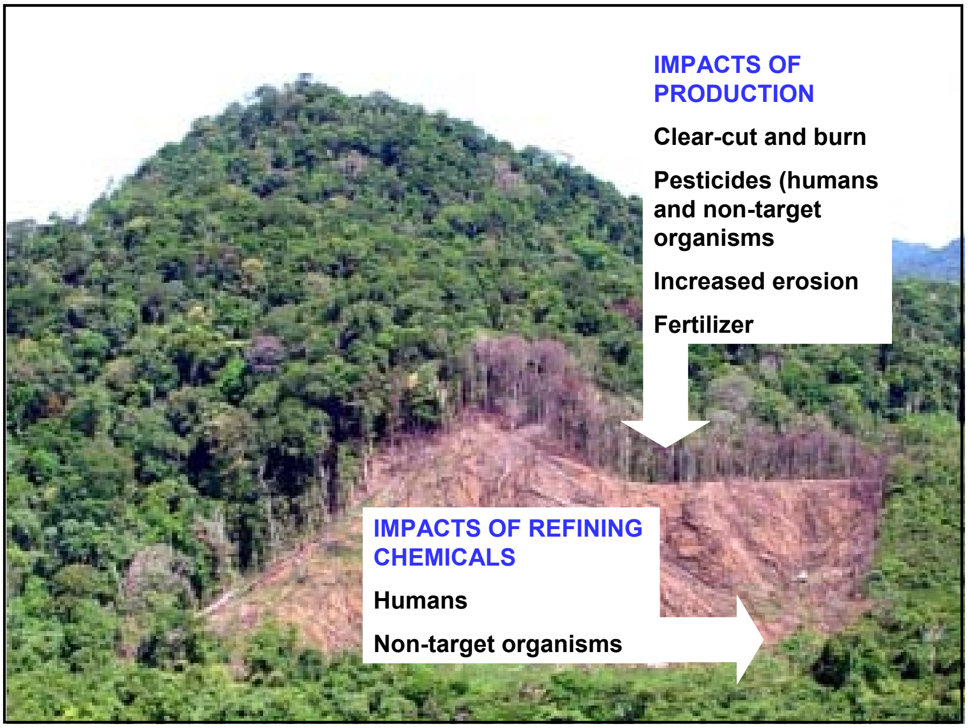
- Dr. Keith R Solomon
  - University of Guelph, Canada
- Dr. Arturo Anadón
  - Universidad Complutense de Madrid, Spain
- Dr. Antonio Luiz Cerdeira
  - EMBRAPA, Brazil
- Dr. Jon Marshall
  - Marshall Agroecology, Somerset, UK
- Dr. Luz-Helena Sanin
  - University of Toronto, Canada and Autonomous University of Chihuahua, Mexico

APPROACH

- **Scientific team with expertise in several areas**
- **Followed the standard approach to risk assessment**
  - **Problem formulation and stressor characteristics**
  - **Exposure characterization**
  - **Effects characterization**
  - **Risk assessment**
- **Reviewed the open scientific literature and government reports**
- **Conducted special studies in Colombia and elsewhere to characterize effects and exposures**
- **Science-based assessment for publication in the scientific literature**


IMPACTS OF
PRODUCTION
Clear-cut and burn
Pesticides (humans
and non-target
organisms
Increased erosion
Fertilizer


humitron


IMPACTS OF PRODUCTION
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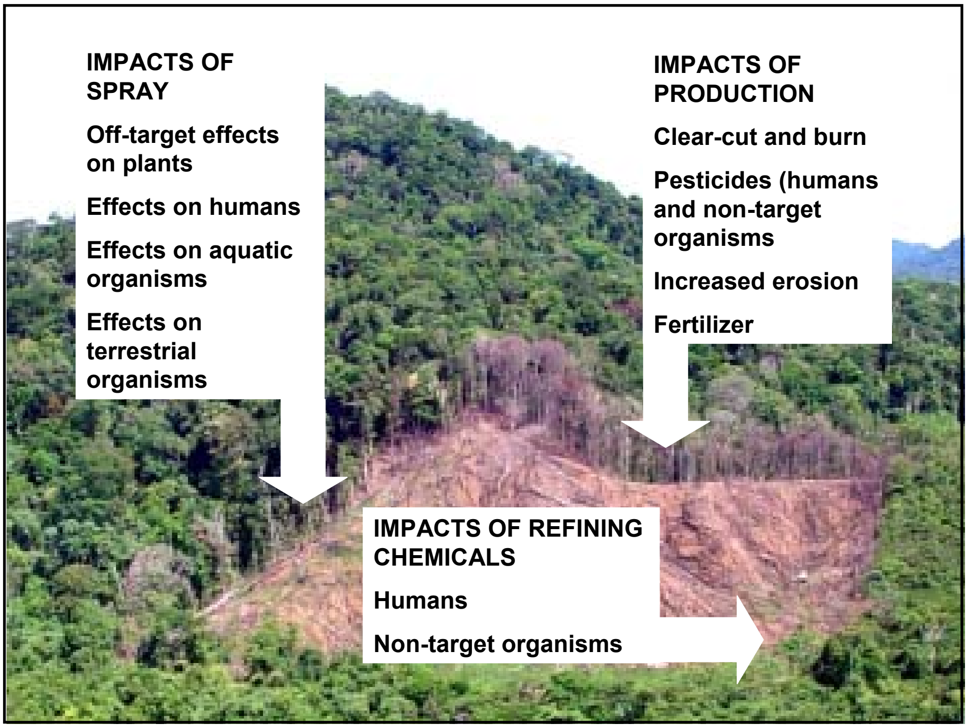
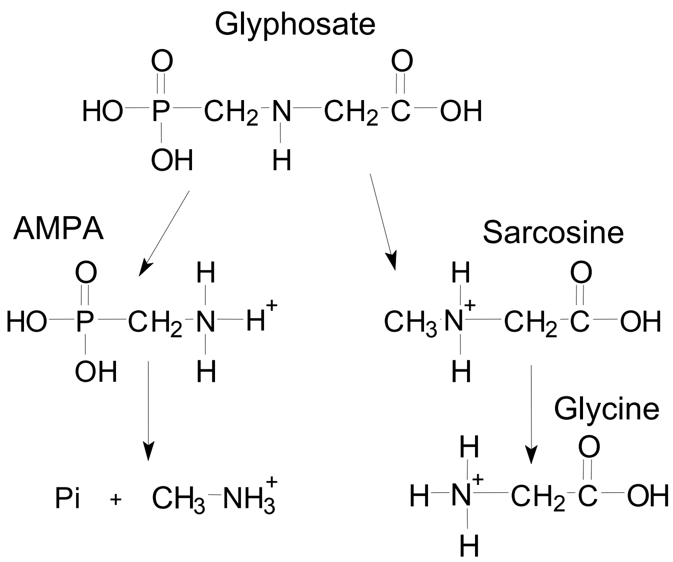
Increased erosion
Fertilizer
IMPACTS OF REFINING CHEMICALS
Humans
Non-target organisms

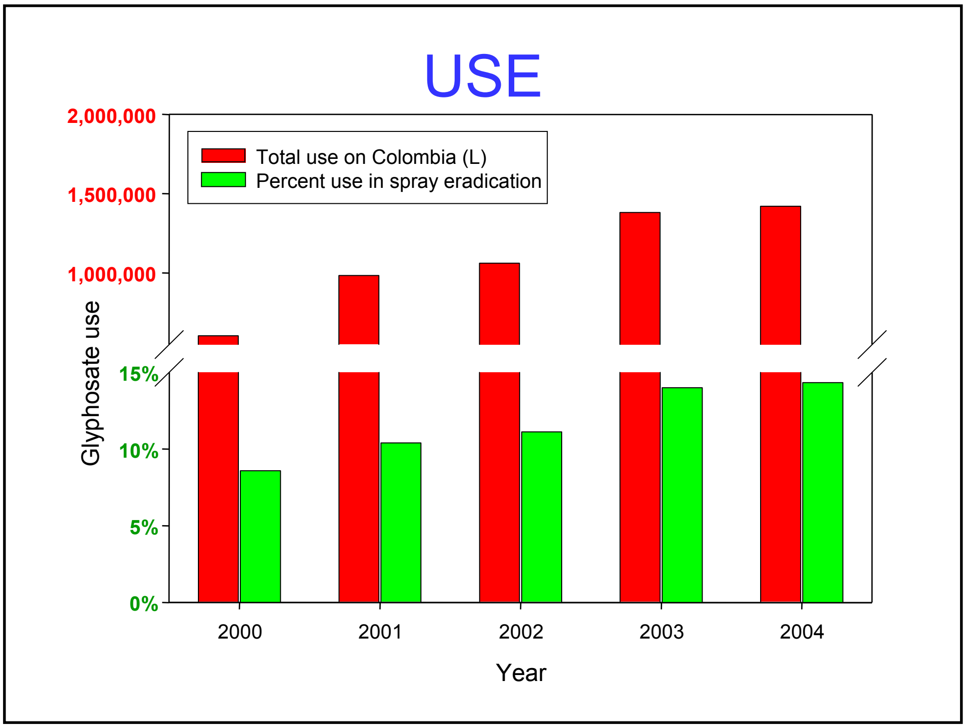

IMPACTS OF SPRAY
Off-target effects on plants
Effects on humans
Effects on aquatic organisms
Effects on terrestrial organisms
IMPACTS OF PRODUCTION
Clear-cut and burn
Pesticides (humans and non-target organisms
Increased erosion
Fertilizer
IMPACTS OF REFINING CHEMICALS
Humans
Non-target organisms

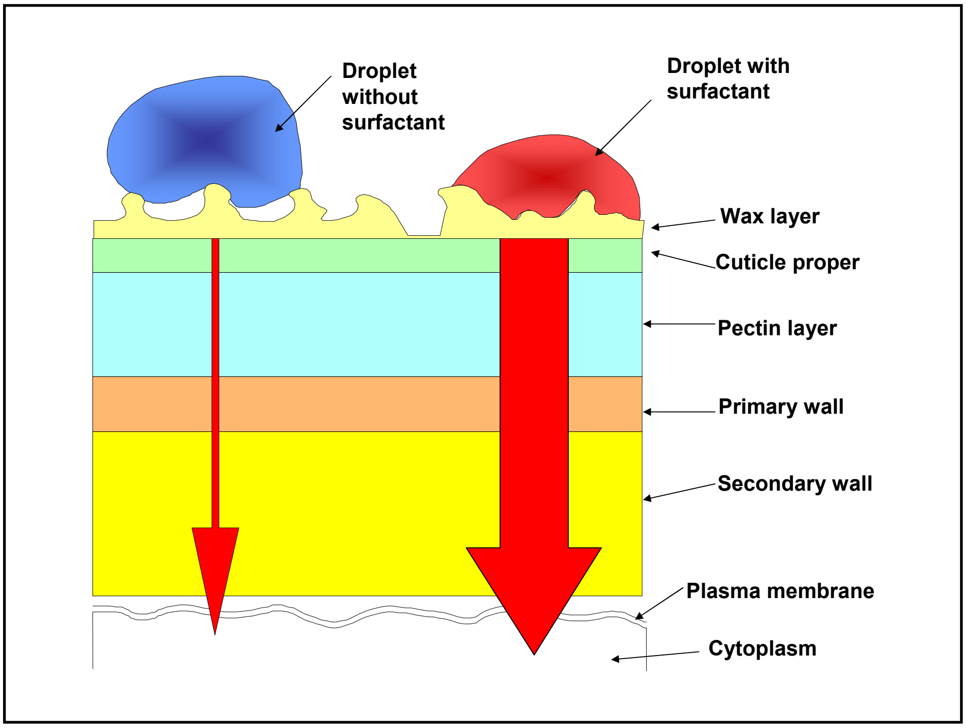
CHARACTERISTICS

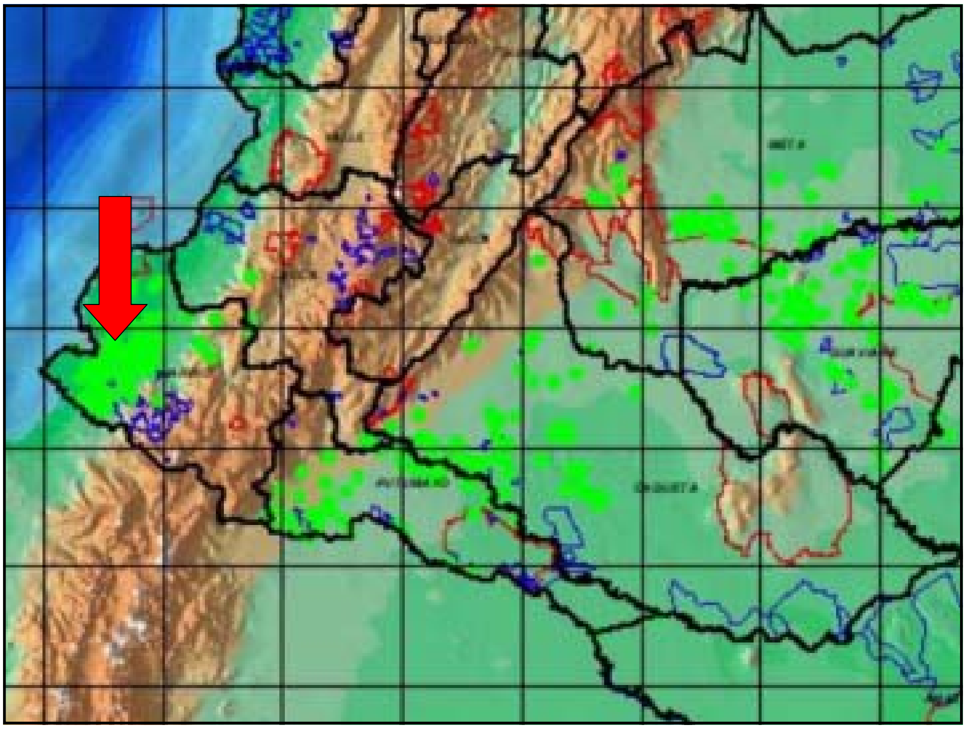


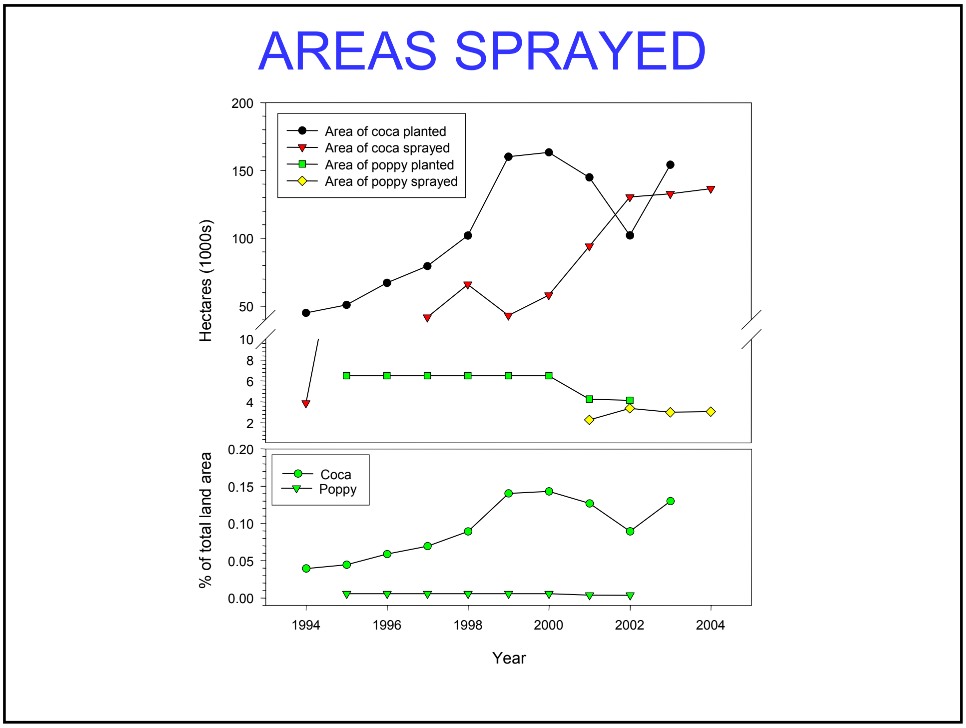
GLYPHOSATE

- Glyphosate is not highly mobile in the environment
- Rapidly and tightly bound on contact with soil and aquatic sediments
- Very short biological activity in soils and water
- Does not biomagnify or move through the food chain
- Does not leach into groundwater from soil.


USE
2,000,000
1,500,000
1,000,000
15%
10%
5%
0%
Glyphosate use
Total use on Colombia (L)
Percent use in spray eradication
2000
2001
2002
2003
2004
Year

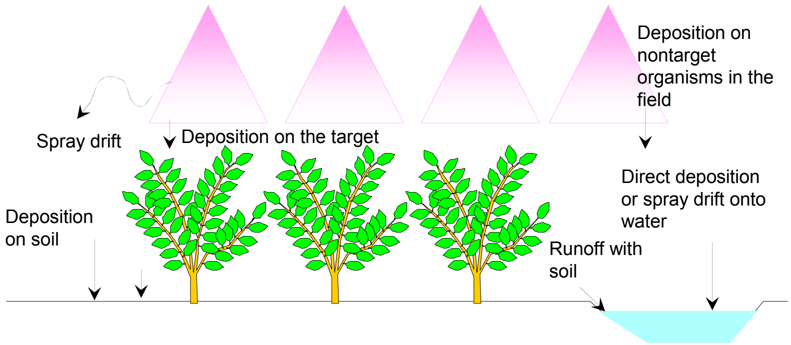

Droplet without surfactant
Droplet with surfactant
Wax layer
Cuticle proper
Pectin layer
Primary wall
Secondary wall
Plasma membrane
Cytoplasm




AREAS SPRAYED
Area of coca planted
Area of coca sprayed
Area of poppy planted
Area of poppy sprayed
Hectares (1000s)
200
150
100
50
10
8
6
4
2
Coca
Poppy
% of total land area
0.20
0.15
0.10
0.05
0.00
1994
1996
1998
2000
2002
2004
Year

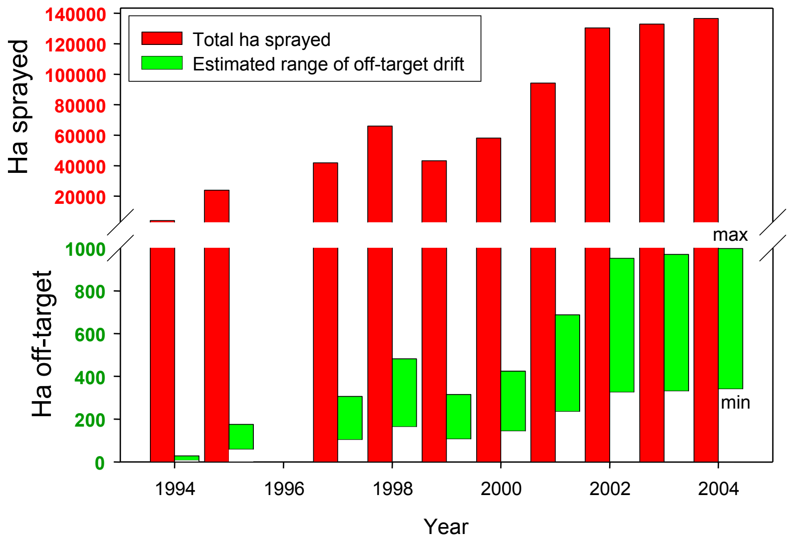
BIODIVERSTY HOTSPOT

PATHWAYS OF EXPOSURE



OFF-TARGET DEPOSITION

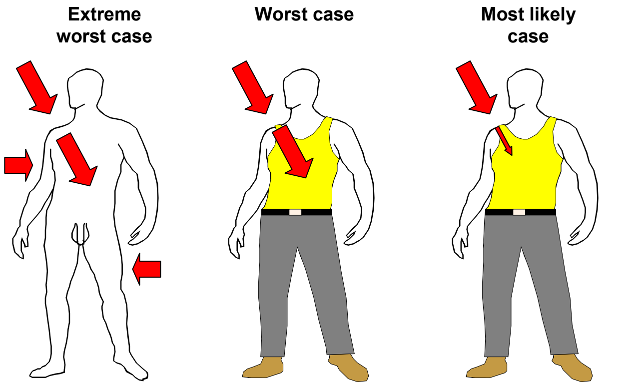
OFF-TARGET DEPOSITION



EXPOSURES

- Applicators
  - Mixer-loader
  - Pilots
  - Technicians
- Bystanders

DIRECT OVERSPRAY



Whole body (2 m^2)	0.25 m^2	**0.25 m^2**
100% absorption	100% absorption	**2% absorption**
14.2 mg/kg bw	1.8 mg/kg bw	**0.04 mg/kg bw**

TOTAL ESTIMATED EXPOSURES

Source of exposure	**Exposure value in mg/kg bw**	
	Coca	Poppy
Direct overspray	0.04	0.01
Reentry	0.26	0.06
Inhalation	0.01	0.01
Diet and water	0.75	0.18
Worst case total exposure from all sources	1.05	0.26

ENVIRONMENTAL EXPOSURES

Surface water scenario	Exposure in µg/L	
	Coca sprayed at 4.982 kg/ha (3.69 kg AE/ha)	Poppy sprayed at 1.2 kg/ha (0.89 kg AE/ha)
2 m deep, rapid mixing and no absorption to sediments, no flow.	185	44
0.3 m deep, rapid mixing and no absorption to sediments, no flow.	1,229	296
0.15 m deep, rapid mixing and no absorption to sediments, no flow.	2,473	595
0.15 m deep, rapid mixing and 50% absorption to sediments, no flow.	1,237	297

SAMPLING IN COLOMBIA

Site name	Location	Altitude (m)	Major crop types	Known pesticide use
Valle del Cauca, Río Bolo	N 03°27.642' W 076°19.860'	1002	Sugar cane	Glyphosate and other pesticides
Boyacá, Quebrada Paunera	N 05°40.369' W 074°00.986'	557	Coca	Manual eradication, no aerial spraying of glyphosate
Sierra Nevada, Quebrada La Otra	N 11°13.991' W 074°01.588'	407	Organic coffee	None
Putumayo, Río Mansoya	N 00°43.259' W 076°05.634	329	Coca	Aerial eradication spraying
Nariño, Rio Sabaletas	N 01°27.915' W 078°38.975'	15	Coca	Aerial eradication spraying

DETECTION OF GLYPHOSATE

Surface water collection site	Total number of samples	Frequency of detection (n and %) for site	
		Glyphosate	AMPA
Valle del Cauca, Río Bolo	17	1 (5.9%)	0 (0%)
Boyacá, Quebrada Paunera	18	1 (5.5%)	0 (0%)
Sierra Nevada, Quebrada la Otra	18	0 (0%)	0 (0%)
Putumayo, Río Mansoya	16	0 (0%)	0 (0%)
Nariño, Rio Sabaletas	17	0 (0%)	0 (0%)

MDL = 25 µg/L

Other pesticides detected at Nariño - 2,4-D, endosulfan I, endosulfan II, endosulfan sulfate

EFFECTS IN MAMMALS

- **Glyphosate**
  - Very low acute and chronic toxicity
  - Not teratogenic
  - Not mutagenic
  - Not carcinogenic
  - Not immunotoxic in mammals
  - **Cancer epidemiology**
    - No strong association with cancer
  - **Neurological epidemiology**
    - No strong association
  - **Reproductive epidemiology**
    - Association with reproductive responses – Time to Pregnancy

GLYPHOSATE AND COSMOFLUX®

- **ACUTE STUDIES (GLP guideline studies)**
  - Very low acute oral toxicity
  - Very low acute dermal toxicity
  - Low to moderate inhalation toxicity
  - Low to moderate skin irritant
  - Moderate eye irritant (recovery)
  - Not a skin sensitizer
- Addition of the adjuvant Cosmo-Flux® to the glyphosate did not change its toxicological properties to mammals

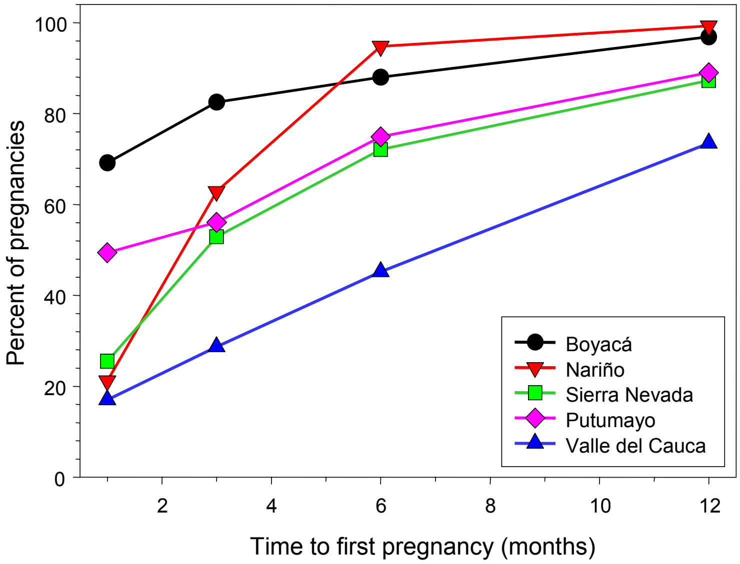
EPIDEMIOLOGY STUDY IN COLOMBIA

- Questionnaire study in 5 regions in Colombia
- Time to (1st) Pregnancy (TTP)
- 600 women in each location (3000 total)
- Ecologic study based on region – use of glyphosate for eradication
- Other factors were also assessed

EPIDEMIOLOGY REGIONS

Site name	Focal crop	Known pesticide use
Valle del Cauca	Sugar cane	Glyphosate and other pesticides. Glyphosate applied by air.
Boyacá	Coca	Manual eradication, no aerial spraying of glyphosate. Use of other pesticides unknown.
Sierra Nevada	Organic coffee	No pesticide use and no coca known to be grown. Use of other pesticides unknown.
Putumayo	Coca	Aerial eradication spraying with lower intensity. Use of other pesticides unknown.
Nariño	Coca	Aerial eradication spraying with higher intensity. Use of other pesticides unknown.

TIME TO PREGNANCY



ALTERNATIVE MODEL

Variable	OR	95% CI
Region		
Boyacá	1.00	--
Nariño	0.56	0,47; 0,66
Sierra Nevada	0.36	0,31; 0,43
Putumayo	0.35	0,29; 0,41
Valle del Cauca	0.15	0,13; 0,18
Age at first pregnancy > 20 years	0.81	0,73; 0,91
Irregular relationship	0.76	0,68; 0,84
Consumption of coffee		
Medium (1-3 cups per day)	0.91	0,81; 1,04
High (4 and more cups per day)	0.84	0,69; 1,02
Perception of contamination of water	0.91	0,81; 1,01

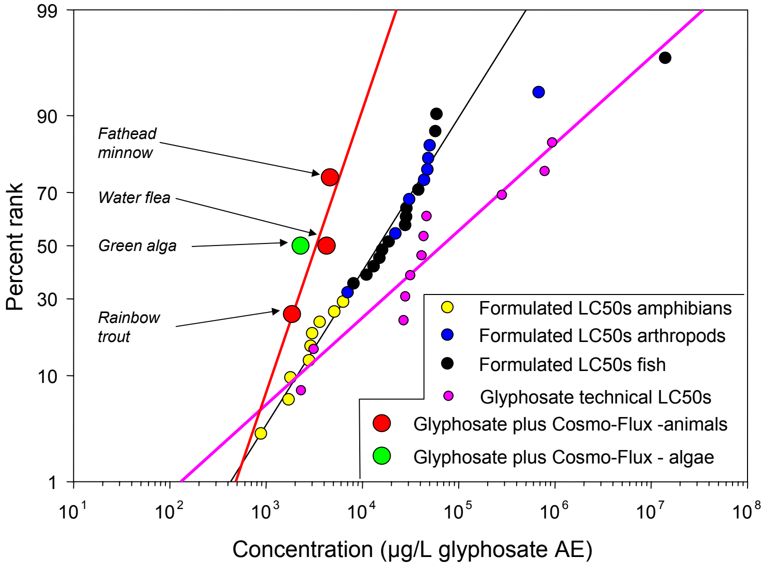
RESULTS OF EPIDEMIOLOGY

- The greatest risk (TTP) was in the Valle del Cauca region
- No association between TTP and eradication of illicit crops
- Reason(s) for the increased risk for longer TTP in the Valle del Cauca region not known
  - Not due to exposure to pesticides alone - Sierra Nevada (organic crops) also showed a significant difference from reference (Boyacá)
- Study designed to test hypotheses related to the use of glyphosate in eradication spraying - data cannot be used to identify causality associated with other risk factors
- To test this question in Valle del Cauca or any other region, a new study would have to be designed and conducted

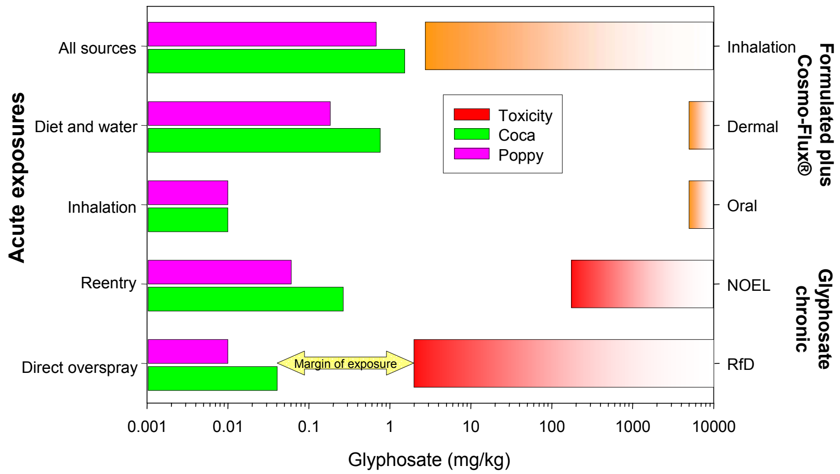
EFFECTS IN THE ENVIRONMENT

- **GLYPHOSATE AND ROUNDUP®**
  - Published papers
  - Government documents (U.S.EPA, EU, etc)
- **GLYPHOSATE AND COSMOFLUX®**
  - Special studies on the mixture
  - Honey bee
  - *Daphnia magna* (aquatic invertebrate)
  - Aquatic alga
  - Two fish (fathead minnow, rainbow trout)

ECOTOXICOLOGY DATA

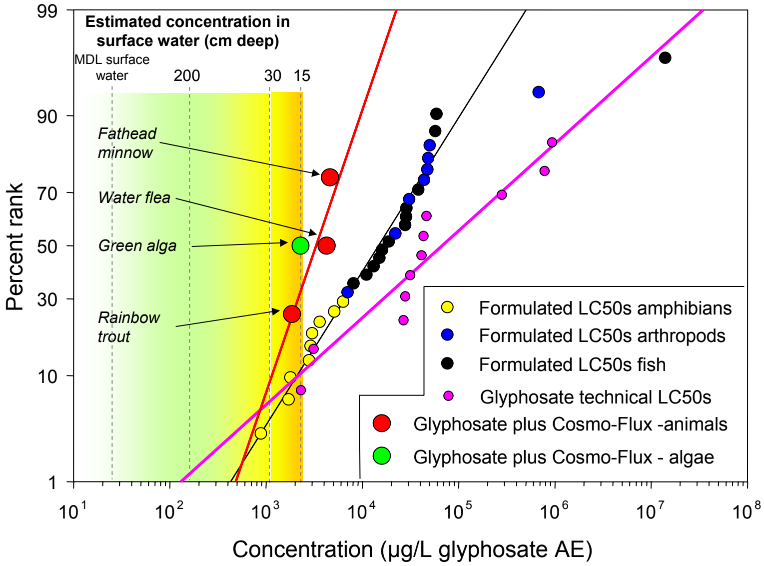


HUMAN RISK ASSESSMENT



Margin of exposure is protective for all sources of contamination and is even lower because acute exposures are compared to chronic effect doses

ENVIRONMENTAL RISK



HUMAN HEALTH CONCLUSIONS

IMPACTS	INTENSITY SCORE	RECOVERY SCORE	FREQUENCY %	IMPACT SCORE	% IMPACT
Clear cutting and burning	5	3	3	45	**16.7**
Planting the coca or poppy	0	1	100	0	**0.0**
Fertilizer inputs	0	0.5	10	0	**0.0**
Pesticide inputs	5	3	10	150	**55.5**
Eradication spray	**<0.1**	**0**	**1**	**<0.1**	**<0.1**
Processing and refining	5	3	5	75	**27.8**

ENVIRONMENTAL CONCLUSIONS

IMPACTS	INTENSITY SCORE	RECOVERY TIME (Y)	IMPACT SCORE	% IMPACT
Clear cutting and burning	5	60	300	**97.6**
Planting the coca or poppy	1	4	4	**1.3**
Fertilizer inputs	1	0.5	0.5	**0.2**
Pesticide inputs	2	0.5	1	**0.3**
Eradication spray	**1**	**0.5**	**0.5**	**0.2**
Processing and refining	2	1	2	**0.7**

RECOMMENDATIONS FOR CURRENT PRACTICES

Practice	Benefit of continuance	Rank
Mixer-loader, worker, and environmental protection in storage, mixing, and loading operations.	Protection of the humans and the environment from excessive exposures.	5
Use of state of art application technology.	Accurate records of location and areas sprayed	5
Replace the respirator worn by the mixer-loader with a full face shield to reduce the potential exposure of the eyes.	Reduce the risk of splashes of concentrated formulation into the eyes.	5
Use of glyphosate in the eradication program.	Risk to humans and the environment is judged to be lower than any currently-available alternatives. New candidate products should only be considered after an appropriate risk assessment has been conducted.	4

NEW RECOMMENDATIONS (1)

Recommendation	Benefit of new data	Rank
Conduct a study to identify other factors associated with time to pregnancy (TTP).	Better understand and manage human health risks.	3
Including proximity to surface waters in Geographic Information System (GIS) analysis of locations and areas of coca and poppy fields.	Better indication of likely frequency of contamination of these habitats.	2
Identify mixtures of glyphosate and adjuvants that are less toxic to aquatic organisms than the currently used mixture. The priority of this recommendation would depend on the results of the GIS analysis.	Reduction in possible environmental impacts to non-target organisms in shallow surface water environments.	2
Testing of the glyphosate-Cosmo-Flux® formulation for toxicity to amphibians.	Decrease in uncertainty regarding the toxicity to amphibians.	2

PROXIMITY TO WATER

NEW RECOMMENDATIONS (1)

Recommendation	Benefit of new data	Rank
Conduct a study to identify risk factors associated with time to pregnancy (TTP).	Better understand and manage human health risks	3
Including proximity to surface waters in Geographic Information System (GIS) analysis of locations and areas of coca and poppy fields.	Better indication of likely frequency of contamination of these habitats.	2
Identify mixtures of glyphosate and adjuvants that are less toxic to aquatic organisms than the currently used mixture. The priority of this recommendation would depend on the results of the GIS analysis.	Reduction in possible environmental impacts to non-target organisms in shallow surface water environments.	2
Testing of the glyphosate-Cosmo-Flux® formulation for toxicity to amphibians.	Decrease in uncertainty regarding the toxicity to amphibians.	2

NEW RECOMMENDATIONS (2)

Recommendation	Benefit of new data	Rank
Use of GIS to quantify areas of coca and poppy production in biodiversity hotspots.	Better understand potential effects on important sources of biodiversity from clear-cutting and planting of coca and poppy.	2
Use of GIS to quantify size of fields planted to coca and poppy and track these over time.	Allow more accurate quantification of potentially impacted areas as well as recovery.	2
Review the regulatory status of glyphosate on a regular basis.	Ensure that new testing and toxicity data on glyphosate are included in the risk assessment of its use in eradication spraying in Colombia.	2
If new mixtures are used, measurement of exposures to glyphosate in bystanders to sprays and reentry into sprayed fields.	Better characterization of human exposures under conditions of use in Colombia.	1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THANK YOU

Annex 118

CICAD, R.A. BRAIN ET AL., "THE TOXICOLOGY OF SUBSTANCES USED IN THE PRODUCTION AND REFINING OF COCAINE AND HEROIN: A TIER-TWO HAZARD ASSESSMENT", OAS, WASHINGTON, D.C., 31 JULY 2005, (CICAD I)

(Complete Report without appendices. Full Report available at: http://www.cicad.oas.org/Desarrollo_Alternativo/ENG/Projects%20By%20Country/Colombia/OAS_CICAD_Tier_2_Hazard_Assessment_July_2005%5B1%5D.pdf (last visited 7 March 2010))

THE TOXICOLOGY OF SUBSTANCES USED IN THE PRODUCTION AND REFINING OF COCAINE AND HEROIN: A TIER-TWO HAZARD ASSESSMENT

CICAD OAS

WASHINGTON, DC, USA

JULY 31, 2005

THE TOXICOLOGY OF SUBSTANCES USED IN THE PRODUCTION AND REFINING OF COCAINE AND HEROIN: A TIER-TWO HAZARD ASSESSMENT

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Executive Summary

A number of substances are used in the production of cocaine and heroin in Colombia. These range from pesticides used to control pests in the coca and poppy fields to substances used in the extraction and refining processes. The practice of illicit crop production may have potential adverse effects on human and environmental health due to the large quantities of chemicals required to cultivate the crops under the conditions of growth in Columbia. Poor nutrient availability, competition from other vegetation and damage from various insects necessitate large chemical inputs. A total of 67 substances used in significant quantities for these purposes were reviewed in a Tier-1 assessment (CICAD/OAS 2004). Of these, 20 were selected for a more detailed assessment of toxicological properties and their fate in the environment.

Three different ranking systems were employed to select the 20 highest priority compounds based on toxicological and physiochemical data. Two ranking systems where based on scoring criteria while the third was based on weighting factors and strictly for pesticides. Substances lacking in one or more data categories were assigned default worst-case values and further assessed by expert judgment for inclusion or exclusion from the priority list. Good agreement was attained between the three selection methods, where 13 out of 20 compounds appeared on all three lists and 16 out of 20 appeared on two or more. The final priority list integrated the three different approaches by assimilating the ranks of each compound from each method as well as supplemental material characterizing the nature of these compounds where data was missing or not available. These 20 substances are reviewed in detail in the appendices to this report. Eighty percent of the substances included in the Tier-2 assessment were pesticides, and all of the 16 pesticides are registered for use in Columbia with the exception of endosulfan. Toxicological and physiochemical data were obtained from primary literature sources, databases, and compilations. Supplementing the hazard assessment, and contained in the appendices are the tabulated human and environmental toxicity data sets for each compound as well as appropriate discussions of chemical mode of action, oncology, teratology, toxic symptoms, and biological receptors and effects. All data used in the Tier-2 hazard assessment was reviewed for quality to ensure that quality sources were used for evaluation.

A comparative hazard assessment approach was used to evaluate the relative hazard posed by individual compounds to human and environmental health. The hazard quotient is typically the ratio of highest exposure value and the lowest effects value, where ratio values above 1 indicate potential hazard, and values below one indicate less potential for hazard. For the 16 pesticide compounds, estimates of exposure to humans and the environment were made using worst-case (conservative) assessment scenarios from standard procedures to evaluate potential hazards. Little or no information was available with respect to the application and use of these substances for the production of cocaine and heroin, requiring exposures to be estimated. The human hazard quotient exposure value (or body dose) was estimated based on the pesticide application rate, surface area of skin exposed and dermal absorption per 70 kg adult, which was divided by the reference dose (RfD). For the environmental hazard quotient, exposures were calculated based on standard values

for pond depths adjusted for the pesticide application rate, assuming direct overspray, and divided by the lowest aquatic toxicity value. Similarly, hazard quotients were generated for honeybees and earthworms. To assess hazards to earthworms, the data for the most sensitive soil organism was compared to the concentration in the top 2.5 or 5 cm of soil that would result if the soil was sprayed directly with the substance. However, for the honeybee hazard assessment, the pesticide application rate was divided by the topical LD_{50} for the pesticide, where a hazard ratio of < 50 indicates low risk; 50 - 2,500 indicates moderate risk; and > 2,500 indicates high risk. Glyphosate, which is used in the illicit crop control program, was used as a basis of comparison for the degree of hazard posed by other pesticide compounds used in the production of illicit crops. The four remaining non-pesticide compounds were assessed in a different manner.

Comparison of the hazard quotient values for the human health hazard assessment indicated that a number of pesticides used in coca and poppy production present much greater hazard to humans as compared to glyphosate. Based on conservative exposure scenarios, hazard quotients (HQ) for methamidophos, monocrotophos, endosulfan, profenofos, methomyl, and diazinon were all greater than 10, compared to glyphosate (<1). With the exception of endosulfan, these pesticides are largely acetylcholinesterase (AChE) inhibitors, which is consistent with observations of adverse effects in terrestrial animals and humans in other jurisdictions. Hazard quotients calculated for the aquatic environmental health component were also greater than 10 for several pesticides, where most of the pesticides used in coca and poppy production presented significantly greater hazards to aquatic organisms than glyphosate (and Cosmo-Flux®). For shallow waters, only pendimethalin and glyphosate (plus Cosmo-Flux®) had HQs less than 10. Comparatively, the HQ for endosulfan was, 41,000. Not surprising, several of the pesticides, present significant hazards to bees and other pollinators. By comparison, tests conducted with the formulation of glyphosate plus Cosmo-Flux® showed that it was essentially non-toxic to honey bees. Similar results were found for the earthworm hazard assessment, where a number of other pesticides such as diazinon and carbendazim were found to present significantly greater hazards to earthworms than glyphosate with hazard quotients greater than 1. However, it should be clarified that, since the frequency of exposures and the number of individuals involved is unknown, it is uncertain whether these identified hazards translate into greater risk.

The four non-pesticide compounds could not be assessed under the hazard quotient framework due to lack of precise knowledge of how humans may be exposed to these substances and how they may enter the environment. Although nitric acid is a strong skin and gastrointestinal irritant, potassium permanganate may cause toxic and reproductive effects in humans, fuel oil is toxic to mammals if consumed and is toxic to organisms in the environment during spills or other large releases, the use of these chemicals is not expected to represent a major human or environmental hazard. Only in cases where large releases or direct consumption occurs, are adverse effects on human and environmental health expected.

In general, many of the substances used in cocaine and heroin production and refining are potentially hazardous to human and environmental health. Comparatively, several of the short-listed pesticides are considerably more toxic to humans and non-target organisms in the environment than glyphosate (plus Cosmo-Flux®). Most of the more hazardous pesticides were found to be insecticides, which are toxic to mammals and other wildlife, as well as to insects. These chemicals are registered in Colombia with the exception of endosulfan, and their inclusion in this report does not imply that they should be further restricted or banned. However, if used improperly, particularly in the production of coca and heroin, these compounds have the potential to present significant hazards to human and environmental health, much more so than the hazards identified for glyphosate as used in the eradication of the illicit crops.

TABLE OF CONTENTS

APPENDICES

1 INTRODUCTION

This report is focused on a hazard assessment of twenty high priority substances used in the production of the illegal drugs, cocaine and heroin, in Colombia. Cocaine and heroin are produced in a number of regions of the world, including several countries in Latin America. A previous report addressed hazards associated with 67 substances that are used in the production and refining of these drugs in Colombia (CICAD/OAS 2004). Because of the large number of substances involved, this earlier report was designed to be a Tier-1 hazard assessment for the purposes of categorizing and ranking the substances in terms of hazard to humans and the environment. This report is a detailed hazard assessment of twenty of these substances with respect to their possible adverse effects to human health and the environment. As with the previous report (CICAD/OAS 2004), the document is focused on the illicit production of cocaine and heroin in Colombia, one of the largest producers in the region. It is recognized that both cocaine and heroin are produced in neighboring countries such as Venezuela, Ecuador, Peru, and Bolivia.

1.1 BACKGROUND

1.1.1 Cocaine

Cocaine is the primary drug produced in Colombia, however, some heroin and marijuana are also produced (DEA 2002). There is a history of coca use in Colombia that goes back as far as 500 BCE when the leaves of the coca plant, *Erythroxylum coca,* and related species were used in religious ceremonies by the pre-Inca, pre-Mayan, and other peoples. The cocaine alkaloid, produced in the leaves of coca plant, was first isolated in purified form in the 1800s. It was used a medicine, a drug, as a poison, and even as a flavoring in cola soft drinks until the early 1900s, when harmful effects and the addictive properties were recognized.

Although over 200 *Erythroxylum* species have been described, only seventeen of these are suitable for use in cocaine production and only two of the seventeen have a high enough alkaloid content in their leaves to warrant cultivation. Based on personal observations and information in the literature, there are a number of steps in the production of cocaine from growing to the production of the pure alkaloid. These are summarized the following sections:

1.1.1.1 Cultivation

If the coca is to be planted in a new field in a forested area, the field is initially cleared by cutting most of the larger trees and then burning those parts of the trees that are not used a source of wood for construction. The source of the coca plants is either from seeds or from cuttings. The preferred methods vary with region. Seedbeds are prepared in humus-enriched soil and are kept well watered and free of weeds until germination occurs within 20 to 30 days. Seedlings generally reach transplanting size (approximately 30 cm tall) within two months. At this point, they are planted in rows of holes about a 30 cm deep in the farmer's field. Cuttings are obtained from mature bushes and are planted directly in the soil where they root. A coca plant cultivated from seed generally reaches full maturity and its leaves ready for harvest between 12 and 24 months after transplantation. Plants grown from cuttings may be ready for harvesting in less than 6 months, depending on growing conditions and inputs.

Although coca is a robust plant that will live for years and produce multiple leaf harvests, when grown in monoculture for maximum yield it requires nutrients, fertilizers, herbicides, fungicides, and insecticides for sustained growth and protection from natural enemies (Figure 1). The most serious threat to the coca plant is the larvae of the moth *Eloria novesi*. The larva will develop in approximately a month and will eat up to 50 leaves in its lifetime. Also, the leaf-cutting ant, *Acromyrmex* and the beetle, *Aegoidus pacificus*, are both known to seriously damage coca cultivation. Other insects such as spider mites and grasshoppers can attack the coca plant, but usually only do so when there is a shortage in their normal food supply. Coca growers use insecticides to defend against attack from these pests. Coca plants are also susceptible to numerous species of pathogenic fungi, especially during the wet season (DEA 1993) and fungicides are used to combat these. Micronutrients are often applied as foliar sprays.

1.1.1.2 Harvesting

Depending on the climate, harvest of the coca leaf can occur between two and six times per year, with one larger harvest that accounts for around half of the total production usually occurring after the rainy season. At harvest, the majority of the leaves are removed from the plant, leaving just a few at the tips of the branches. The leaves are packed into bags for transport to nearby processing areas. After harvest, leaves may be spread in thin layers in direct sunlight to dry prior to processing.

1.1.1.3 Cocaine production

As in cultivation, the processing of the coca leaves into the cocaine alkaloid varies, but involves several common steps and substances. Many of these substances are quite common such as industrial acids, bases, and solvents. Processing takes place in three major steps: conversion of the coca leaf into coca paste, followed by conversion to cocaine base, and finally to cocaine hydrochloride (DEA 1993).

Figure 1 Coca laboratory in Nariño (2005)

The first step, conversion of the coca leaf into coca paste is performed in a coca paste pit, or “pozo”, usually a simple hole in the ground lined with thick, heavy plastic or in containers such as drums (Figure 1). Although the steps vary significantly, a general formula for production of the coca paste is as follows. An alkaline material, such as sodium carbonate, water and an organic solvent, such as kerosene are added to the leaves in the plastic-lined pit to allow for extraction of the cocaine alkaloid from the leaf into the solvent. The mixture is then agitated by stomping the leaves. The solvent is separated from the water and leaves, and the cocaine alkaloids are further extracted into an aqueous acid solution to which an alkaline material is then added. A precipitate forms that can be filtered and dried to produce coca paste (DEA 1993).

The second step is conversion of the coca paste to cocaine base. Although procedures vary, a common procedure for production of cocaine base is as follows: the coca paste is dissolved into an acid solution and combined with diluted potassium permanganate to remove undesired alkaloids and contaminants. Once this precipitate is discarded, ammonia water is added to the filtered solution to form another precipitate that is separated and dried. The resulting powder is cocaine base (DEA 1993).

The third step is the conversion of cocaine base to cocaine hydrochloride (conducted in a so-called acid laboratory). Methods only vary slightly at this point in the processing. Acetone or ether is added to dissolve the cocaine base and the solution is filtered to remove undesired material. Hydrochloric acid is then added to the cocaine solution to precipitate (crystallize) the cocaine, forming cocaine hydrochloride which is dried to produce the final product (DEA 1993).

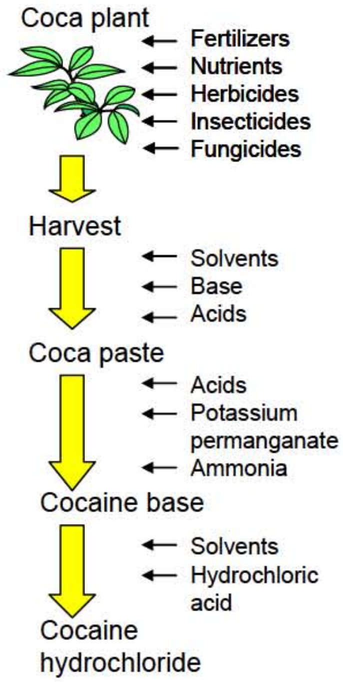

Figure 2 Steps in the production of cocaine from coca

1.1.2 Heroin

Opium poppies (*Papaver somniferum*) are cultivated for the naturally occurring morphine found in the seedpods. The morphine is further processed to produce heroin (ONDCP 2004).

1.1.2.1 Cultivation

In areas of new development, opium poppy fields are cleared using slash-and-burn methods (DEA 2002). Once the fields have been seeded, it takes approximately 3 months for the plants to mature. Opium poppies, like any other crop, are subject to damage by various insects, fungi, and competition by weeds. Aphids attack the leaves and stems, and root weevils cause damage to the root system. Other insects attack the flower, or the capsule itself. Various seed-borne diseases, such as leaf blight and capsule infection, cause seedling decay and a reduction in germination. There are also a variety of fungal, bacterial, and viral diseases affecting opium poppies, which necessitates the use of pesticides to control their spread. Herbicides are also used to control weed populations, which would otherwise consume valuable soil nutrients (CBN 2004).

1.1.2.2 Harvesting

After flowering, the petals fall off after a week or so, leaving a seed capsule. The capsule is scored, and the sap (opium gum) that oozes out is collected by hand. The capsule is scored several times until the gum is exhausted.

1.1.2.3 Heroin production

The opium gum is converted into the intermediate product, morphine. This process involves mixing the opium with lime in boiling water, which causes the formation of a white layer (morphine) on the surface. The morphine is drawn off and reheated with ammonia, which is then filtered and boiled again until a brown paste is obtained. The process of converting morphine into heroin requires several substances, mainly acetic anhydride. Morphine and acetic anhydride are mixed and heated, and then water and chloroform are added to produce a precipitate containing organic wastes, which can then be removed. Sodium carbonate is used to precipitate the heroin, and it is filtered out of solution using activated charcoal. The next step involves the use of ethanol to purify the heroin. The ethanol is evaporated off, and the heroin is further purified with ether and hydrochloric acid.

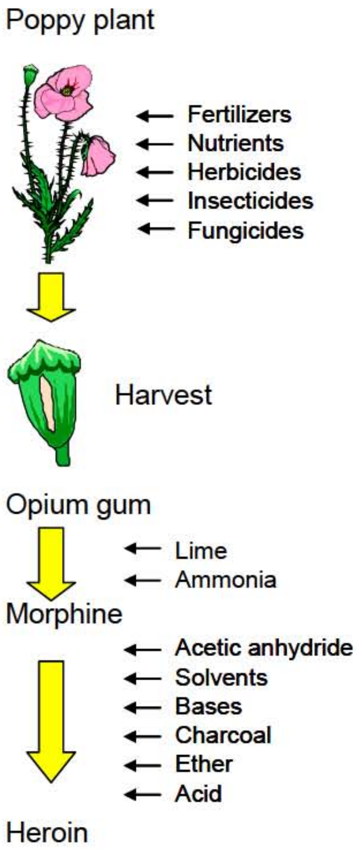

Figure 3 Steps in the production of heroin

1.2 ENVIRONMENTAL IMPLICATIONS OF ILLICIT DRUG PRODUCTION

The practice of the cultivation of crops for the production of illicit drugs may have adverse effects on the environment. These begin with clear-cut and slash-and-burn methods employed by the farmers to clear new land. Without the protective vegetative cover, soil erosion occurs and landslides and run-off can contaminate nearby streams and other bodies of water with sediments. These impacts will also occur with the clearing of land for agricultural purposes and are severe. However, they are not the subject of this Tier-2 hazard assessment.

The many substances that are used in the cultivation, processing, and refinement of illicit drugs have been described and a Tier-1 hazard assessment carried out previously (CICAD/OAS 2004). These represent a potential threat to the environment. Over 90% of farmers use various forms of biocides and fertilizers on their crops. Since the quality of the tropical soil found in the areas where illicit production occurs is poor, fertilizers and growth stimulants are used to increase crop production. As discussed above, pesticides are also used to control weeds, and to protect the crops from insects, fungi, and other pests (OAS 2004). Pesticides as well as the substances used in the refining process may enter surface waters, contaminating drinking water of both humans and animals, as well as affecting freshwater aquatic life.

2 SUBSTANCES USED IN THE PRODUCTION AND REFINING OF COCAINE AND HEROIN

The substances included in this review are a subset of those selected from the compounds reviewed in a Tier-1 assessment conducted in 2004 (CICAD/OAS 2004). These substances and, where known, the amounts seized by authorities in Colombia between 1999 and 2002 are listed in Tables 1 and 2. Although the quantities seized were known for some of the substances, these quantities may not reflect the total amounts used as it is expected that significant amounts were not seized or confiscated. It is unknown how accurately the reported amounts reflect the total amounts used but they likely significantly underestimate the actual use. In the absence of other data, it was assumed for this project that the amounts seized were proportional to the total use.

No use data were available for the pesticides and all of those identified were included. Substances that were seized as both solids and liquids were assessed only as solids. Substances that were used in only minor amounts (less than 100 kg or 100 L per year) or the use of which had declined to less than 100 kg per year between 1999 and 2002 were not included in the original review (CICAD/OAS 2004) and are also excluded here.

Table 1. Pesticides used in the production of coca and opium poppy in Colombia (CICAD/OAS 2004).

Pesticide[1]	Substance class	Use
2,4-D	Phenoxy	Herbicide
Atrazine	Triazine	Herbicide
Carbaryl	Carbamate	Insecticide
Carbendazim	Benzimidazole	Fungicide
Carbofuran	Carbamate	Insecticide
Chlorpyrifos	Organophosphorus	Insecticide
Copper Oxychloride	Metal salt	Fungicide
Cypermethrin	Synthetic pyrethroid	Insecticide
Diazinon	Organophosphorus	Insecticide
Diuron	Urea	Herbicide
Endosulfan	Organochlorine	Insecticide
Furadan	Carbamate	Insecticide
Glyphosate[2]	Organophosphate	Herbicide
Lambda Cyhalothrin	Synthetic pyrethroid	Insecticide
Malathion	Organophosphorus	Insecticide
Mancozeb	Dithiocarbamate	Fungicide
Metamidophos	Organophosphorus	Insecticide
Methomyl	Carbamate	Insecticide
Methyl Parathion	Organophosphorus	Insecticide
Monocrotophos	Organophosphorus	Insecticide
Paraquat	Bipyridilium	Herbicide

Table 1. Pesticides used in the production of coca and opium poppy in Colombia (CICAD/OAS 2004).

Pesticide[1]	Substance class	Use
Prophenophos	Organophosphorus	Insecticide
Wax up Waxal (Dinitroaniline)	Dinitroaniline	Herbicide

[1] In alphabetical order, no priority implied.

[2] Glyphosate was omitted from further assessment in this report as it is the subject of a more detailed review.

A number of solid substances used in the refining of drugs of natural origin were seized between 1999 and 2002. Solids are listed in Table 2 and liquids in Table 3.

Table 2. Solid substances used in the production of cocaine and opiates in Colombia (CICAD/OAS 2004).

	Amount seized per year (kg)			
Substance[1]	1999	2000	2001	2002
Activated charcoal	36,681	49,323	84,141	93,057
Ammonium chloride	480	7	450	350
Ammonium nitrate	-	-	2390	9,350
Ammonium sulfate	-	-	-	900
Calcium carbonate	500	150	255	1570
Calcium chloride	7,371	33,073	56,985	146,040
Cement, grey	142,818	197,646	502,857	1,053,372
Cement, white	-	-	-	18,700
Lime	24,807	49,783	155,507	220,259
Potassium chloride	2,290	4,766	1,456	34,750
Potassium hydroxide	375	1,425	-	4,700
Potassium nitrate	2	-	2,150	2,390
Potassium permanganate (sum)	71,284	171,798	51,641	80,639
Sodium bicarbonate	52	4,827	8,538	9,939
Sodium carbonate	531,095	248,136	59,521	128,571
Sodium chloride	28,154	17,046	31,594	35,161
Sodium hydroxide	73,776	69,100	111,540	122,619
Sodium hypochlorite	-	16	4,208	1,720
Sodium sulfate	5,755	970	1,852	8,667
Urea	62,685	37,995	226,394	360,237

[1] In alphabetical order, no priority implied.

Table 3. Liquid substances used in the production of cocaine and opiates in Colombia (CICAD/OAS 2004).

Substance[1]	Amount seized per year (L) 1999	2000	2001	2002
Butyl acetate	23,732	469	13,089	11,908
Ethyl acetate	97,723	76,156	23,289	15,336
Acetone	1,666,474	894,070	1,546,651	1,841,860
Hydrochloric acid	144,804	62,303	126,884	140,650
Sulfuric acid	303,732	200,404	241,903	277,538
Isopropyl alcohol	59,379	6,938	16,408	19,330
Ammonia	131,104	154,180	102,512	431,485
Acetic anhydride	9,938	284	10,855	1,045
Chloroform	465	1,457	1	273
Ethyl ether	205,984	67,704	53,989	110,098
Gasoline	621,686	1,034,880	2,013,650	2,612,820
Hexane	35,963	4,497		16,991
Kerosene	127,316	90,855	159,818	210,408
Methyl ethyl ketone MEK	88,402	69,209	10,674	41,332
Methanol	269,027	14,107	2,961	3,512
Methyl isobutyl ketone MIBK	55,943			2,086
Thinner	226,657	78,156	100,829	203,459
Toluene	3,630	208	19	6,469
Acetic acid	11	14	208	212
Nitric acid	59	6	1	5,300
Isobutyl alcohol	170		3	1,136
Petroleum ether				35,579
Methylene chloride	416	4	45	4,182
Unknowns				
Fuel oil (A.C.P.M)	32,082	325,250	346,460	948,083
Solvent No 1	203,603	116,498	435,816	280,921
Solvent No 2	6,505	3,819	5,621	11,942

[1] In alphabetical order, no priority implied.

3 SELECTION OF A PRIORITY LIST OF SUBSTANCES.

The nature of this project imposed two major considerations on the selection criteria. The assessment considered both agrochemicals as well as “laboratory” substances used for the purification of the illicit products. The assessment also integrated hazards to ecosystems as well as humans, including farm workers and “chemists” alike.

To meet these challenges, three approaches were used to select the 20 highest priority substances. Two ranking procedures were developed, a Relative Rank approach and a scoring system based upon guidelines from the Ontario Ministry of the Environment and Energy (Ontario Ministry of the Environment and Energy 1990). The third approach, Environmental Impact Quotient (EIQ) (Kovach et al. 1992), which only considered the pesticides used in the production of coca and opium crops, is also presented here.

The final selection of the priority was achieved by assimilating the three aforementioned approaches. Good agreement was found between the different ranking procedures, suggesting that the approach taken was satisfactory for the task at hand.

3.1 RELATIVE RANKING

The relative rank approach sorted the substances used in the production of cocaine and heroin by the addition of relative rank positions for the following selection categories; mammalian toxicity (oral LD50), most sensitive terrestrial LD50, most sensitive aquatic LC50, and persistence (half-life). For each selection category, the substances were ranked and given a score as determined by their relative position. The final score was determined by a summation of the scores from all categories.

The scoring of substances in each category was based upon the most sensitive value reported in the Tier-1 document (CICAD/OAS 2004). For the toxicity categories, which included mammalian toxicity, most sensitive terrestrial species, and the most sensitive aquatic species, the lowest LC50 or LD50s respectively were given the lowest score. For the persistence category, values with the longest half-life were given the lowest scores. Thus, substances identified in the Tier 1 assessment (CICAD/OAS 2004) were ranked from most toxic to least toxic and assigned a score consecutively, beginning from one. For the persistence category, substances were ranked from the longest half-life to the shortest and given a score from one. Substances with the same toxicity value or half-life were given the same score and the subsequent score was not used, similar to the classification for a sporting event.

To flag data insufficiencies and to ensure thorough selection of the priority list, a series of fractions were included in the relative ranking score. Within each category, there were substances with no readily available data, and these substances were labelled and given a “worst case” score, to ensure these substances ranked high and were only excluded by further evaluation. The assigned fractions are presented below in Table 4. Where there were no reported values within the Tier-1 assessment document, a fraction was added to the scoring system for each category missing data. Because the relative rank selects high hazard substances based upon the lower scores, those substances with missing data were promoted to the top of the ranking list. The data missing from such substances can be identified by the decimal value associated with the final score. Extra information would be required to exclude these compounds from the final group of twenty. Conversely, integer scores indicate a complete data set for respective compounds.

Table 4. Insufficient data; interpretation of decimals within the scoring system

Missing Data	Assigned score	
	Relative Rank Approach	OMEE
Terrestrial LD50	0.5	10.1
Aquatic LD50	0.5	10.01
Half life	0.25	0.0001[a]
Mammalian LD50	0.01	10.001

[a] Note that no "worst case" score was applied to the OMEE so as to avoid skewing score results - almost 50% of substances do not have clear persistence values.

The resultant rank and respective scores of about half of the identified substances are presented in Table 5. Immediately obvious are the lowest scores for Solvents 1 and 2 and Thinner (Petroleum 50), an artifact of limited toxicity data. Many of these data insufficiencies arise from the inability to expose an organisms in a toxicity test to sufficient quantities to cause an observable effect. These scores also represent the worst case where no data for any of selection categories was available and the final score is entirely from the assigned fractions. These two substances were not considered further.

Cement and urea were also excluded from the Tier-2 assessment based upon similar justification. The final score for cement (Table 5) indicates that there were no readily available data for persistence or oral mammalian toxicity. Although no values were given, cement was found to be non toxic to mammals via oral ingestion and a lack of persistence data does not indicate extended toxic exposure. Because urea is a very common substance used for agriculture as well as a common intermediary in ecosystem processes, and not expected to cause significant toxic effect, it was not considered further in this assessment.

From the remaining list, it is clear that the pesticides show the greatest hazard (Table 5). The integration of mammalian oral exposure and ecosystem hazard resulted in pesticides representing half of the top 30 substances. This is not a surprising result because pesticides are designed to be biologically active. With the solvents and thinner excluded, endosulfan was at the top of the relative ranking list, with a full data set as indicated by the integer score. Some non-pesticide substances were found in the top 20. For example, nitric acid and potassium chloride can be found in the list although the persistence of these substances is not characterized. This indicates that acute exposure would be the main concern for these two substances.

Table 5. The position of substances determined by the relative hazard scoring approach

Rank	Substance	Relative Score[a]
1	Solvents 1 and 2[b]	1.26
2	Thinner (Petroleum 50)[b]	1.26
3	Endosulfan	13

Table 5. The position of substances determined by the relative hazard scoring approach

Rank	Substance	Relative Score[a]
4	Diazinon	26
5	Methyl parathion	26
6	Lambda cyhalothrin	30
7	Carbofuran	36
8	Cypermethrin	38
9	Chlorpyrifos	38
10	Methomyl	40
11	Monocrotophos	41
12	Paraquat	41.25
13	Nitric acid	45.76
14	Potassium chloride	49.25
15	Carbendazim	50
16	Methamidophos	55
17	Potassium nitrate	58.25
18	Cement (White/Grey)[b]	58.76
19	Urea[b]	63.5
20	Potassium permanganate	69.25
21	Prophenophos	70
22	Ammonium chloride	70.25
23	Fuel oil (ACPM)	70.25
24	Copper oxychloride	72.25
25	Sodium hydroxide	73.25
26	2,4-Dichlorophenoxyacetic acid	74
27	Carbaryl	74
28	Potassium hydroxide	84.25
29	Hydrochloric acid	86.25
30	Chloroform	90
31	Ammonia	90
32	Malathion	91

[a] Integers represent complete data set; 0.5 assigned for lack of either mammalian or aquatic toxicity values; 0.25 assigned for lack of persistence data; 0.01 assigned for no mammalian oral toxicity. [b] Excluded substance; no readily available evidence to show significant toxicity

The relative rank and subsequent scoring approach integrated potential human exposure, potential ecotoxicological exposure, and persistence, from the readily available data. From the list of substances used in the production and purification of heroin and cocaine, the majority of the substances identified within the top 20 were pesticides. A number of substances were identified as having limited data, however, on closer inspection, they were found not to pose a large hazard. They were commonly used substances, such as cement, for which there is widespread experience of low hazard other than issues of lesser importance, such as skin irritation. These were excluded from further assessment. As this approach did not provide a magnitude of hazard, two other approaches, EIQ and OMEE were used for the final selection of the priority list.

3.1.1 The Ontario Ministry of the Environment and Energy scoring system

To ensure rigor in the selection process, a regulatory approach was used in conjunction with the other approaches. A scoring system based upon The Ontario Ministry of the Environment and Energy (Ontario Ministry of the Environment and Energy 1990) hazard assessment protocol was also used to fulfil the project criteria, namely, that government criteria, other than those from the United States or Colombia, were used to ensure fairness and objectivity.

The OMEE procedure involved assigning a score for each selection category and subsequent ranking. The final rank was determined by a summation of values assigned to data for selected categories, including mammalian toxicity (oral LD50), fish toxicity (LC50), daphnia toxicity (LC50) and persistence (Ontario Ministry of the Environment and Energy 1990). Also Appendix A-1 for a more detailed explanation of the scoring system. In contrast to the relative approach, the scores were given based upon the magnitude of toxic value, whereas, for the relative approach, the score was assigned by relative toxicity. The higher the score for the OMEE approach, the greater the hazard associated with the substance.

Similarly to the relative hazard approach, a "worst case" score and fractions (as detailed in Table 4) were included in the procedure to flag data insufficiencies. Where there were no reported values, high scores were assigned because the OMEE approach selects high hazard based upon the largest numbers. Table 4 summarises these assigned values and fractions. Compounds with limited available data were given high scores that promoted them towards the top of the selection list. Other selection criteria would be required to exclude these compounds from the final group of high priority chemicals. Also, similarly to the relative ranking approach, integers represent a complete data set for respective compounds.

The resultant ranking based upon the OMEE scoring method is presented in Table 6. There appears to be good agreement between the two methods. Similarly to the relative ranking, pesticides are heavily represented at the top of the list. Endosulfan and diazinon fill the top two positions, concordant with the relative ranking approach.

Those substances with insufficient data to enable a meaningful comparison, including solvents-1 and -2, thinner (Petroleum 50), and urea are also identified in the top section of the list, showing further agreement between the two approaches (see Tables 5 and 6). The concordant identification of these compounds by two different approaches shows that the assigning of worst case numbers where there were no readily available data ensures no substances were overlooked. Such compounds are marked by *superscript "b"* in Table 6, and after additional review appear not to pose a significant hazard. As such, these substances were not included in the final priority list.

Table 6. The results of the hazard scoring system based upon The OMEE hazard assessment methodology (Ontario Ministry of the Environment and Energy 1990)

Rank	Substance	OMEE Score[a]
1	Endosulfan	38
2	Diazinon	36
3	Carbendazim	34
4	Chlorpyrifos	34
5	Cypermethrin	34
6	Lambda cyhalothrin	33
7	Carbofuran	32
8	Solvents 1 and 2[b]	30.1111
9	Thinner (Petroleum 50)[b]	30.1111
10	Urea[b]	28.011
11	Methomyl	28
12	Methyl parathion	26
13	Pendimethalin	26
14	Carbaryl	24.001
15	Malathion	24.001
16	Prophenophos	24
17	Nitric acid	22.1011
18	Activated charcoal[b]	22.0111
19	Atrazine	22
20	Chloroform	22
21	Diuron	22
22	Petroleum ether[b]	20.011
23	Potassium chloride	20.0101
24	Monocrotophos	20
25	Fuel Oil (ACPM)	18.0011
26	Potassium hydroxide	18.0011
27	Sodium hydroxide	18.0011
28	Hydrochloric acid	18.0011
29	2,4-Dichlorophenoxyacetic acid	18.001
30	Paraquat	18.0001
31	Potassium permanganate	18.0001
32	Methamidophos	18

[a] Integers represent complete data set; 10.1 assigned for no mammal oral tox; 10.01 assigned for no fish tox; 10.001 assigned for no daphnia tox; 0.0001 assigned for no persistence data.

[b] Excluded substance; no evidence to show significant toxicity

The Relative Hazard approach combined ecotoxicity and human health hazards well. No obvious skewing of the scoring system was observed when separate criteria rankings were combined. (NB: mammalian toxicity values were included in the ecotoxicity assessment if they were the most sensitive terrestrial value. When this was done no obvious bias was observed).

3.1.2 Environmental impact quotient

The environmental impact quotient (EIQ) scoring system used for this assessment was developed by the Integrated Pest Management Program at Cornell University (Kovach et al. 1992) and is outlined in Figure 4. Briefly, the EIQ scores the potential hazard for a pesticides based on measures of toxicity such as the LD50 and LC50 (dose or concentration at which 50% mortality is observed in treated groups as compared to controls), and measures of potential exposure such as half-life, runoff or leaching potential, and pattern of use (Gallivan et al. 2001). The EIQ equation is based on the average of three principal components of agricultural production systems: a farm worker component, a consumer component, and an ecological component. The farm worker component includes potential effects to applicators and fieldworkers; the consumer component includes the potential effects of residues on the consumer and of groundwater contamination; and the ecological component includes the potential effects on aquatic organisms, bees, birds, and beneficial arthropods (Gallivan et al. 2001). Each component in the equation is given equal weight in the final analysis, but within each component, individual factors are weighted differently (Kovach et al. 1992). Coefficients used in the equation to give additional weight to individual factors are also based on a one to five scale. Factors carrying the most weight are multiplied by five, medium-impact factors are multiplied by three, and those factors considered to have the

$$EIQ = \{\overbrace{\boxed{C[(DT*5) + (DT*P)]}}^{\text{Farm Worker Component}} + \overbrace{\boxed{[(C*((S+P)/2)*SY) + (L)]}}^{\text{Consumer Component}} + \overbrace{\boxed{[(F*R) + (D*((S+P)/2)*3) + (Z*P*3) + (B*P*5)]}}^{\text{Ecological Component}}\}/3$$

DT = dermal toxicity, C= chronic toxicity, SY = systemicity, F = fish toxicity, L = leaching potential,
R = surface loss potential, D = bird toxicity, S = soil half-life , Z = bee toxicity,
B = beneficial arthropod toxicity, P = plant surface half-life

Figure 4 Formula for calculating the Environmental Impact Quotient (EIQ) for individual pesticides (Kovach et al. 1992).

least impact are multiplied by one (Kovach et al. 1992). A consistent rule throughout the model is that the impact potential of a specific pesticide on an individual environmental factor is equal to the toxicity of the substance multiplied by the potential for exposure (Kovach et al. 1992).

Environmental impact quotient values for 17 of the 21 listed pesticides were directly obtained from Kovach et al. (2005). For the remaining 4 pesticides, EIQs were calculated using input data obtained from the British Crop Protection Council (BCPC 2002-2003) according to the equation outlined in Figure 3. For pesticides with missing data fields, a worst case value was inserted into the equation for the purposes of caution. Pesticides were ranked with respect to EIQ value from highest to lowest, with those pesticides obtaining the highest score (highest hazard) ranked at the top. Table 7 outlines the results of the EIQ ranking classification.

Table 7. Results of the EIQ ranking of pesticides (Kovach et al. 1992)

SUBSTANCE	(Farm Worker+ Consumer+ Toxicity Ecological)/3	C(DT*5) +C(DT*P) Farm Worker	C*((S+P)/2) *SY)+L Consumer + Leaching	(Fish)+(Bird) +(Bee)+ (Beneficial) Ecology	Rank
Carbofuran	56.8	72.0	29.0	69.4	1
2,4-D	56.3	72.0	9.0	88.0	2
Chlorpyrifos	43.5	18.0	4.0	108.6	3
Lambda cyhalothrin,	43.5	20.7	3.5	106.5	4
Diazinon	43.4	6.9	2.5	120.9	5
Endosulfan	42.1	36.0	7.0	83.2	6
Methamidophos	36.8	45.0	9.5	56.0	7
Methyl parathion	35.2	54.0	4.0	47.7	8
Monocrotophos	34.3	30.0	8.0	65.0	9
Paraquat	31.0	8.0	5.0	80.0	10
Methomyl	30.7	6.0	11.0	75.0	11
Pendimethalin	29.7	8.0	5.0	76.0	12
Cypermethrin	27.3	9.0	4.0	69.0	13
Prophenophos	26.0	18.0	2.0	58.0	14
Malathion	23.2	21.0	4.5	44.0	15
Atrazine	22.9	8.0	7.0	53.6	16
Carbaryl	21.7	9.0	2.5	53.7	17
Carbendazim	20.7	6.0	14.0	42.0	18
Diuron	20.5	15.0	10.5	36.0	19
Mancozeb	14.6	12.0	3.0	28.9	20

Based upon comparison of the three selection methods, there were some obvious choices regarding the final priority list. Those compounds that appear in all ranks were included; Table 8 lists these substances. The integration of the final priority list from the information provided by the three approaches was based upon the assimilation of the ranks of each compound in each method as well as background material regarding the nature of the substances, especially when no data were available for use in the scoring approaches.

Many of the compounds, 13 out of 20, were selected by all three of the ranking approaches, 16 out of 20 were selected by 2 or more, where both human and ecotoxicological hazards were integrated. The use of the combined ecotoxicity and human health ranking might marginally weight the human health hazard, because similar data (terrestrial toxicity and mammalian toxicity) are included. It was considered acceptable to tolerate this possible small bias, as there is good reason to suspect that good industrial hygiene and good personal protection from pesticides are not used.

Table 8 contains the final priority list, derived from an integration of all three methods. Most of the substances in the priority list are pesticides. Without adequate education, training and proper precautions, pesticides can cause acute and chronic effects to humans and the ecosystem. Because pesticides are designed to inflict biological damage, to kill, or otherwise reduce the population of pest species, the relatively large representation of these compounds in the final priority list was expected.

Table 8. Final priority list

Ranking	Compounds	Notes[a]
1	Endosulfan	O, E, R
2	Methyl parathion	O, E, R
3	Diazinon	O, E, R
4	Lambda cyhalothrin	O, E, R
5	Carbofuran	O, E, R
6	Cypermethrin	O, E, R
7	Chlorpyrifos	O, E, R
8	Methomyl	O, E, R
9	Monocrotophos	O, E, R
10	Carbendazim	O, E, R
11	Methamidophos	O, E, R
12	Prophenophos	O, E, R
13	Carbaryl	O, E, R
14	Pendimethalin	O, E, high ecological toxicity
15	2, 4-D	E, high human toxicity
16	Paraquat	R, E, and human exposure
17	Fuel oil (ACPM)	R, O, and volume of use
18	Potassium chloride	R, O, and human exposure
19	Nitric acid	Human toxicity and volume used
20	Potassium permanganate	Human toxicity and volume used
Exclusions	Sodium hydroxide	Low ecotoxicity, probable low exposure – Tier-1
	Copper oxychloride	R, E, (persistent not active) – Tier-1
	Atrazine	Low mammalian toxicity – Tier-1
	Malathion	Low E and R – Tier-1
	Potassium nitrate	Low exposure probable – Tier-1
	Ammonium chloride	Low exposure probable – Tier-1
	Solvent 1 and 2	Low mammalian toxicity – Tier-1
	Activated charcoal	Low toxicity indicated – Tier-1
	Petroleum ether	Low toxicity indicated – Tier-1
	Urea	Low toxicity indicated – Tier-1
	Thinner	Low mammalian toxicity – Tier-1

[a] Explanation of notes; O= selected by OMEE approach; R= selected by Relative Rank Approach; E= selected by EIQ approach.

There are four non-pesticide substances included in the priority list (Table 8). These substances were included because of their high scores in the two approaches that combined both human and ecotoxicological hazards. As previously mentioned, non-pesticide substances were not included in the EIQ method. The inclusion of fuel oil

(ACPM), potassium chloride, nitric acid, and potassium permanganate in the priority list was mainly because of potential hazard to humans and terrestrial ecosystems, as well as the relatively high volume of use (Tables 2 and 3).

A number of substances were excluded from the priority list, despite being ranked relatively high by the selection criteria. Most of these substances, as listed in Table 8, were found to be of relatively low toxicity to humans and the ecosystem. They were present in the respective rankings because of the “no data” condition included in the selections. Therefore, after review, sodium hydroxide, potassium nitrate, ammonium chloride, solvents 1 and 2, activated charcoal, petroleum ether, urea, and thinners were excluded from the priority list. Three pesticides, copper oxychloride, atrazine, and malathion were also excluded from the final priority list to enable the inclusion of the non-pesticides substances, believed to be more of a hazard, especially after consideration of the human health risks.

4 CONDITIONS OF USE OF THESE SUBSTANCES

Many of the substances selected for this Tier-2 hazard assessment are pesticides. Because they are toxic to one or more groups of organisms, they tend to rank high in scoring systems that consider human and ecological hazard. All substances can present a hazard if the exposure is sufficient to exceed the threshold of toxicity. Because of their properties, these substances generally have greater toxicity to humans, the environment, or both and therefore have greater intrinsic hazard.

Because these substances present potential hazards to human or the environment does not mean that they cannot be used safely. It is important to note that the word “safely” does not imply that these substances are absolutely safe; it merely indicates that, with the proper use directions, application equipment, protective equipment, and applicator training, they can be used without an unacceptable risk to humans or the environment. These pesticides are registered for use in a number of jurisdictions, as well as in Colombia (with the exception of endosulfan). Their registration is predicated on the assumption that they will be used correctly and with appropriate knowledge. Their inclusion in this report does not imply that they should be further restricted or banned; it merely means that they have the greatest potential for hazard.

Little factual information is available as to how these substances are used in the production of cocaine and heroin in Colombia. Anecdotal information suggests that, in some cases, the products are not correctly stored; workers are not trained, not able to read the appropriate instructions on the label, use greater than recommended rates, use inappropriate application techniques, mix products together in inappropriate ways, and do not use adequate protective equipment. In other instances, they may be correctly used; however, the frequency and extent of correct and incorrect uses have not been documented. It is for this reason that doses received by bystanders and off-target drift cannot be estimated from other situations where more data are available. It is also for this reason that a full risk assessment is not possible. For some substances, such as paraquat, information from other jurisdictions shows that, when incorrectly used, serious injury can result.

5 MAMMALIAN AND ENVIRONMENTAL DATA – METHODS

5.1 SOURCES AND SELECTION OF TOXICITY AND OTHER DATA

Toxicological and other data on the selected substances were obtained from the literature. Primary sources were published works such as reference texts, books, and reviews. Extensive use was made of databases and compilations of data from National and International agencies such as the United States Environmental Protection Agency (USEPA), the Food and Agricultural Organization (FAO), and the World Health Organization (WHO). Many of these sources are available on the internet and these are referenced where appropriate to allow the user of this report access to additional information and to future updates. These sources of information are listed in the Table below:

Table 9. List of internet sources of data

Database	Web address
Chemical Registry System	http://www.epa.gov/srs/
ChemWeb	http://www.chemweb.com/databases
ECOTOX: Database of Toxic Effects to Aquatic and Terrestrial Species	http://www.epa.gov/ecotox/ecotox_home.htm
EXTOXNET – EXTension TOXicology NETwork	http://ace.orst.edu/info/extoxnet/
MSDS search	http://www.msdssearch.com/
National Library of Medicine Specialized Information Systems	http://toxnet.nlm.nih.gov
NIOSH – National Institute for Occupational Safety and Health	http://www.cdc.gov/niosh/database.html
NTP-Health and Safety reports-National Toxicology Program	http://ntp-server.niehs.nih.gov
SRC-Environmental Fate Database	http://esc.syrres.com/efdb.htm
Environmental Health Criteria Monographs (EHCs)	http://www.inchem.org/pages/ehc.html
WHO Environmental Health Criteria	http://www.who.int/ipcs/publications/ehc/en/

Other sources of information are referenced in the individual appendices for each substance. The information on these substances was compiled in a standardized format under the following headings:

IDENTITY
GENERAL CHARACTERISTICS
  Physical/chemical properties
  Uses
ENVIRONMENTAL FATE
  Persistence
  Movement
  Bioaccumulation and biomagnification
HUMAN HEALTH EFFECTS
  Mammalian toxicological data
    Acute
    Chronic
  Toxicokinetics
    Mechanism of action
    Adsorption, distribution, metabolism, and excretion
    Biological half-life
    Major health effects
ENVIRONMENTAL EFFECTS
  Toxicological data
    Acute
    Chronic
  Effects on organisms in the environment
REGULATORY STATUS IN OTHER JURISDICTIONS
SUMMARY CONCLUSIONS
REFERENCES

5.2 PROCESSING AND SELECTION OF MAMMALIAN TOXICITY DATA

Mammalian toxicity data were tabulated where appropriate and discussed in the text with respect to the mechanisms of action and other relevant interpretive information. All key data that could be obtained were included. Since the objective of the report was hazard assessment, the main focus was on data relevant to description of hazard to mammals (including data from humans where available) and the environment. Thus, the information is not totally inclusive; however, appropriate sources of data are referenced should the reader desire additional information. Where appropriate, the structure of the substance is shown and pathways of metabolism are illustrated with diagrams.

5.3 PROCESSING AND SELECTION OF ENVIRONMENTAL TOXICITY DATA

Environmental effects information and toxicity values were obtained from the USEPA ECOTOX database, from other databases, and from peer-reviewed literature. The comparable endpoints were separated, units standardized, and organisms were sorted according to taxonomy and sensitivity.

Acute toxicity data were selected to include only responses related to survival and growth. These included LC50 based on mortality, EC50 based on morbidity or growth for organisms such as algae. Acute exposures were defined as those lasting for between 24 and 120 h. Where multiple data values for a species were available, they were selected for the quality of the study and its design. The order of selection of studies for inclusion was flow-through > renewal > static and measured > nominal concentration. For organisms with more than one data value that met the criteria of selection (N>1), the geometric mean for the LC/EC50s were calculated. The N-value for number of data points is presented in the Tables.

Chronic toxicity data were usually less numerous but were treated in a manner similar to that for acute data. Chronic toxicity tests were generally conducted over a period of more than 120 h.

Each of these substances is described in a series of appendices to this document. Each is a stand-alone document with its own tables and references. They are arranged in alphabetical order with no implied priority.

6 COMPARATIVE HAZARD ASSESSMENT

Since no exposure data were available for any of the 20 compounds selected for more detailed hazard assessment, estimates of exposures in humans and the environment were made. These exposures were calculated for the pesticides only as the other substances assessed using a different method. These pesticide exposure estimates were conducted using the same procedures as were used for worst case estimates of glyphosate exposures during the aerial application of glyphosate and Cosmo-Flux® for the purposes of eradication of coca (Solomon et al. 2005). This allowed the exposures to these pesticides to be compared to those of glyphosate.

6.1 PESTICIDE EXPOSURES

6.1.1 Humans

Pesticides are applied with hand-operated backpack sprayers in coca fields (Figure 5). Formulated products are diluted with local sources of water from a nearby stream, river, or well. Mixing and loading of the sprayer usually takes place close to the water source and empty containers are discarded in the field. Other than anecdotal information, there are little data on the use of protective equipment, however, from field observations; it appears to not be widely used.

Figure 5 Backpack sprayer in coca field, container of pesticide (a glyphosate formulation) and measuring containers, and backpack sprayers. (Photographs in San Jose del Guaviare and Nariño, 2005).

As for the glyphosate risk assessment (Solomon et al. 2005), the most likely scenario is the partially clothed human with a cross-sectional area of 0.25 m² exposed to the spray (Figure 6). For the purposes of this assessment, it was assumed that people conducting pesticide applications would be exposed via the same route as a bystander receiving an accidental overspray. However, this is likely an underestimate as an applicator would be handing concentrated material more often. In general, applicators have higher exposures than bystanders (Ecobichon 1998).

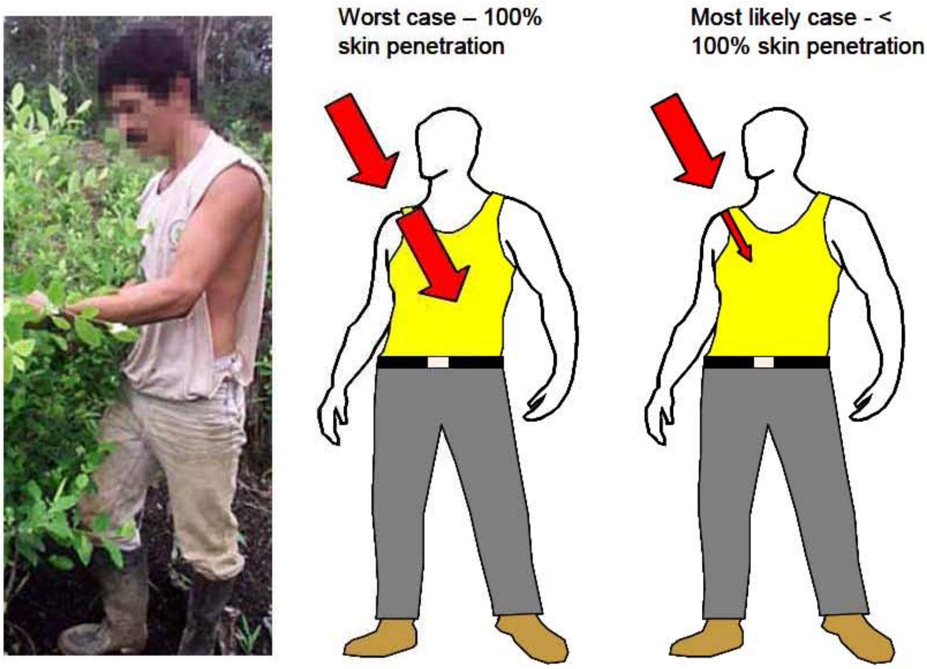

Figure 6 Example of clothing used by a coca grower and illustrations of likely exposure scenarios for pesticide exposure

Total body dose for each of the sixteen pesticides contained in the priority list was calculated from the pesticide application rate, dermal absorption of the pesticide, average human body mass, and surface area exposed. As for glyphosate, body dose calculations were computed using two different surface areas 0.25 m^2 (face, forearms, and hands) and 2 m^2 (face, hands, arms, feet, legs, and torso), which correspond to different clothing coverage scenarios. Pesticide absorption values (expressed as percent absorption) and application rates were obtained from government reports and the primary literature (See Table 11 for references).

The following equation was used to estimate the body dose in mg/kg:

$$\text{Body dose} = \frac{[\text{Application rate (kg/m}^2)] * [\text{surface are (m}^2)] * [\text{dermal absorption (\%)}]}{\text{Body mass (70 kg)}}$$

Table 11. References for dermal penetration, application rates and RfDs.

Chemical	Reference for dermal penetration	Reference for application rate	Reference for RfD
2,4-D	(Harris and Solomon 1992)	(BCPC 2002-2003)	(USEPA 2005)
Carbaryl	(Wester and Maibach 1985)	(BCPC 2002-2003)	(USEPA 2005)
Carbendazim	(Dorn and Keller 1980)	(BCPC 2002-2003)	(USEPA 1997b)
Carbofuran	(Liu and Kim 2003)	(DCC 2005)	(USEPA 2005)
Chlorpyrifos	(USEPA 2000a)	(Dow Agrosciences 2005)	(USEPA 2005)
Cypermethrin	(Woollen et al. 1992)	(IPCS 1992)	(USEPA 2005)
Diazinon	(Wester et al. 1993)	(BCPC 2002-2003)	(USEPA 2000c)
Endosulfan	(USEPA 2000b)	(BCPC 2002-2003)	(USEPA 2005)
Lambda cyhalothrin	(PMRA 2003)	(IPCS 1990)	(USEPA 2005)
Methamidophos	(Bagos and Beatty 1991)	(BCPC 2002-2003)	(USEPA 2005)
Methomyl	(USEPA 1998)	(IPCS 1996)	(USEPA 2005)
Monocrotophos	(Wester and Maibach 1985)	(NRA 2000)	(USEPA 1999b)
Paraquat	(Wester and Maibach 1985)	(BCPC 2002-2003)	(USEPA 2005)
Parathion	(Wester and Maibach 1985)	(IPCS 1978)	(USEPA 1992)
Pendimethalin	(USEPA 1997a)	(BCPC 2002-2003)	(USEPA 2005)
Profenophos	(USEPA 1999a)	(BCPC 2002-2003)	(USEPA 1999c)

6.1.2 Environmental

As for the human exposures, similar procedures to those used to estimate surface water concentrations for glyphosate (Solomon et al. 2005) were used to estimate concentrations of pesticides in water. The maximum concentration of pesticide water used for the hazard assessment of surface waters was estimated based on worst-case procedures, where direct overspray of water of different depths is assumed. Three assumptions of water depth were used, the USEPA assumption of a water depth of 2 m (farm pond SETAC 1994), the European assumption of a farm pond, 0.3 m, (Riley 1993), and a depth of 0.15 m (forest pool or wetland). For an application rate of 1 kg/ha (1×10^{-4} kg/m^2), the assumed maximum concentrations are for these three depths are 50, 333, and 670 µg/L, respectively. These base values were adjusted by multiplying the assumed concentration at an application rate of 1 kg/ha by the suggested label rate (Table 11 and 13) in order to obtain specific exposure concentrations for individual pesticides.

Exposures to bees were determined from the recommended application rates (Table 11 and 14) based on recommended procedures (Felton et al. 1986).

Concentrations of pesticides in soil were estimated using the assumptions based on a rate of application of 1 kg/ha to soil with a bulk density of 1.5 kg/L. For even distribution in the top 2.5 and 5.0 cm, this would give concentrations of 2.67 and 1.34

mg/kg soil, respectively. These values were adjusted for recommended application rates (Table 11 and 15).

6.2 HUMAN AND ENVIRONMENTAL HAZARD ASSESSMENT OF THE PESTICIDES

6.2.1 Human hazards

The exposure value obtained from calculations divided by the effects value from experimental data, results in a Hazard Quotient (HQ). A HQ which exceeds one indicates a potential for toxicity; values less than one indicate toxicity is not likely to occur. For the human assessment, hazard quotients were computed by dividing the Reference Dose (RfD) obtained from the EPA IRIS database or other EPA sources (Table 11) by the calculated body dose (Table 12). The RfD (also known as the Acceptable Daily Intake or ADI) is a commonly-used criterion for judging exposure to a number of substances, especially pesticides. The RfD is the estimated maximum amount of an agent or pesticide, expressed on a body mass basis, to which an individual in a (sub) population may be exposed daily over their lifetime without appreciable health risk (IPCS 2002). This is used to assess chronic risk and therefore provides a conservative estimate of risk. It is the same estimator that was used to assess risks of glyphosate exposures that occur spray eradication (Solomon et al. 2005) and thus serves as a useful criterion for comparative assessment of hazard. The data used in the calculation of the hazard quotients for humans are summarized in Table 12. Toxicity and estimated exposure data for glyphosate in humans are included in Table 12 for the purpose of comparison.

Table 12. Hazard quotient values for human risk to pesticide exposure based on body dose estimates and reference dose values

Chemical	Species in which absorption was measured	Percent absorption	Application rate (kg/ha)	Body dose (mg/kg/day) for and exposed area of		Reference Dose (mg/kg/d)	Hazard quotient for area exposed	
				$2\ m^2$	$0.25\ m^2$		$2\ m^2$	$0.25\ m^2$
Methamidophos	Rat	44	1.2	1.5	0.2	0.00005	30,171	3,771
Monocrotophos	Human	14.7	1.6	0.7	0.08	0.00005[d]	13,440	1,680
Endosulfan	Rats	45	2.5	3.2	0.4	0.006	536	67
Profenofos	------------------	50	1	1.0	0.2	0.005	286	36
Methomyl	------------------	100[b]	1	2.9	0.4	0.025	114	14
Diazinon	Human	3.9	0.6	0.07	0.01	0.0007	96	12
Carbofuran	Rat	7.9[a]	1	0.2	0.03	0.005	45	6
Chlorpyrifos	Human	3	1.5	0.1	0.02	0.003	43	5
Carbaryl	Human	73.9	2.0	4	0.5	0.1	42	5
Parathion	Human	8.6	1.0	0.2	0.03	0.006	41	5
2,4-D	Human	4.43	2.3	0.3	0.04	0.01	29	4
Pendimethalin	Monkey	10[c]	2.4	0.7	0.09	0.04	17	2
Lambda cyhalothrin	Rat/human	21	0.02	0.01	0.002	0.005	2	0.3
Paraquat	Human	0.3	1	0.01	0.001	0.0045	2	0.2

Table 12. Hazard quotient values for human risk to pesticide exposure based on body dose estimates and reference dose values

Chemical	Species in which absorption was measured	Percent absorption	Application rate (kg/ha)	Body dose (mg/kg/day) for and exposed area of		Reference Dose (mg/kg/d)	Hazard quotient for area exposed	
				$2\ m^2$	$0.25\ m^2$		$2\ m^2$	$0.25\ m^2$
Cypermethrin	Human	1.2	0.015	0.001	0.0001	0.01	0.1	0.01
Carbendazim	Rat	0.2	0.6	0.003	0.0004	0.08	0.04	0.01
Glyphosate[e]	Several	2	4.9	0.280	0.0350	2	**0.14**	**0.02**

[a] Calculated from the dermal absorption factor (DAF) given in units of µg/cm²/h from the surface area tested and test duration
[b] No dermal penetration data were available, therefore a default value of 100% was assigned as specified by the EPA
[c] This value was estimated by the EPA based on similar compounds
[d] This reference dose value is for dicrotophos as no RfD was available for monocrotophos
[e] Data from (Solomon et al. 2005).

From the data in Table 12, it is obvious that, compared to glyphosate, a number of pesticides used in the production of coca and poppy have much greater hazard to humans. Based on a likely exposure scenario, hazard quotients (HQ) for methamidophos, monocrotophos, endosulfan, profenofos, methomyl, and diazinon were all greater than 10. In comparison, the HQ for glyphosate was 0.02. In situations where exposures are similar, these pesticides would present a significantly greater hazard than glyphosate. With the exception of endosulfan, these pesticides are all inhibitors of acetylcholinesterase. The fact that they present a greater hazard is consistent with observations of adverse effects in terrestrial animals as well as humans in other jurisdictions. Whether this increased hazard translates into greater risk is uncertain as the frequency of exposures and the number of individuals using these substances in Colombia is unknown.

6.2.2 Hazards to aquatic organisms

The environmental HQ was calculated by dividing maximum estimated concentration in surface water by the lowest acute toxicity value for aquatic organisms obtained from the data as summarized for the individual chemicals in Appendices 1-20. Again, this is a conservative estimate but is similar to that used for the assessment of glyphosate to non-target aquatic organisms (Solomon et al. 2005) and allows for a comparative assessment of hazard. The hazard assessment data for surface water exposures are summarized in Table 13. Toxicity and estimated exposure data for glyphosate and for the mixture of glyphosate and Cosmo-Flux® as used in Colombia are included in these Tables for the purposes of comparison.

Table 13. Hazard quotient values for environmental hazard (aquatic) from pesticide exposure based on direct overspray of surface waters at the applied label rate and the lowest toxicity value for each chemical (Appendices 1-20)

Chemical	Application rate (kg/ha)	Concentration resulting from direct overspray (µg/L) Water depth (m)			Species from which lowest toxicity value was obtained	Lowest toxicity value (µg/L)	Hazard Quotient Water depth (m)		
		2	0.3	0.15			2	0.3	0.15
Endosulfan	2.5	125	832.5	1675	*Penaeus duorarum*	0.04	3,125	20,813	41,875
Chlorpyrifos	1.5	75	499.5	1005	*Gammarus pulex*	0.07	1,071	7,136	14,357
Carbofuran	1	50	333	670	*Brachythermis contaminata*	0.1	417	2,775	5,583
Monocrotophos	1.6	80	532.8	1072	*Daphnia magna*	0.2	333	2,220	4,467
Lambda cyhalothrin	0.02	1	6.66	13.4	*Americamysis bahia*	0.004	244	1,624	3,268
Diazinon	0.6	30	199.8	402	*Gammarus fasciatus*	0.2	150	999	2,010
Parathion	1	50	333	670	*Americamysis bahia*	0.6	85	564	1,136
Paraquat	1	50	333	670	*Navicula pelliculosa*	0.6	83	555	1,117
Cypermethrin	0.015	0.75	4.995	10.05	*Crangon septemspinosa*	0.01	75	500	1,005
Carbaryl	2	100	666	1340	*Oncorhynchus gilae apache*	2	50	333	670
Profenophos	1	50	333	670	*Daphnia magna*	1	45	303	609
Methamidophos	1.2	60	399.6	804	*Macrobrachium rosenbergil*	4	15	100	201
2,4-D	2.3	115	765.9	1541	*Anabaena variabilis*	10	12	77	154
Methomyl	1	50	333	670	*Daphnia magna*	13	4	26	52
Carbendazim	0.6	30	199.8	402	*Daphnia magna*	20	2	10	20
Pendimethalin	2.4	120	799.2	1608	*Daphnia magna*	280	0.4	3	6
Glyphosate (with Cosmo-Flux®)[a]	4.9	245	1,632	3,283	*Oncorhynchus mykiss*	1,850	**0.1**	**0.9**	**1.8**

[a] Data from (Solomon et al. 2005)

The hazard quotients calculated from environmental exposures in surface waters and the effect measure for the most sensitive aquatic organisms were also greater than 10 for several pesticides. In fact, for shallow waters (15 cm), only pendimethalin and glyphosate (plus Cosmo-Flux®) had HQs less than 10. The HQ for endosulfan was, by comparison, 41,000. Once again, most of the other pesticides used in the production of coca and poppy present a significantly greater hazard to aquatic organisms than glyphosate (and Cosmo-Flux®). Again, whether this represents a significant risk to the environment is uncertain as the frequency of use is not known. However, proximity of coca and poppy fields to surface waters is a constant. Although not known exactly, the likelihood of contamination by pesticides used by coca and poppy growers and that from the use of glyphosate for eradication spraying is the same and these hazards can be used for comparative purposes.

6.2.3 Hazards to bees

Bees and other pollinating insects are important in agriculture and in the survival of many insect-pollinated plants. For this reason, they are tested for sensitivity to pesticides as part of the registration process. A general guideline has been suggested for assessing hazard of pesticides to honeybees (Felton et al. 1986). This is based on empirical observations in field tests with a number of pesticides. To use this, the grams of active pesticide ingredient applied per ha of field is divided by the topical LD50 for the pesticide in µg/bee as determined in laboratory tests. The quotient is then compared to the hazard ratio criteria and the risk estimated. A hazard ratio of < 50 indicates low risk; 50 - 2,500 indicates moderate risk; and > 2,500 indicates high risk. This procedure was applied to the data in Appendix 1-20. The results are summarized in Table 14.

Table 14. Toxicity values for honey bees and risk classifications

Chemical	**Lowest toxicity value (µg/bee)**	**Applic-ation rate (kg/ha)**	**Hazard ratio**	**Risk to bees**
Chlorpyrifos	0.01	1.5	150,000	High
Profenophos	0.10	1	10,526	High
Carbofuran	0.16	1	6,250	High
Methyl Parathion	0.20	1	5,000	High
Diazinon	0.27	0.6	2,222	Moderate
Carbaryl	1.20	2	1,667	Moderate
Methamidophos	1.37	1.2	876	Moderate
Endosulfan	6.9	2.5	362	Moderate
Cypermethrin	0.08	0.015	188	Moderate
Paraquat	6.0	1	166	Moderate
Monocrotophos	10	1.6	160	Moderate
Lambda cyhalothrin	0.20	0.02	100	Moderate
Pendimethalin	50	2.4	48	Low
2,4-D	>18	2.3	NA	NA
Carbendazim	>50	0.6	NA	NA
Glyphosate	**>100**	**4.9**	**NA**	**NA**
Fuel oil	NA	NA	NA	NA
Methomyl	NA	1	NA	NA
Nitric Acid	NA	NA	NA	NA
Potassium chloride	NA	NA	NA	NA
Potassium permanganate	NA	NA	NA	NA

Several substances could not be assessed because of lack of data (NA) or no route of exposure (NA) to bees. [a] Toxicity values are greater than the maximum dose tested and ratios cannot be calculated.

Several of the pesticides used in the production of coca and poppy have high hazard to bees, and by extension, to other pollinators. This is not surprising as these pesticides are insecticides and are highly toxic to insects. Compared to these substances, glyphosate is essentially non-toxic to honey bees (Table 14). Tests conducted with the formulation of glyphosate plus Cosmo-Flux® as used in the spray program in Colombia showed that it was also non-toxic to honey bees with no observed effects at exposures ≤ 58 µg/bee.

6.2.4 Hazards to soil organisms

Soil organisms such as earthworms are important in maintaining soil quality and are routinely tested in the registration of pesticides. To assess hazards to earthworms, the data for the most sensitive soil organism (Appendices 1-20) were compared to the concentration that would result if the soil was sprayed directly with the substance and it was evenly distributed in the top 2.5 or 5 cm of soil. The application rates from Table 11 were used for this purpose. Hazard ratios are shown in Table 15.

Table 15. Toxicity values for soil organisms and hazard quotients

Chemical	Application rate (kg/ha)	Concentration in soil (mg/kg) Depth (cm)		Species from which lowest toxicity value was obtained	Lowest toxicity value (mg/kg)	Hazard Quotient Soil depth (cm)	
		2.5	5			2.5	5
Diazinon	0.6	1.60	0.80	*Lumbricus terrestris*	0.072	22	11
Carbendazim	0.6	1.60	0.80	*Eisenia andrei*	0.6	2.7	1.3
Carbofuran	1	2.67	1.34	*Eisenia fetida*	11	0.24	0.12
Methomyl	1	2.67	1.34	*Lumbricus terrestris*	23	0.12	0.06
Methamidophos	1.2	3.20	1.60	*Eisenia fetida*	29	0.11	0.06
Methyl parathion	1	2.67	1.34	*Eisenia fetida*	40	0.07	0.03
Carbaryl	2	5.34	2.67	*Eisenia fetida*	106	0.05	0.03
Monocrotophos	1.6	4.27	2.14	*Eisenia foetida*	132	0.03	0.02
Chlorpyrifos	1.5	4.01	2.00	*Lumbricus rubellus*	152	0.03	0.01
Profenophos	1	2.67	1.34	*Aporrectodea caliginosa*	127	0.02	0.01
2,4-D	2.3	6.14	3.07	*Lumbricus terrestris*	680	0.009	0.005
Endosulfan	2.5	6.68	3.34	*Eisenia fetida*	6,700	0.001	<0.001
Cypermethrin	0.015	0.04	0.02	*Aporrectodea caliginosa*	73	0.001	<0.001
Lambda cyhalothrin	0.02	0.05	0.03	*Eisenia fetida*	>1,000	<0.001	<0.001
Paraquat	1	2.67	1.34	*Lumbricus terrestris*	>1,380	<0.002	<0.001
Glyphosate	**4.9**	**13.08**	**6.54**	***Lumbricus terrestris***	**>5,000**	**<0.002**	**<0.001**
Pendimethalin	2.4	6.41	3.20	Not available			

From these results, it is clear that a number of other pesticides that are used in the production of coca have greater hazards to earthworms than glyphosate. Diazinon and carbendazim both have hazard quotients greater than 1, suggesting that they may be hazardous to earthworms when used in coca and/or poppy production.

6.3 HUMAN AND ENVIRONMENTAL HAZARD ASSESSMENT FOR NON-PESTICIDAL CHEMICALS

Fuel oil (ACPM), potassium chloride, nitric acid, and potassium permanganate were included in the priority list of 20 chemicals but could not be assessed in the above manner because of lack of precise knowledge of how humans may be exposed to these substances and how they may enter the environment. However, based on the data in Appendices, some general discussion and comments can be offered.

Nitric acid is a strong irritant that will cause severe burns to exposed skin, the eyes, the respiratory tract, and the gastrointestinal tract in humans. Damage can be permanent unless treated immediately and, in some cases, can be fatal. If not correctly used, hazards to the user and to bystanders are large. If released into the environment, nitric acid will lower the pH of the soil or surface water that it comes into contact with. This may be lethal to soil and aquatic organisms. However, with sufficient dilution, nitric acid will react with substances in soil and water, such as carbonates and bicarbonates. This will result in the formation of nitrates which are less acutely toxic and would become nutrients for plants. Long term effects in the environment are unlikely except in regions where large amounts are released for extended periods of time.

Potassium permanganate is not highly toxic to mammals and is used as an antiseptic in human medications. Toxic effects in humans have been reported at exposures of the order of 100 mg/kg and reproductive effects at 25 mg/kg in male rats. Environmental effects have been reported at concentrations as low as 30 µg/L. If potassium permanganate is accidentally consumed or released into the environment in large quantities, it will present a hazard. However, given the use of potassium permanganate as a chemical reactant, it is unlikely that large amounts would be released into the environment before it is consumed in the reaction.

Potassium, as a component of potassium chloride is an essential nutrient for most organisms and is essential for plant growth. High exposures in humans are hazardous and, as potassium chloride could be mistaken for salt (sodium chloride) it may be inadvertently consumed. Potassium chloride is not expected to be toxic in the environment. Potassium is a widely used component of agricultural fertilizers and is likely used in large quantities in agriculture in Colombia.

Fuel oil is toxic to mammals if consumed and is toxic to organisms in the environment in situations where spill or other large releases to the environment occur. Again, this material is widely used industry and commerce in Colombia and use in the production of cocaine and heroin represents a small fraction of the total use and does not represent a major human or environmental hazard.

7 GENERAL CONCLUSIONS

Many of the substances used in the production and refining of cocaine and heroin are potentially hazardous to the environment. Since there is scant information as to how these substances are used and how humans and the environment may be adversely affected, standardized scenarios were used to estimate exposures of humans and components of the environment such as surface waters and soil. For the purposes of comparison, glyphosate was also included in these hazard assessments, although it has been the subject of a more detailed risk assessment (Solomon et al. 2005).

Several of the short-listed substances are considerably more toxic to humans and non-target organisms in the environment than glyphosate. Greater toxicity is reflected in the higher hazard of these substances to humans and to the environment. These hazards are illustrated graphically in Figures 7 and 8.

Most of the more hazardous pesticides (Figure 7) have hazard quotients (HQs) >1, are insecticides, are toxic to mammals, and other wildlife, as well as to insects. It should be noted that the HQs are shown on a logarithmic scale to allow presentation in a small graph. These insecticides are organophosphorus compounds which are frequently associated with human poisonings and adverse effects in wildlife (Appendices 1-20). The HQ for glyphosate was less <1 as were those for carbendazim, cypermethrin, lambda cyhalothrin and paraquat. Carbendazim is a fungicide and would not be expected to be hazardous to mammals. Cypermethrin and lambda cyhalothrin are pyrethroid insecticides, are not highly toxic to mammals, and are used at low rates of application. The low HQ for paraquat is reflective of its poor penetration through skin, the basis for the calculation of these hazards. In fact, paraquat (Appendix 16) can be much more hazardous if there are cuts or abrasions in the skin that facilitate penetration. If consumed orally, paraquat is highly hazardous and is responsible for many human deaths, particularly where it is not used and stored properly (Appendix 16).

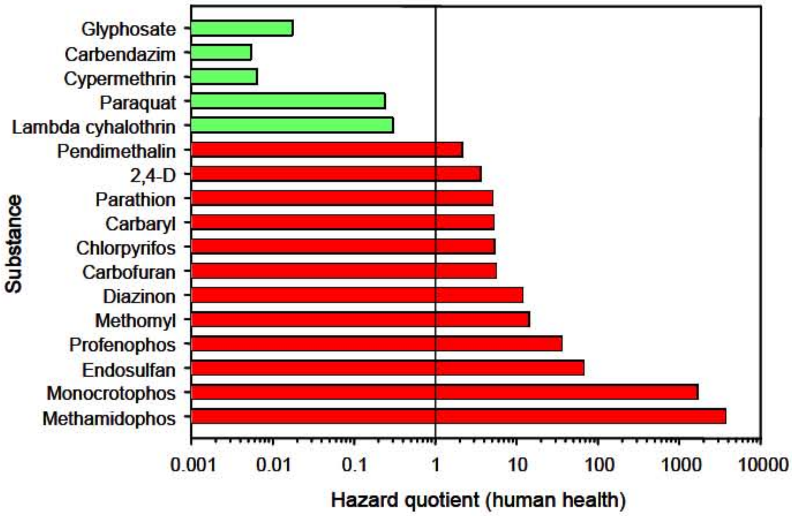

Figure 7 Graphical illustration of the human health hazard quotients of pesticides used in the production of coca and poppy

The environmental hazards of the pesticidal substances are illustrated in Figure 8. The HQs for aquatic organisms are illustrated for direct application to water that is 30 cm deep and were all >1, except for glyphosate. Some of these pesticides are highly toxic to non-target aquatic organisms and endosulfan had an HQ in excess of 20,000. Endosulfan is highly toxic to aquatic organisms, has been associated with fish kills in surface waters in other jurisdictions (Appendix 8), and its use in Colombia is banned. Endosulfan was one of the pesticides detected in surface waters in Nariño in 2004-2005 (Solomon et al. 2005) where it was obviously being used illegally.

Hazards to bees (Figure 8) were high for chlorpyrifos, profenophos, carbofuran, and methyl parathion. Pendimethalin is an herbicide and is not highly toxic to bees and had a low HQ. Glyphosate, 2,4-D, and carbendazim all had HQs less than the indicated values on the graph as the toxicity values were all greater than the highest value tested. The other pesticides had HQs that indicated moderate risks to bees. Thus, significant effects on bees and other pollinators (for which bees are surrogates) may occur when coca and/or poppy are treated with insecticides.

HQs for soil organisms were based on complete mixing in the upper 2.5 cm of the soil and were >1 for only carbendazim and diazinon (Figure 8). These HQs were small, suggesting that the risks to soil organisms from the use of these substances in the production of coca and/or poppy would be small in general. The HQs for glyphosate, paraquat, and lambda cyhalothrin were all less than the indicated values as toxicity was not observed at the highest concentration tested in the bioassays. The low toxicity of glyphosate and paraquat is likely the result of strong binding to soil particles and low bioavailability.

7.1 DATA GAPS AND UNCERTAINTY

A number of data gaps were identified in this study. Some related to missing toxicity values for pesticides, particularly in bees and earthworms. For humans and other organisms in the environment, toxicity data were judged to be good. An additional uncertainty related to toxicity is the use of mixtures of pesticides. These may interact to increase toxicity to humans and non-target organisms in the environment.

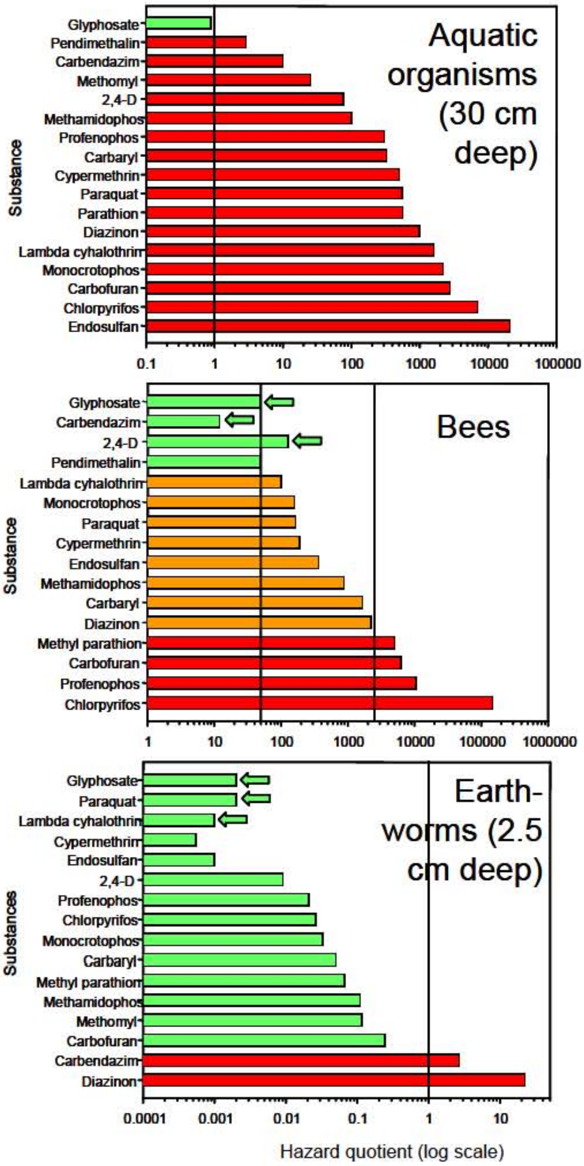

Figure 8 Hazard quotients for aquatic organisms, bees, and earthworms for pesticides used in the production of coca and poppy. Green arrows indicate that the HQs were less than the indicated value.

There were significant data gaps and uncertainties with respect to the exposure estimates for the substances assessed in this Tier-2 process. These data gaps are discussed in the introductory sections and relate to the rates of application, the frequency of the application and the protective equipment used by the applicators. Additional uncertainties relate to other routes of exposure in bystanders and other workers who may re-enter the fields shortly after application of chemicals. Biomarkers of exposure, such as concentrations of pesticides and metabolites in urine and blood or inhibition of red blood cell acetylcholinesterase would be more appropriate indicators of exposure but are almost impossible to obtain for logistical reasons. For this reason we used HQs in the assessment.

A general uncertainty related to the use of chemicals in the refining and production of cocaine and heroin is the purity of these substances. In some cases, impurities may increase toxicity and hazard to humans and the environment.

Additional uncertainties result from some of the conservative assumptions used in the characterizing of exposures and toxicity. For environmental exposures, it was assumed that direct overspray of water or soil occurred. If surface water was not over-sprayed and the only contamination was from drift, concentrations would be smaller. Similarly, soil concentrations were calculated without factoring in interception of the plant canopy which may reduce deposition on soil to less than 50% if plants are mature and the canopy is closed. For the environmental hazard assessment, toxicity values for the most sensitive organism were used. This organism may not be present in Colombia but, as is the case with all hazard and risk assessments, these organisms are surrogates for those that may be present and have not been tested for sensitivity. In assessing human health hazards, the reference dose was used. This reference dose is based on daily exposure to the chemical for a lifetime and is somewhat conservative for assessing risks from single and infrequent exposures.

For these reasons, it was not possible to estimate risks with any certainty and was the reason for the use of HQs. The HQ is not an indicator of risk from a substance but the substances may be compared on the basis of the relative HQs. In all cases, these substances presented greater hazards to humans and the environment than glyphosate, whether this herbicide is used in spray eradication or in the production of coca and/or poppy.

7.2 RECOMMENDATIONS

Specific recommendations are not made; however, it is obvious that, as has been noted in other jurisdictions, training and education in the use of pesticides would reduce risks to humans and the environment. With the exception of endosulfan, all of the pesticides reviewed here are used routinely in agriculture in Colombia and (including endosulfan) in other jurisdictions. With the use of proper storage, application equipment, protective clothing, and mixing and loading procedures, all of these substances can be used safely and will therefore not present an unacceptable risk to humans or the environment. In addition to training and proper use, inspection and environmental monitoring are useful in assessing compliance with correct use. Several educational and training programs related to correct pesticide use practices have been set up by government and industrial groups in Colombia. However, these programs may be very difficult to implement in areas where coca and poppy are grown. Nonetheless, increased education and training would be generally beneficial and should be encouraged.

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Annex 119

2006 MEMORANDUM OF UNDERSTANDING BETWEEN THE GENERAL SECRETARIAT OF THE ORGANIZATION OF AMERICAN STATES (SG/OAS) AND THE GOVERNMENT OF COLOMBIA FOR THE EXECUTION OF THE STUDY ON THE EFFECTS OF THE PROGRAM FOR THE ERADICATION OF ILLICIT CROPS BY AERIAL SPRAYING WITH GLYPHOSATE HERBICIDE (PECIG) ON HUMAN HEALTH AND THE ENVIRONMENT, 23 MAY 2006

(*Archives of the Ministry of Foreign Affairs of Colombia*)

MEMORANDUM OF UNDERSTANDING BETWEEN THE GENERAL SECRETARIAT OF THE ORGANIZATION OF AMERICAN STATES (SG/OAS) AND THE GOVERNMENT OF COLOMBIA FOR THE EXECUTION OF THE STUDY ON THE EFFECTS OF THE PROGRAM FOR THE ERADICATION OF ILLICIT CROPS BY AERIAL SPRAYING WITH GLYPHOSATE HERBICIDE (PECIG) ON HUMAN HEALTH AND THE ENVIRONMENT

[PAGE 2]

MEMORANDUM OF UNDERSTANDING BETWEEN THE GENERAL SECRETARIAT OF THE ORGANIZATION OF AMERICAN STATES (SG/OAS) AND THE GOVERNMENT OF COLOMBIA FOR THE EXECUTION OF THE STUDY ON THE EFFECTS OF THE PROGRAM FOR THE ERADICATION OF ILLICIT CROPS BY AERIAL SPRAYING WITH GLYPHOSATE HERBICIDE (PECIG) ON HUMAN HEALTH AND THE ENVIRONMENT

The Parties to this Memorandum of Understanding, the General Secretariat of the Organization of American States (hereinafter SG/OAS), through the Executive Secretariat of the Inter-American Drug Abuse Control Commission (hereinafter, SE/CICAD), represented by its Assistant Executive Secretary, Abraham Stein, and the Government of Colombia through the Ministry of Foreign Affairs, represented by the Minister of Foreign Affairs, Carolina Barco:

CONSIDERING

That the SG/OAS, is the main and permanent organ of the Organization of American States (hereafter OAS), and is authorized to establish and promote relations of cooperation with member States pursuant to Article 112(h) of the OAS Charter and with its General Assembly resolution AG/RES. 57 (l-O/71).

That the Inter-American Drug Abuse Control Commission (hereafter CICAD or the Commission) is an agency of the OAS, established by Article 52 of the Charter of the Organization. This agency is technically autonomous and carries out its duties within the context and scope of the Rio de Janeiro Action Plan against Consumption, Production, and Illicit Trafficking on Drugs and Psychotropic Substances, the mandates of the General Assembly, and the decisions internally adopted by the Commission.

That the purpose of CICAD is to contribute to eliminate illicit trafficking and drug abuse. Pursuant to its Statutes, it has attributions with regard to the field of prevention, assistance and social rehabilitation of drug-addicts, as well as to that of the prevention, control and punishment of the production and illicit trafficking of drugs and psychotropic substances.

That within the framework of its Hemispheric Strategy, CICAD promotes actions against the illicit crops of raw materials destined for the production of illicit drugs, while always taking into account the preservation of the environment, through the promotion of programs and/or projects to encourage the development of lawful economies in the areas of illicit drug production in Member States.

[PAGE 3]

That the Colombian State implemented the Program for the Eradication of Illicit Crops by Aerial Spraying with Glyphosate Herbicide (PECIG) in Colombia, in accordance with paragraph g) of Article 91 of Law 20 of 1986, whereby Colombia adopted the National Anti-Narcotics Statute that assigns to the National Narcotics Council the duty to "provide for the destruction of marihuana, coca and other crops from which substances causing dependency may be extracted, using the most adequate means, following a favourable opinion of the agencies entrusted with protecting the health of the population and the preservation and balance of the ecosystem in the country". [The Program] is regulated through resolution 0013 of 2003 and operates in all the regions in the country the presence of illicit crops is evidenced.

That for the Colombian State, the adoption and implementation of the Program for the Eradication of Illicit Crops by Aerial Spraying with Glyphosate Herbicide (PECIG) has become an inexorable necessity in view of the fact of the extended presence of illicit crops in the national territory and the security problems that, in many cases, preclude resort to other eradication methods.

That the Government of Colombia understands the PECIG as the plan of the State for the mitigation of the adverse environmental impact caused by illicit crops and the subsequent processing of illicit drugs.

That, in accordance with Colombian law and abiding by the provisions of the 1961 Single Convention on Narcotic Drugs as amended by its 1972 Protocol and the 1988 United Nations Convention Against Trafficking of Illicit Drugs and Psychotropic Substances as regards the obligation to adopt the necessary measures to eradicate the poppy crops, coca bushes and cannabis plants that are illicitly grown, and in light of the unusual increase of illicit crops in the national territory, the Government of Colombia set out to strengthen its strategy to confront the problem of illicit drugs production and trafficking through forced eradication by aerial spraying with glyphosate herbicide.

That in view of the growing domestic and international concern as to the alleged effects of the Program for the Eradication of Illicit Crops by Aerial Spraying with Glyphosate Herbicide (PECIG), the Governments of Colombia, the United States and the Untied Kingdom requested CICAD to conduct a study in order to document such effects in a scientific and independent manner.

That the panel of scientists contracted by SE/CICAD to carry out that study, conducted under the Memorandum of Understanding between the OAS and the Government of Colombia for the execution of the study on the effects of the PECIG on human health and the environment, concluded in the city of Bogotá, D.C., Republic of Colombia, on the 4th day of February 2004, identified certain queries in their reviews of the data and on the basis thereof makes certain recommendations aimed at resolving the queries identified in the study.

[PAGE 4]

That having learned of the results of the Initial Phase, the Government of Colombia and the Government of the United States request the cooperation of CICAD in order to be able to conduct a complementary phase.

That scientific team identified the strengths and queries as a result of the assessment and recommended to maintain the current practices of the PECIG, additional data collection for a longer period with the purposes of gathering a between characterization of the impacts of coca and poppy crops in areas of the Andean region characterized by their biodiversity and the definition of the alleged effects on superficial waters adjacent to the crops. It is also recommended that other adjuvants be tested, that represent a higher efficacy and, at the same time, eliminate or minimize any risk that could affect aquatic organisms. Although no relation was observed between aerial sprayings with glyphosate herbicide and the results in human reproduction, it is recommended to conduct additional studies in order to identify possible risk factors associated to other human activities or environmental factors.

STATING the importance of coordinating their efforts with the purpose of fulfilling their objectives,

AGREE to conclude the present Memorandum of Understanding that will be governed by the following provisions:

FIRST CLAUSE: Object and purpose

The object and purpose of the present Memorandum is to conclude an agreement that serves as framework for the development of an independent scientific study on the alleged effects of the PECIG on human health and the environment.

The description of the study is set out in detail in Annex I that is an integral part of the present Memorandum, that was vetted by the Government of Colombia and the SE/CICAD.

SECOND CLAUSE: Framework for cooperation

Cooperation and assistance provided in pursuance of the present project will be carried out in observance of the respect for national sovereignty, confidentiality, transparency and veracity of conclusions.

THIRD CLAUSE: Study areas

For comparative purposes and of statistic and methodological precision, the study will focus both on the areas where the Program for the Eradication of Illicit Crops is implemented, as well as on areas where glyphosate herbicide is used for the cultivation of lawful produce,

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on areas where manual eradication programs are carried out and in areas of organic production. By mutual agreement between the Parties, other areas the assessment of which is considered relevant may be included.

FOURTH CLAUSE: Responsibilities of the Parties

A. SE/CICAD undertakes to:

1. Supervise and follow-up on the works carried out by the Scientific Assessment Team (SAT) and the Permanent Technical Group for Mobile Monitoring (PTGMM [shortened form PTG]).
2. Contract and supervise the required personnel and laboratories for conducting the study that is the object of the present Memorandum.
3. Conduct and follow-up on the study that is the object of the present Memorandum.
4. Coordinate and supervise the adequate progress of the activities foreseen in Annex I, "Monitoring of the Aerial Spraying Program for the Control of Illicit Coca and Poppy Crops on the Environment and Human Health in Colombia."
5. Take all actions required for the effective and timely execution of the project's activities mentioned in Table 6 of Annex I.
6. Review and approve periodical reports on the progress of the established work plan.
7. Periodically inform the Government of Colombia on the progress of the completion of the study that is the object of the present Memorandum.
8. In accordance with the provisions of the Fifth Clause, publicly present the results of the study and widely publicize the corresponding final report that will have been previously presented to the Government of Colombia for its information. The results of the study and the final report to which this paragraph refers will be presented in Spanish and English.

B. The Government of Colombia undertakes to:
   1. Facilitate the compliance with and implementation of the present Memorandum.
   2. Provide any information required for the formulation and implementation of the project as requested by SE/CICAD, including, among other, information relating to the areas considered within the aerial spraying program.
   3. Appoint an agency that, in direct coordination with the Ministry of Foreign Affairs (Division of Multilateral Political Affairs, Sub-division for Drug Affairs), will be entrusted with the following responsibilities:
      a. To facilitate communication between SE/CICAD, implementing personnel and the Government of Colombia.
      b. To arrange the required logistics required for the mobilization of the personnel to and within the areas under study described in Annex I.

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      c. To ensure the timely and coordinated action of the different authorities in charge of providing security to the personnel implementing the study.

4. To provide the required elements for the correct execution of the components of the study.
5. To provide a security detail for the mobilization of the personnel involved in the study to and within its areas, in accordance with the resources allocated for these purposes in the project budget. All field visits to the areas under study shall be conducted by mutual agreement with the Colombian authorities in charge of providing security, and under the terms recommended by such authorities according to the security situation. Pursuant to these same reasons, any scheduled visit may be suspended prior to the agreed date.

FIFTH CLAUSE: Confidentiality

The Parties to this Memorandum undertake to preserve the strictest confidentiality while the study is being developed. Neither Party may, without the express prior consent of the other, publish partial results of the study under way.

Once the Parties have learned, under reserve, the results of the study, the final report will be made public and will be widely publicized.

SIXTH CLAUSE: Termination

The present Memorandum may be terminated by mutual agreement or by either Party, through written advance notice of at least three months to the other.

SEVENTH CLAUSE: Settlement of disputes

The Parties undertake to settle controversies that may arise of the interpretation or application of the present Memorandum of Understanding, preferably by mutual agreement. In case a satisfactory solution is not reached, recourse will be had to the arbitration procedure mutually agreed by the CICAD and the Government of Colombia. If there is no agreement on the procedure, arbitration will be conducted pursuant to the arbitral procedures in force of the United Nations Commission on International Trade Law (UNCITRAL). The arbitral tribunal constituted in accordance with those Rules will rule as amiable mediator or *ex aequo et bono* and its decision will be final and binding.

None of the provisions in this Memorandum signifies or shall be construed as a relinquishment of the privileges and immunities

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enjoyed by the Parties in accordance with the relevant agreements and laws on the matter and the general principles of international law.

EIGHTH CLAUSE: Entry into Force, Duration and Amendments

The present Memorandum shall enter into force on the date of its signature by the last of the Parties, and shall be in force until the completion of the study and the publication of its results.

Addition or amendment to this Memorandum will be made by mutual agreement between the Parties, following compliance with legal requirements. The instruments registering those modifications will be appended as annexes to the present Memorandum and shall become integral parts thereof.

In witness whereof, the present Memorandum between the General Secretariat of the Organization of American States (SG/OAS) and the Government of Colombia for the Execution of a Study on the Effects of the Program for the Eradication of Illicit Crops by Aerial Spraying with Glyphosate Herbicide (PECIG) on Human Health and the Environment, is signed by the duly authorized representatives of the Parties, in two copies in Spanish, both equally authentic.

For the General Secretariat of the
Organization of American States

[signed illegibly]
ABRAHAM STEIN
Assistant Executive Secretary of the
Inter-American Drug Abuse Control
Commission

Date: 23 May 2006

For the Government of Colombia

[signed illegibly]
CAROLINA BARCO
Minister of Foreign Affairs

Date:

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ANEXO I

FOLLOW-UP ENVIRONMENTAL AND HUMAN HEALTH ASSESSMENT OF THE AERIAL SPRAY PROGRAM FOR COCA AND POPPY CONTROL IN COLOMBIA

Introduction

There are several issues that have been identified with respect to the production and eradication of coca in Colombia that require further investigation and understanding. These issues relate to spray drift, which has not been measured under conditions of use in Colombia, toxicity of glyphosate and other pesticides used by growers of illicit crops to amphibians, risks to amphibians of production of and eradication of illicit crops. The following are proposals to address these research needs. This work will be conducted in collaboration with Capt. James Roa and other experts from Colombia and other countries.

The proposed studies are summarized in the Table 1 and described in summary form in the following sections.

Table 1. Summary of proposed follow-up studies related to the spray eradication program in Colombia

Study	Comment	Start	Likely completion
Frog toxicity studies	*Xenopus laevis* acute toxicity study of glyphosate+Cosmo-Flux® at two rates, one for coca, and one for poppy. GLP study is being conducted by Wildlife International and is underway. Hypothesis – The mixture is not differently toxic from formulated glyphosate alone. *Depending on the results of this study, further studies will be conducted to compare the risks from glyphosate plus Cosmo-Flux® to the pesticides used by the growers of illicit crops and some or all of the following:*	May 2006	June, 2006
Preliminary study of mapping of shallow water habitat for amphibians in coca fields	This study will require satellite images that can distinguish and identify shallow water with emergent vegetation. Hypothesis – all coca fields in all regions have shallow surface water that is suitable as frog habitat. It is a preliminary study to test the feasibility of using satellite imagery for this purpose.	May 2006	June 2006
Mapping of shallow water habitat for amphibians in coca fields	This study will be a follow-up to the above preliminary study. Hypothesis – all coca fields in all regions have shallow surface water that is suitable as frog habitat. This study will use satellite imagery, or if this is not feasible, will require that the Gyrocam is	Jun 2006	Sept 2006

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Table 1. Summary of proposed follow-up studies related to the spray eradication program in Colombia			
Study	**Comment**	**Start**	**Likely completion**
	operational and is being used to evaluate efficacy of the spray program. It will also require that the operators and evaluators are able to identify potential habitat. Once all fields have been categorized once, only new fields will have to be evaluated as these are established.		
Distribution of Colombian frogs in relation to spray programs	Will require person(s) in with local knowledge. Hypothesis – populations of rare, threatened, and endangered frogs in Colombia are only found in areas where coca is being produced and is sprayed for eradication purposes. Discussions are underway to identify the appropriate people.	June, 2006	August, 2006
Toxicity of glyphosate to Colombian frogs (tadpoles and terrestrial juveniles).	Will require a person in Colombia with local knowledge and the ability to raise frogs in the laboratory. Hypotheses – frogs from Colombia are not differently sensitive to glyphosate and Cosmo-Flux® than frogs from other countries.	Jun 2006	Dec 2006
Toxicity of pesticides used by coca growers to amphibians and the effects of habitat alteration on amphibians.	This study is important to conduct as it will allow the potential effects of the eradication spraying on amphibians to be compared to the effects of the other pesticides used by growers, the effects of clear-cutting, the effects of a monoculture, the effects of reductions in food supply, and potential spread of diseases on frogs. Hypotheses – the risks to amphibians from eradication spraying are the same as those from all of the processes and procedures used by growers of illicit crops.	May, 2006	July, 2006
Field studies where frogs are exposed under field conditions to a direct overspray in a coca field	Will require person in Colombia with local expertise and availability of a test species of frog that has also been tested in the laboratory. In addition, a test field plot will be needed. Hypothesis – frogs are equally sensitive to glyphosate and Cosmo-Flux® in the field as in the laboratory.	Jan 2007	Jun 2007
Testing of other adjuvants for formulated glyphosate that are equally efficacious but are less toxic to aquatic organisms.	Will require mature coca plants in VG and potential products selected for likely low toxicity. Hypothesis – other adjuvants are as efficacious for coca control as is Cosmo-Flux®. Products that are as good as or better than Cosmo-Flux® will be further tested to identify products less hazardous to aquatic organisms. This study will require a field site with 220 small plots with 9 plants each. A total area of 0.5 ha will be needed and this must be separated by a suitable	Jan 1 2007	Jun 30 2007

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Table 1. Summary of proposed follow-up studies related to the spray eradication program in Colombia			
Study	Comment	Start	Likely completion
	buffer from other areas that may receive aerial applications. It is assumed that the test plots will be ready in Jan 2007.		
Toxicity testing of new adjuvants.	If more effective adjuvants are identified, these will be tested with formulated glyphosate to determine toxicity to the standard suite of aquatic test organisms (fathead minnow, rainbow trout, *Daphnia*, algae) and to the African clawed frog, *Xenopus laevis*. Hypothesis – there is no difference in toxicity between glyphosate + Cosmo-Flux® and glyphosate + other formulants and adjuvants.	Jun 2007	Dec 2007
Spray drift study – spray droplet spectrum.	This study will be conducted in a wind-tunnel in Australia to characterize the spray droplet spectrum for the nozzles and speed of spraying in Colombia. These data will be used to better model spray drift under conditions of use in Colombia and to determine whether a surrogate for spray that can be used to measure spray drift under actual conditions of use in Colombia.	May 2006	August 2006
Spray drift study in Colombia.	A field experiment will be conducted with aerial application of a surrogate mix for glyphosate + Cosmo-Flux® under conditions in Colombia to determine spray drift. Water-sensitive paper and/or a spray dye will be used to assess off-target drift. Hypothesis – modeled spray drift is the same as measured spray drift.	Sep 2006	Jan 2007
Human health effects of eradication spraying using the "comet" assay on human lymphocytes	A protocol has been developed and will assess genotoxicity using the comet assay on lymphocytes from people in 5 areas previously identified in the 2004 epidemiology study. Blood samples will be taken prior to, about 5 days after, and 5 months after spraying. Other areas of Colombia will be used as control regions. Hypotheses – genetic effects in human lymphocytes in people from areas of coca spraying are not different from those in areas where no spraying is undertaken and there is no correlation between genetic effects in lymphocytes and closeness to the sprayed fields.	May 2006	May 2007

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AMPHIBIAN RISK CHARACTERIZATION

The outline of the decision tree for the characterization of risks to amphibians in shown in Figure 1. Note that the follow-up studies are dependent on the results of the earlier studies.

Toxicity testing of glyphosate-Cosmo-Flux® mixture in Xenopus laevis

The African clawed frog, *Xenopus laevis*, is the most sensitive frog species to formulated glyphosate (Edginton et al. 2004). This study will determine the acute toxicity (96-h LC50) of glyphosate + Cosmo-Flux® at two rates, one for coca, and one for poppy. This is a good Laboratory Practice (GLP) study and is being conducted by Wildlife International in the US, one of the few laboratories that have appropriate experience with this test species. The null hypothesis being tested is that the mixture formulated glyphosate and Cosmo-Flux® is not differently toxic from formulated glyphosate alone.

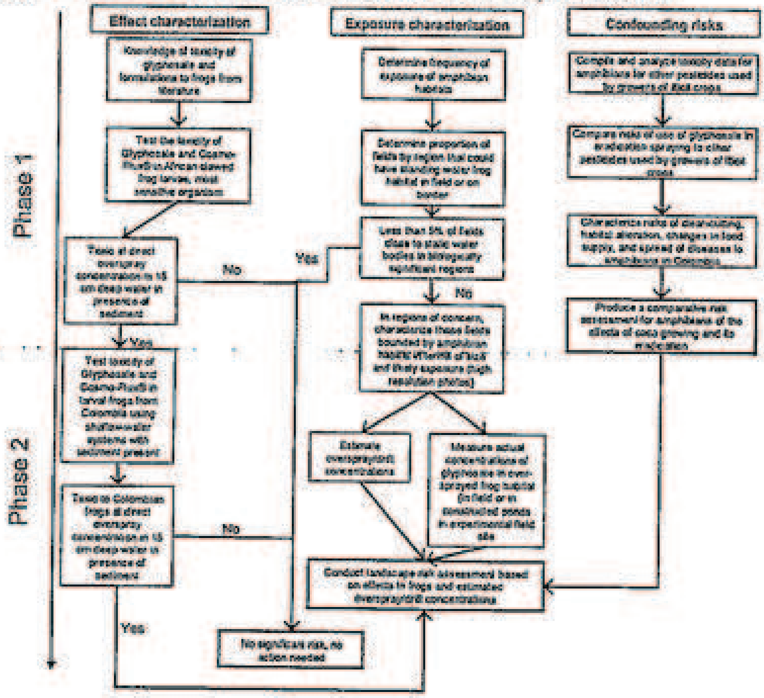

Figure 1 Diagrammatic outline of the amphibian risk characterization.

Preliminary study of mapping of shallow water habitat for amphibians in coca fields

This is a preliminary study to determine if high resolution satellite images can distinguish and identify shallow water with emergent vegetation. This work will be conducted through DOS in the US. The initial focus is on are area around Nariño and Tumaco where direct observations suggest that amphibian habitats are more closely associated with coca fields than in other regions. The null hypothesis being tested is that all coca fields in all regions have shallow surface water that is suitable as frog habitat. It is a preliminary study to test the feasibility of using satellite imagery for this purpose but, if it is successful, this technique could be used in place of that discussed below in Section 0.

Mapping of shallow water habitat for amphibians in coca fields

This study will be a follow-up to the preliminary study above and will use a larger sample of fields. If the satellite-based method can be used, it will be extended to a larger sample of fields. If not, the study will require that the Gyrocam is operational and is being used to evaluate efficacy of the spray program. It will also require that the operators and evaluators are able to identify potential amphibian habitat. Once all fields have been categorized once, only new fields will have to be evaluated as these are established by the growers and identified by the DNE. The null hypothesis being tested is that all coca fields in all regions have shallow surface water that is suitable as frog habitat.

Distribution of Colombian frogs in relation to spray programs

This is an important question as it is needed to address the risks to frogs from two sources, the use of glyphosate and adjuvants in the eradication program and the risks from the production of coca (see Section 0). This task will require person(s) with local knowledge of the distribution of amphibians in Colombia and the overlaying of this information on the distribution of the coca and poppy fields and those that are being sprayed. The null hypothesis being tested is that populations of rare, threatened, and endangered frogs in Colombia are only found in areas where coca is being produced and is sprayed for eradication purposes. Discussions are underway to identify the appropriate people.

Toxicity of glyphosate to Colombian frogs (tadpoles and terrestrial juveniles)

To properly conduct a risk assessment on amphibians in Colombia, it is necessary to measure the susceptibility of Colombian amphibians to formulated glyphosate and Cosmo-Flux®. This will allow the appropriateness of the extrapolation of toxicity data from *X. laevis* and other frogs to Colombian amphibians to be judged and used in a risk assessment. This study will require a person(s) in Colombia with local knowledge and the ability to raise frogs in the laboratory. The null hypothesis being tested is that both larval and terrestrial frogs from Colombia are not differently sensitive to glyphosate and Cosmo-Flux® than frogs from other countries.

Procedures used in these tests will be similar to those used for testing larval *X.laevis* as discussed in Section 0 above. Standard test methods are not available for juvenile terrestrial stages of frogs and the only publication on this procedure (Relyea 2005) used unrealistic exposures. It is proposed that tests would be done in open-topped plastic containers (0.25 m^2) with a bottom layer of soil and plant matter typical of that found in a coca field. Ten juvenile terrestrial stages of a test frog would be randomly selected from a supply of animals and placed in each container. Containers would be covered to prevent escape of frogs. Three replicates would be set up for each concentration tested. Frogs would sprayed with water (control) and 5 concentrations of formulated glyphosate-Cosmo-Flux® mixture as used in coca control in these containers. The greatest concentration will be twice that of the coca application rate and the others will be a geometric dilution series (2x, 1x, 0.66x, 0.33x, and 0.16x). A sample of the 1x spray solution will be analyzed for glyphosate to confirm concentrations. The test units will be covered and the frogs observed at 0.5, 3, 6, 12, 24, 48, and 96 h for mortality. The data will be analyzed using appropriate probit methods. If possible, GLP procedures will be used.

Toxicity of pesticides used by coca growers to amphibians and the effects of habitat alteration on amphibians

This study is important to conduct as it will allow the potential effects of the eradication spraying on amphibians to be compared to the effects of coca production. It is known that several of the other pesticides used by growers in the production of coca are more toxic to aquatic organisms than glyphosate (CICAD/OAS 2005). Amphibian toxicity data will be obtained from the ECOTOX database and from recent literature, compiled, and characterized using tabular and graphical techniques to allow comparison to the data from glyphosate. In addition, the effects of clear-cutting and of a monoculture of frogs will be characterized from the literature. Since the insecticides used in coca and poppy production are toxic to insects, they will reduce the supply of food items to frogs and may also cause secondary poisoning of native frogs. Thus, the effects of reductions in food supply and also the potential spread of diseases on frogs will also be characterized from the literature. The null hypothesis being tested is that the risks to amphibians from eradication spraying are the same as those from all of the processes and procedures used by growers of illicit crops.

Field studies where frogs are exposed under field conditions to a direct overspray in a coca field

While laboratory toxicity tests may show that glyphosate and Cosmo-Flux® are toxic to frogs, these tests are not representative of the field. In the field, frogs utilize shallow water systems that have emergent vegetation and sediments on the bottom. It is known that glyphosate and its adjuvants are strongly absorbed to sediments and organic matter and that this reduces biological availability and thus reduces the observed toxicity to aquatic organisms (Wang et al. 2005). Thus, under field conditions, glyphosate and its formulations will be less toxic than in the laboratory. This may reduce to risk to a negligible level. This study will require persons in Colombia with local expertise and availability of a test species of frog that has also been tested in the laboratory (for comparison). In addition, a test field plot will be needed. The null hypothesis being tested is that frogs are equally sensitive to glyphosate and Cosmo-Flux® in the field as in the laboratory.

To conduct these tests, 12 small field microcosms (2 m^2), such as plastic swimming pools will be set up partially buried in the soil with local sediments typical of shallow pools added in a layer 2.5 cm deep. The pools will be filled to a depth of 15 cm with local water and allowed to equilibrate for 7 days. At this time, 50 randomly selected tadpoles from the test species of frog will be will be placed in each microcosm. The microcosms will be covered with shade cloth to exclude predators and the tadpoles allowed to acclimatize to their environment for 24 h. Any tadpoles that die will be removed and replaced with fresh tadpoles. The shade cloth will be removed and two microcosms each sprayed with water (control) and 5 concentrations of formulated glyphosate-Cosmo-Flux® mixture as used in coca control. The greatest concentration will be twice that of the application rate and the others will be a geometric dilution series (2x, 1x, 0.66x, 0.33x, and 0.16x). The tadpoles will be observed every 6 h and dead tadpoles removed and counted. Samples of water will be taken at 0.5, 6, 12, 24, 48, and 96 h after application from the 2x and 2x treatments for analysis of glyphosate to determine persistence in the system. If methods are available, analyses of the surfactant will also be undertaken. Observed toxicity will be compared to that noted in laboratory tests.

Testing of other adjuvants for formulated glyphosate that are equally efficacious but are less toxic to aquatic organisms

At this time, glyphosate is mixed with Cosmo-Flux® prior to application. The mixture is somewhat more toxic to aquatic organisms than the formulated glyphosate. If this mixture is shown to present a significant risk to amphibians, other adjuvants should be tested. Other adjuvants are potentially less toxic to aquatic organisms than Cosmo-Flux® and there are several other commercial formulations of glyphosate that are less toxic to aquatic organisms than Roundup®. These formulations and/or mixtures of other adjuvants may be less toxic to non-target aquatic organisms that the currently used mixture, however, they may not be as effective as the current mixture in controlling coca. It is proposed that a number of formulations and adjuvants be tested for efficacy in controlling coca and, if they are as, or more effective, than the current mixture, they be tested for toxicity to key aquatic non-target organisms such as rainbow trout and frog larvae. This would allow the identification of more effective and less hazardous formulations and mixture of surfactants.

The null hypothesis being tested is that other adjuvants are equally efficacious for coca control as is Cosmo-Flux®. Products that are as good as or better than Cosmo-Flux® will be further tested to identify products less hazardous to aquatic organisms. This study will require a field site with 220 small plots with 9 plants each. A total area of 0.5 ha will be needed and this must be separated by a suitable buffer from other areas that may receive aerial applications. It is assumed that the test plots will be ready in Jan 2007.

Several adjuvants have already been tested for efficacy (Collins and Helling 2002). The more active of these that also have low environmental toxicity will be included in the trial (Table 2). Additional surfactants will be sought on the recommendations of users of glyphosate in similar uses such as in aerial application for forestry. It is proposed that the current formulation of glyphosate be tested as a reference point and that additional adjuvants, including those listed in Table 3, will be used. Additional surfactants will be added to this list as they are identified.

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Table 2. Glyphosate and surfactant mixtures as previously tested at 2.2 and 4.4 kg/ha

Mixture	Rank order of efficacy[a]
Glyphosate without surfactant (Rodeo®) + 2%[(Agri Dex® - Heavy-range paraffin-based petroleum oil + polyethoxylated derivatives thereof + sorbitan ester based emulsifiers) + (Silwet L77®) – 50:50 mix] diluted in water.	1
Glyphosate (Roundup® original) + 2%[Optima® - Polyethoxylated alkyl amines [C8--C18] + alkyl polyoxyethyleneglycols + organic acids] diluted in water.	2
Glyphosate without surfactant (Rodeo®) + 2%[X-77® - Alkylarylpolyoxyethylene glycols 1 free fatty acids + isopropanol] diluted in water.	3
Glyphosate without surfactant (Rodeo®) diluted in water.	4
Glyphosate without surfactant (Rodeo®) + 2%[Cide-Kick II® D-Limonene + nonylphenol polyethyleneglycol ether] diluted in oil.	5

[a] Data from (Collins and Helling 2002).

Three rates of glyphosate will be tested. These will be 1.25, 2.5 and 5 kg/ha (X, Y, and Z). This will allow identification of more effective materials and the approximate rates of application needed for equivalent efficacy.

Table 3. Proposed adjuvants to be tested.

Treatment	Adjuvants (2.5%) added to glyphosate as currently used in Colombia
A-0	Unsprayed control
A-1	Glyphosate only
A-2	Glyphosate + Cosmo-Flux®
A-3	Glyphosate + [(Agri Dex® + Silwet L77®) - 50:50 mix]
A-4	Glyphosate + Silwet L77®
A-5	Glyphosate + Optima®
A-6	Glyphosate + X-77®[a]
A-7	Glyphosate + LI-700®[b] a lecithin-based surfactant consisting of a mixture of phosphatidylcholine, alkyl phenol ethoxylates, and methylacetic acid
A-8	Glyphosate + etc., etc.

[a] May be omitted as this surfactant is toxic to aquatic organisms (Solomon and Thompson 2003).
[b] Shown to have low toxicity aquatic organisms (Solomon and Thompson 2003).

A series of small plots of coca will be planted from seedlings or from cuttings of *Erythroxylum coca* var. *coca* and *E. novogranatense* var. *novogranatense*, (A and B, respectively) will be used that represent the most commonly used strains. These plots will be planted with the aid of a person(s) with local expertise. All appropriate fertilizing and pest management will be done on these plots to ensure that the plants are healthy and representative of those grown locally. Each will have nine plants in a 3 x 3 pattern. Spacing will be 80 cm and the space between plots will be 200 cm. All treatments will be replicated four times and will be allocated to plots at random arranged within four blocks. All treatments will be replicated four times and will be allocated to plots at random arranged within four blocks. A total of more than 220 small plots will be set up and planted with coca bushes; >168 of which will be used for experimental work and 24 others kept as additional plots.

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Provisional layout of the plots is shown in Table 4.

Table 4. Adjuvant plot allocations

	Strain 1				Strain 2			
Treatment	Block A	Block B	Block C	Block D	Block A	Block B	Block C	Block D
A-1-X	16	18	9	21	5	17	5	13
A-1-Y	8	12	1	9	16	1	10	15
A-1-Z	11	1	16	11	1	12	14	14
A-2-X	18	17	17	1	2	6	11	9
A-2-Y	10	21	6	19	11	7	13	12
A-2-Z	12	2	19	16	20	21	4	6
A-3-X	19	10	5	14	18	19	8	4
A-3-Y	6	16	14	3	3	20	21	20
A-3-Z	9	19	20	4	12	3	19	11
A-4-X	3	7	8	8	9	18	12	5
A-4-Y	4	14	3	7	13	10	6	18
A-4-Z	5	6	12	13	6	13	2	21
A-5-X	1	3	15	17	19	14	3	1
A-5-Y	17	15	7	20	10	8	1	19
A-5-Z	21	9	18	18	17	9	18	17
A-6-X	20	20	4	2	15	4	16	2
A-6-Y	15	11	10	5	21	11	17	3
A-6-Z	13	4	11	15	7	16	20	10
A-7-X	14	8	2	6	4	5	15	8
A-7-Y	7	5	21	12	8	2	9	7
A-7-Z	2	13	13	10	14	15	7	16

Once the coca crop has reached a stage equivalent to the age when it would be sprayed with glyphosate (1 m tall) it will be subjected to the treatments summarized in Table 4. The mixtures will be applied to the plots using backpack sprayers between the hours of 7h00 and 15h00 on a day when rain is not predicted within the next 24 h.

The following observations will be made on the treated and blank plants (Table 5).

Table 5. Observation on treated and blank plants

Observations	Measures	Times of observation (days after treatment)
Disease incidence	Number of lesions per leaf, n = 10 per plant, 3 plants per plot.	-7, 0
Insect damage	Area of leaf eaten n = 10 per plant, 3 plants per plot.	-7, 0
Glyphosate effects	Scoring system of 0-5 with 0 = no visible damage, 5 = extensive damage. Per plant, 3 plants per plot.	1, 3, 7, 14, and 28 d after spraying

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Table 5. Observation on treated and blank plants

Observations	Measures	Times of observation (days after treatment)
Yield	Wet mass and dried leaf mass.	28 d after spraying
Alkaloid yield	Mg/kg dry leaf tissue.	28 d after spraying

Toxicity testing of new adjuvants

If testing suggests that glyphosate and Cosmo-Flux® pose a significant risk to amphibians (Sections 0, 0, and 0 above) and if more effective adjuvants are identified (Section 0 above), these will be tested with formulated glyphosate to determine toxicity to the standard suite of aquatic test organisms (fathead minnow, rainbow trout, *Daphnia*, algae) and to the African clawed frog, *Xenopus laevis*.

The null hypothesis being tested is that toxicity of other adjuvants identified in Section 0 above have the same toxicity profile as glyphosate + Cosmo-Flux®. These tests will be conducted in the laboratory using standard guidelines (OECD 1984a, b, 1992, 1998a, USEPA 1996a, b) and under the principles of GLP (OECD 1998b).

SPRAY DRIFT

Spray drift study – spray droplet spectrum

This study will be conducted in a wind-tunnel in Australia to characterize the spray droplet spectrum for the nozzles and speed of spraying in Colombia. These data will be used to better model spray drift under conditions of use in Colombia and to determine whether a surrogate for spray that can be used to measure spray drift under actual conditions of use in Colombia.

The emission droplet size spectrum from a spray application is one of the most important factors affecting the fate of the pesticide with respect to on-target performance and spray drift exposure. The present study aims at measuring the emission droplet size spectra for various tank mixes containing Glyphosate and a surfactant used under simulated aerial application conditions. Particular attention will be given to the volume median diameter (Dv0.5) droplet size and the spray volume contained in droplets with diameter below 150 µm, which is more prone to possible off-target drift under unfavorable conditions.

The objective of this study is to measure the droplet size spectra produced by tank mixes containing glyphosate herbicide with Cosmo-Flux®, when sprayed in a wind tunnel under application scenarios representative of aerial applications by fixed wing aircraft at various application speeds using a range of nozzle types. Two different tank mixes will be tested and compared to water. If the Dv0.5 droplet size for a water spray is >5% different from that of the two test substances, then

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additional tests will be made to determine the optimum composition of an appropriate surrogate formulation using water with surfactant.

Test Substances - The test substances will be the spray solutions that are released from the nozzle. Prepare the test substances from component materials provided by the Sponsor. The test substances are as follows (all amounts on volumetric basis):

- C1: 55% water, 44% glyphosate, 1% Cosmo-Flux
- P1: 94.6% water, 4.9% glyphosate, 0.5% Cosmo-Flux
- Water
- Optional depending on test results:
  Additional test substances will be prepared using water with Cosmo-Flux at various rates until the droplet size spectrum provides one with a Dv0.5 within ±5% of the values for test substances C1 and P1.

The test system consists of a wind tunnel facility equipped with a laser-diffraction particle sizing instrument for measuring drop size distribution of several test substances as they are atomized through agricultural nozzles in a high speed airstream. A Sympatec HELOS VARIO laser diffraction system with a 3500 mm focal length lens can be used for the measurement of the sprays.

There will be at least 18 treatments involving at least three test substances with various application parameters. The treatment list is provided in Addendum A. Additional treatments may be needed with the Accu-Flo nozzle to determine appropriate surrogate tank mixes to simulate C1 and P1. This will involve testing candidate rates of Cosmo-Flux® in water until the appropriate concentration is determined for representing the Dv0.5 of C1 and P1 within ±5% of their respective values. The test substance components (except water) will be provided by the sponsor. The nozzles will include types commonly used in spray applications for these systems/ application volume rates in the U.S. when spray drift potential is to be minimized. Application speeds (wind tunnel velocity settings) are based on those used for fixed wing aircraft operating at flight speeds between 140 and 180 kn.

Three replications of data will be collected for each treatment. The atomization data will be reported for droplet size spectra and also to perform some assessments (with selected atomization data covering the study range) to determine application efficiency (on-target) and spray drift exposure risk (off-target) using the AGDISP or AgDRIFT model as appropriate. Assessments will include the effect of boom length (comparing boom lengths of 60-75% of the wing semi-span) and release height (comparing applications at altitudes of 100-1000m for treatments with tank mix C1 and 3000m for treatments with tank mix P1) as well as relative humidity levels of 10-100%.

Analyses of the data will be as outlined in Standard Operating Procedure entitled "Standard Operating Procedures for Determining Cross-Section Average Drop-Size Distributions of Agricultural Sprays in a Wind Tunnel" (SOP No. SDTF-11A/5).

Spray drift under Colombian conditions

A field experiment will be conducted with aerial application of a surrogate mix for glyphosate + Cosmo-Flux® under field conditions in Colombia to assess spray drift. The null hypothesis being tested is that modeled and measured spray drift are the same.

Three non-overlapping spray swaths will be sprayed and spray targets (water-sensitive paper and filter papers for dye catching) set out in transects so that a spatial representation of deposition can be mapped. Applications will be repeated for several wind speeds (such as 1, 4, and 8 knots). Different spray heights will be used as well (30 and 70 m). The location will be a secure location such as an airfield or farm.

Three spray applications will be conducted for each set of conditions of wind speed and height. Two times of day will be used to bracket high humidity (morning) and low humidity (noon). Number of applications will be 3 wind speeds x 2 heights x 2 times x three replicates = 36 applications.

On-site records will include wind speed, temperature, humidity, plane height. The spray targets will be water sensitive papers.

Four transects at 90° to the spray run, comprising 15 locations: swath centre, swath edge and at 1, 2, 5, 10, 15, and 20 m each side. Two further transects at each end of the spray area, with targets located at the swath edge, 2, 5, 10, and 20 m into the spray area and 1, 2, 5, 10, 15, 20, and 30 m outside the spray area (Figure 2).

Sample analysis for water-sensitive paper will include measures of the proportion of cover. Image analysis will be used for this purpose.

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Drift experiment: proposed layout of spray collectors
(distances in metres)

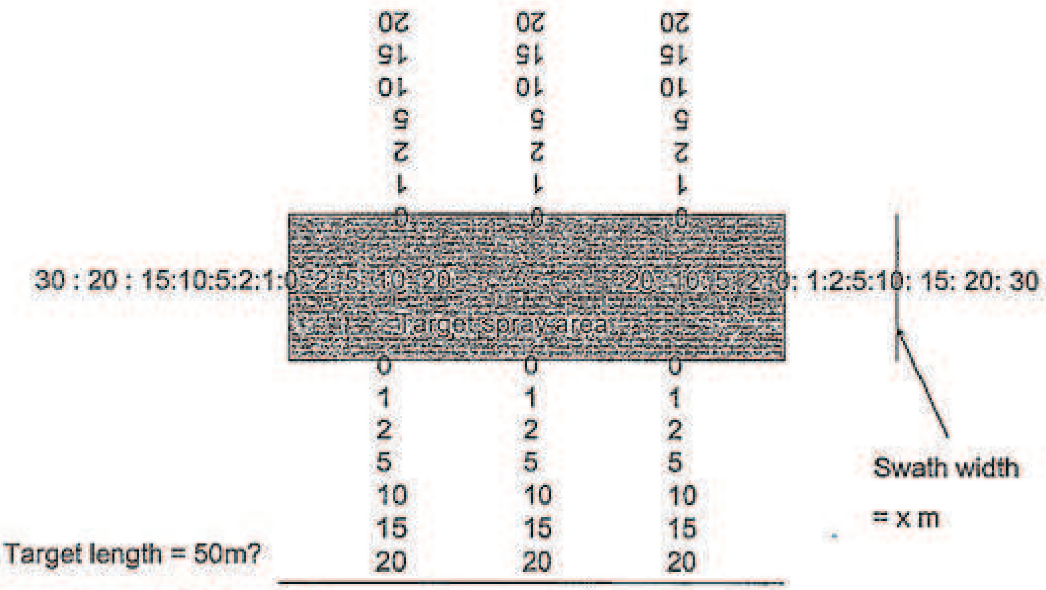

Figure 2 Layout of drift samples

HUMAN HEALTH STUDY

Glyphosate is a broad-spectrum herbicide acting through the inhibition of a biological pathway specific for plants. This mechanism is not considered to be a risk for humans. Glyphosate is widely used in agriculture. In Colombia, it is used as herbicide in several crops, for sugar cane maturation, and for illicit crop eradication. In the country, Roundup® is classified in group IV (low toxicity) and in class III by EPA in the USA. Glyphosate has a mean life of 3-5 days in humans and the only metabolite is AMPA.

Acute, sub-acute, and chronic effects of the exposure to glyphosate have been assessed. Among the acute effects both skin and eye irritation have been documented and both resolve easily, with no complications. Chronic effects, especially related to potential carcinogenesis are, so far, not conclusive and its assessment requires long lasting and highly costly observational studies. Although recent epidemiological studies suggest a potential association with Non Hodgkin Lymphoma (NHL) and with multiple myeloma, other agrochemicals, may explain better this increased incidence of the above referred tumours. Chronic feeding studies of glyphosate did not reveal carcinogenic effects in mice or rats, but a

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number of studies demonstrated a weak genotoxic effects in mammals at large exposures and in vitro.

Coformulants and surfactants contained in glyphosate formulations have an important role in the induction of toxic effects mainly genotoxic ones, as it has been demonstrated in a number of papers (Bolognesi et al. 1997, Peluso et al. 1998) and also very recently as differential effects as endocrine disruptor on human placental cells (Richard et al. 2005). Reproductive health still has unsolved questions regarding glyphosate exposure. Incidence of birth defects or miscarriage has not been completely evaluated. In human lymphocytes Association between glyphosate spraying and time to pregnancy was assessed recently in Colombia (Solomon et al. 2005). No association was established. However, there were differences among regions which were not explained by the data collected.

Glyphosate may cause changes in the DNA. Also damage in DNA has been reported in mice. Studies on cytogenotoxic effects that have been recently evaluated by other investigators in the region (Paz-y-Miño et al. 2005) were not properly designed and sample size was inadequate. Additional studies to evaluate potential risks of glyphosate to exposed population are required to clarify doubts and to answer questions regarding glyphosate exposure and cytogenotoxic effects. Evaluation of cytogenetic damage should be periodically performed in populations exposed to pesticides. The monitoring is carried out in lymphocytes of peripheral blood whose mean life is 4 months, an appropriate time for the assessment of exposures, should these occur.

The micronucleus test, as an index of chromosomal damage is the most appropriate biomarker for monitoring a cumulative exposure. Chromosomal damage, as a result of inefficient or incorrect DNA repair, is expressed during the cell division and represents an index of accumulated genotoxic effects. The test in its comprehensive application, as it has been proposed by Fenech (1993), including a set of markers of gene amplification, cellular necrosis and apoptosis, allows evaluating genotoxic and citotoxic effects induced by the exposure.

The evaluation of the micronuclei frequency in a surrogate tissue, such as the peripheral blood lymphocytes or in buccal exfoliated cells, provides a valid tool to estimate the genetic risk deriving from an integrated exposure to a complex mixture of chemicals.

Micronucleus test in buccal mucosa cells is also used for evaluating DNA damage. The sensitivity and predictive values of this test are lower compared to the method applied in human lymphocytes, but interesting results are obtained for specific inhalation exposure. The collection of the samples, initially for a small group, by a non invasive method (by using a tooth brush) will allow evaluation the suitability of the test for a follow up study in a larger population. The slides of buccal mucosa cells can be scored more rapidly than peripheral lymphocytes. In addition, the samples could be stored for a further analysis.

We propose to carry out a molecular epidemiology study in Colombia to establish prevalence of cytogenetic damage in five areas where an epidemiological study to evaluate time to pregnancy was carried out in women who had had the first pregnancy in the last five years before the interview (Solomon et al. 2005), in order to establish whether there is an association between aerial spraying of glyphosate and cytogenetic alterations. The biomonitoring study in the five regions in Colombia would allow evaluation of differences in genetic risk among the different populations.

<u>HYPOTHESES</u>

Populations exposed to aerial spraying of glyphosate have no difference in incidence of cytogenetic damages compared to non-exposed populations.

<u>OBJECTIVES</u>

1. To determine frequency of cytogenetic alterations in populations from five regions of Colombia, characterized by different kind of exposure

    - Sierra Nevada de Santa Marta where organic coffee is grown without the use of pesticides.
    - Boyacá a zone of illicit crops where manual eradication is performed and use of other chemicals is common
    - Valle del Cauca where aerial spraying of glyphosate is used for sugar cane maturation
    - Putumayo and Nariño where aerial spaying of glyphosate has been and will be performed for coca and poppy eradication.

2. To take samples to evaluate the DNA damage, such as single strand breaks by comet assay, in the same populations.

3. To assess the potential time-dependence of the genotoxic damage through the comparison of the results from different samplings:
    - Before the exposure
    - During (within the following five days) the aerial spraying of glyphosate
    - Five months after the exposure

4. To estimate exposure to glyphosate and to other pesticides or chemicals (by interview and distance from known spray operations).

<u>METHODS</u>

Study area

The study will be carried out in five regions of Colombia with different potential exposure to glyphosate as used in the previous ecologic epidemiology study

(Solomon et al. 2005). Sierra Nevada de Santa Marta where there are crops of organic coffee not exposed to chemicals; Boyacá, a zone of illicit crops, where manual eradication is performed and, therefore, there is not aerial spraying of glyphosate but use of other chemicals may be found; Valle del Cauca where aerial spraying of glyphosate is used for sugar cane maturation; and Putumayo and Nariño where aerial spaying of glyphosate has been and will be performed for coca and poppy eradication.

Study Population
In each of these five areas, 600 women were interviewed in 2004 to assess association between exposure to aerial spraying of glyphosate and time to pregnancy. They were identified at the starting point where environmental samples were taken to evaluate presence of glyphosate and other chemicals in surface water. A random sample of these 3,000 women will be taken for the purpose of this study, their husbands or closest adult male in the same household will be also included in the study and interviews will be performed by using the same questionnaire as for women.

Field data collection
Each subject will be identified by the supervisor of each region who conducted interviews in the previous study. Informed consent will be obtained previously to the interview and sample collection. Because there is already information on demographic characteristics, occupational profile, previous exposure to pesticides, smoking, alcohol, drugs and other habits the interview will update this information and collect more detailed data on exposure to pesticides and other chemicals. A check list will be included in the questionnaire to assure that to all subjects will be asked the same exposure to pesticides, protective measures, recent viral infections, radiation and chemotherapy as well as diseases and other relevant clinical information such as symptoms related to acute effect of exposure to glyphosate.

A simplified food frequency questionnaire that has already been used in other regions of Colombia by experienced researchers at Fundacion Santa Fe de Bogotá[1], including specific questions for intake of folic acid, will be applied in order to identify dietary intake of certain nutrients because deficiency of specific nutrients (e.g. vitamin C, vitamin E, vitamin B12, and folate because statistically significant increase in micronuclei frequency has been observed in subjects with deficiency in folate) on genome instability has been demonstrated. In addition, blood samples will be stored for determination of folate level in plasma at a later time.

Information regarding dates and locations of aerial spraying of glyphosate will be obtained from the antinarcotics police for Tumaco and Putumayo and from ASOCAÑA for Valle del Cauca. In all places, questions regarding use of other

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[1] Heredia, P; Trujillo K & Del Castillo S, 2005

pesticides will be collected in the interview and from environmental and local authorities as well. We will collect additional information on exposure such as distance of the household to the closest point of spraying, time to possible exposure, and length of time living in the area. Another proxy for pesticide use (and exposure) is to interview few retailers in each area as was recently done to evaluate pesticide exposure in flower workers (Varona et al. 2005).

Samples and interviews will be obtained at the beginning of the study, before aerial spraying of glyphosate has occurred, and also within five days after spraying in Putumayo, Nariño, and Valle del Cauca; and again five months after spraying. Samples and interviews from Boyacá and Sierra Nevada de Santa Martha will be obtained at the beginning of the study and one month after the first survey, because in these two areas there is not aerial spraying of glyphosate.

Laboratory analysis

Micronuclei analysis:

A sample (10 mL) of blood will be taken from each subject, after obtaining the informed consent, in heparinized vacutainers. The blood samples for micronuclei analysis in heparinized tubes will be stored at room temperature (15-24°C) for a maximum period of 24 hrs before culturing.

Two sterile cultures of lymphocytes will be prepared and 1000 cells/culture scored blind. The proportion of cells with MN will be obtained. A standardized protocol has been established allowing processing of 100 at the same time.

The samples are coded before culturing. The modified cytokinesis-blocked method of Fenech and Morley (1985) will be used to determine MN frequency. Whole blood cultures are set up for cytogenetic analysis within 24 hrs after collection. An aliquot of 0.3 ml of whole blood is grown in triplicate in 4,7 ml of RPMI 1640 supplemented with 10% foetal bovine serum, 1.5% phytoemoagglutinin, 100 U/ml penicillin and 100 μg/ml streptomycin. At 44 hrs Cytochalsin B is added at a concentration of 6 μg/ml. At the end of incubation at 37°C for 72 hrs, cells are centrifuged (1000 rpm, 10 min). The pellet is treated with 5 ml of 0.075 mM KCl for 3 min at room temperature to lyse erythrocytes then 400 μl prefixative (methanol : acetic acid 3:1) is added. The mixture is centrifuged (1000 rpm, 10 min). The pellet is then treated with cold methanol (-20°C).

The samples can be then shipped or stored at – 20°C. The samples are then further processed through a treatment with fixative (methanol: acetic acid 5:1) followed by centrifugation for 10 min repeated twice. Lymphocytes in fresh fixative are dropped onto clean iced slides, air-dried and stained in 3% Giemsa (Sigma, Milano, Italy). The analysis of MN and other nuclear abnormalities is performed blind only on binucleated lymphocytes with preserved cytoplasm. MN in mononucleated lymphocytes are also recorded. An average of 2000 binucleated cells (1000 cells/culture) are analysed for each subject.

After the analysis of the results further analyses can be carried out on stored samples.

Comet Assay:
The detection of DNA damage by Comet assay reveals a very recent exposure and it is difficult to identify this event in a cumulative exposure. In addition, this test has not been appropriately standardized, mainly in the procedures of slide scoring. Taking into account the relevance of reactive oxygen species in DNA damage induction, the test has to be performed in association to the use of specific enzymes. Different procedures of scoring have been applied considering different parameters and using different software. It has not been established until now the most appropriate parameter to be considered in a comparison of the results from different labs. Therefore, we propose to collect samples and to store them for further analysis in small groups of subjects who are judged to be heavily exposed.

For such a purpose, blood samples to be processed for DNA damage evaluation (alkaline elution, DNA adduct determination, genetic polymorphisms) could be collected in EDTA vacutainers. Samples for comet analysis are drawn into heparinized vacutainers and shipped on ice to the laboratory in Bogotá within 12 hours. Upon arrival, 100 μl blood for comet analysis is aliquoted into iced cryovials containing 1 ml of Hank's balanced salt solution supplemented with 20 mM EDTA and 10% DMSO, pH 7. Samples are then moved to −10°C freezer for 1 h before being transferred to a −80°C freezer.

In the Comet assay the rupture of DNA by the technique of Singh et al will be used. Cells will be placed in an agarose gel for electrophoresis. DNA damaged migrates faster. The tail of the comet (length and intensity) indicates the degree of damage. Damage will be classified according to established criteria in no damage, low, medium, high and sever. Specific software will be used.

Micronucleus assay in buccal mucosa cells
Buccal cells are collected by rubbing the inside of the mouth (both cheeks) with a tooth brush. The samples can be stored in ice for 24 hours.

The cells are then washed twice in a buffer containing 0.01 M Tris HCl, 0.1 M EDTA, and 0.02 M NaCl at pH 7.0. The cell pellet is diluted to a density 1.5 - 2.0 x 10^6/ml and 50 µl of suspension dropped directly onto preheated (37°C) microscope slides. The cells are allowed to air-dry and fixed in methanol (80% v/v) at 0°C for 2-3 hrs. The slides are stained by acridine orange (0.005% w/v) for 4 min, rinsed with distilled water and dried. The slides are covered with a cover slip in a drop of sodium acetate buffer.

Cells are analysed under a magnification of x 1,000 using a fluorescence microscope. 4,000 - 5,000 cells were scored for each individual. Only cells that were not clumped or overlapped and that contain intact nuclei are included in the analysis. Criteria for MN evaluation were those suggested by Tolbert and co-workers (1992). The frequencies of micronucleated cells are calculated based on the number of normal exfoliated cells scored.

Sample size

There only one study that reported cytogenetic alterations due to putative exposure to glyphosate. The report from Ecuador (Paz-y-Miño et al. 2005) stated that prevalence of cytogenetic alterations in those exposed to glyphosate was 22.42%, however, exposures were poorly assessed and the number of experimental subjects was small. An in-vitro study carried out in Colombia evaluating the DNA damage by comet assay in human cell culture reported 20% of cellular damage in cells to the herbicide (Monroy et al. 2005). The glyphosate used in this study was from Sigma Chemicals and was not the technical formulation applied in the fields in Colombia.

Based on these figures, with a population of 600 women and their husbands per region and alpha level of 5% and 10% of error, the required number of subjects would be 55-60 by zone. A total of 60-65 subjects by zone is the minimum taking into account the loss of samples for technical problems (storage, transport, processing, etc.).

There will be 300 interviews and 300 blood samples, twice in each region, and 180 additional for the three zones where glyphosate is sprayed. In total this accounts for 780 interviews and samples.

Data Analysis

Prevalence will be established by the proportion of subjects with cytogenetic alterations of the total population and by region.

Effects of the exposure to aerial spraying will be estimated by calculating cumulative incidence of cytogenetic alterations in two times: immediately after spraying and one month later.

Comparison between areas will be done by cumulative incidence ratio and 95% confidence interval. Risk ratio will be calculated to compare among areas, adjusted for potential confounders, by using multiple regression models.

report

Report content will include presentation of data, analysis, interpretation, and discussion of the following:

Field study methods.

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Discussion of the relevance of findings.

List of any SOPs used.

A draft report containing the preliminary results of the project will be delivered to the within 6 months of the initiation of the study. A final report will be delivered on a mutually agreed date. All data, documentation, records, protocol information, specimens will be archived. The report will be confidential and will not be published without the prior approval of the Sponsor.

TIME LINES

Tentative time lines are shown in Table 1, above.

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Annex 120

ANNUAL REPORT OF THE INTER-AMERICAN DRUG ABUSE CONTROL COMMISSION (CICAD) TO THE GENERAL ASSEMBLY OF THE ORGANIZATION OF AMERICAN STATES AT ITS 36TH REGULAR SESSION, SANTO DOMINGO, DOMINICAN REPUBLIC, 4-6 JUNE 2006

(Available at: http://www.cicad.oas.org/AnnualReports/2005/1474-rev2-AnnualReport_CICAD2005_en.pdf (last visited 7 March 2010), p. 13)

ORGANIZATION OF AMERICAN STATES

INTER-AMERICAN DRUG ABUSE CONTROL COMMISSION cicad

THIRTY-EIGHTH REGULAR SESSION
December 6-9, 2005
Washington, D.C.

OEA/Ser.L/XIV.2.38
CICAD/doc.1474/05 rev.2
22 May 2006
Original: English

**ANNUAL REPORT OF THE
INTER-AMERICAN DRUG ABUSE CONTROL COMMISSION (CICAD) TO THE
GENERAL ASSEMBLY OF THE ORGANIZATION OF AMERICAN STATES
AT ITS THIRTY-SIXTH REGULAR SESSION**

local market for unprocessed and processed produce to strengthen those capabilities that might later be applied to exporting processed products.

Colombia

Study of the Effects of Aerial Glyphosate Spraying and Illicit Crop Cultivation on Human Health and the Environment
In April, the results of the study were presented to the Government of Colombia and made available on the CICAD web site. The scientific team held a news conference in Bogotá, reported the findings to several scientific fora, and prepared responses to commentaries made by several organizations.

Dominica

Organic Banana Production and Pest Management
In 2005, this project expanded its showcase plots to demonstrate the use of organic farming and pest management techniques. This change also brought in new project personnel.

Peru

Tropical Crops Institute (ICT) – Training farmers in the Apurimac and Ene River Valley (VRAE)
The Tropical Crops Institute (ICT) renewed agreements with both CICAD and the Narcotics Affairs Section of the US Embassy in Peru to conduct agricultural extension training in more than 700 locations in Tingo María, Tocache, Juanjui and Tarapoto for 3,000 beneficiaries. Training was provided on topics such as using more technical methods to increase cacao yield, propagation systems, fertilization, pruning, and pest management. Leadership scholarships also enabled farmers to live and study for five days at the ICT-NAS/CICAD Experimental Station in Tarapoto.

Publication

Comité Andino para le Desarrollo Alternativo (CADA), *Estrategia andina de desarrollo alternativo integral y sostenible*. Bogotá, Colombia: 2005

D. LEGAL DEVELOPMENT

Overview

The Legal Development unit provides counseling and legal assistance to the different units of CICAD, giving legal advice on topics and procedures in the areas of drugs and related subjects. One of its most important tasks is to review model regulations. This unit is also in charge of administrative and legal tasks, advising the CICAD on OAS policies and procedures as well as funding obligations. As such, it is responsible for formulating and drafting of Memoranda of Understanding and other agreements.

Control of Arms and Explosives

The Legal Development unit is concentrating on prevention and control of trafficking in firearms through application of the *Inter-American Convention Against the Illicit Manufacturing of and Trafficking in Firearms, Ammunition, Explosives, and Other*

Annex 121

ANNUAL REPORT OF THE PERMANENT COUNCIL TO THE GENERAL ASSEMBLY OF THE ORGANIZATION OF AMERICAN STATES 2006-2007

(OAS, AG/DOC.4698/07, pp. 33, 34)

GENERAL ASSEMBLY

THIRTY-SEVENTH REGULAR SESSION
June 3 to 5, 2007
Panama City, Panama

OEA/Ser.P
AG/doc.4698/07 corr. 1
4 June 2007
Original: Spanish

Item 7 on the agenda

ANNUAL REPORT OF THE PERMANENT COUNCIL
TO THE GENERAL ASSEMBLY
2006-2007

7. Other business

- The Permanent Mission of Brazil requested the distribution of a CD-ROM of the Special Session of Freedom of Thought and Expression that took place on October 26 and 27, 2006. The Alternative Representative of Brazil also informed the Council that his government ratified the Inter-American Convention on Transparency in Conventional Weapons Acquisitions.

- The Permanent Council bid farewell to Ambassador John Maisto, Permanent Representative of the United States.

15. Record of the regular meeting held on January 9, 2007 CP/ACTA 1576/07[24/]

1. Adoption of the order of business

The Council adopted the order of business, document CP/OD-1576/07.

- Remarks by the Chair of the Permanent Council

  Ambassador María del Luján Flores, Permanent Representative of Uruguay, made some remarks on the occasion of her first meeting as Chair of the Permanent Council. She said, among other things, that she intended to promote steadfastly the general principles of international law and, with support from the various diplomatic missions, some topics such as the environment and regional agreements, protection and promotion of the rights of children, and in particular the right of identity and of citizen participation.

- Presentation of the gavel

  As is customary, the Permanent Council presented the gavel to Ambassador Marina Annette Valère, Permanent Representative of Trinidad and Tobago, in recognition for her work as Chair of the Council from October to December 2006.

2. Note from the Permanent Mission of Ecuador requesting inclusion of the topic "Resumption of glyphosate spraying in an area adjacent to the Ecuadorian border"

At the request of the Permanent Mission of Ecuador, the Permanent Council considered the topic "Resumption of glyphosate spraying in an area adjacent to the Ecuadorian border" (CP/INF.5428/07).

Present for consideration of this matter were His Excellency Mr. Francisco Carrión Mena, Minister of Foreign Affairs of Ecuador, and His Excellency Mr. Camilo Reyes, Vice Minister of Foreign Affairs of Colombia.

24. Las declaraciones y comentarios formulados por la Delegaciones se encuentran en el acta de la sesión CP/ACTA 1576/07.

During the meeting, the Minister of Foreign Affairs of Ecuador presented the OAS Secretary General, José Miguel Insulza, with three volumes containing "Studies and documents on aerial spraying of glyphosate and its chemical components." The three volumes have been placed in the Columbus Memorial Library. The statements by the Minister of Foreign Affairs of Ecuador and the Vice Minister of Foreign Affairs of Colombia have been published, respectively, as documents CP/INF.5433/07 and CP/INF.5432/07.

Lastly, the Council decided to take note of the information presented on the topic.

3. Update on preparations for the thirty-seventh regular session of the General Assembly

Ambassador Albert R. Ramdin, Assistant Secretary General, commented on the preparatory work for the thirty-seventh regular session of the General Assembly.

In that connection, the Permanent Council decided:

- To take note of the information presented by the Assistant Secretary General on the preparatory work for the next regular session of the General Assembly.
- To reiterate to the organs, agencies, and entities of the Organization that they should transmit, no later than March 1 of this year, their respective annual reports in order to meet statutory deadlines and as indicated by the Assistant Secretary General.

4. Applications from civil society organizations to participate in OAS activities

Ambassador Marina Annette Valère, Permanent Representative of Trinidad and Tobago and Chair of the Committee on Inter-American Summits Management and Civil Society Participation in OAS Activities, presented the applications from the following civil society organizations (CP/CISC-301/06) to the Permanent Council for consideration:

1.	Transparency International Costa Rica	(CP/CISC-255/07)
2	*Transparência Brasil*	(CP/CISC-256/07)
3	*Caja de Compensación Familiar de Antioquia* (COMFAMA)	(CP/CISC-257/07)
4.	*Coalición Regional contra el Tráfico de Mujeres y Niñas en América Latina y el Caribe, A.C.* (CATW-LAC)	(CP/CISC-258/07)
5.	*Centro Latinoamericano de Estudios y Cooperación para el Desarrollo* (CENLAT)	(CP/CISC-259/07)
6.	*Corporación Participación Ciudadana Ecuador (Participación Ciudadana)*	(CP/CISC-260/07)
7.	*Federación Latinoamericana de Ciudades, Municipios y*	(CP/CISC-261/07)

Annex 122

ANNUAL REPORT OF THE INTER-AMERICAN DRUG ABUSE CONTROL COMMISSION (CICAD) TO THE GENERAL ASSEMBLY OF THE ORGANIZATION OF AMERICAN STATES AT ITS 39TH REGULAR SESSION, SAN PEDRO SULA, HONDURAS, 2-3 JUNE 2009

(OEA/Ser.G, CP/doc.4395/09 corr. 1, 26 May 2009, p. 12)

PERMANENT COUNCIL

OEA/Ser.G
CP/doc. 4395/09 corr. 1
26 May 2009
Original: Spanish

ANNUAL REPORT OF THE INTER-AMERICAN DRUG ABUSE CONTROL COMMISSION TO THE GENERAL ASSEMBLY

Andean Countries Cocoa Export Support Opportunity (ACCESO)

The Andean Countries Cocoa Export Support Opportunity (ACCESO) initiative started in June 2005 with support from the World Cocoa Foundation (private business interests), the U.S. Agency for International Development (USAID) and the Inter-American Institute for Agricultural Cooperation (IICA). The ACCESO initiative aims to strengthen the entire supply chain of cacao production, from the field to the consumer, in Bolivia, Colombia, Ecuador and Peru. CICAD took specific responsibility for developing technical assistance and training for cacao farmers with the "farmer field school" (FFS) methodology. This participatory approach allows farmers to learn by doing. The method integrates farmer and trainer through a two-way channel -- adoption of practical and theoretic knowledge about the cultivation of cacao and the use of simple methodological tools. The activities of farmer field schools incorporate elements of organization, observation, analysis, reflection and action that aim towards developing the skills needed to improve decision-making and problem-solving.

In 2008, CICAD financed the implementation of 30 farm field schools in Peru, which trained 750 growers and certified 60 of them as FFS instructors. The FFS extension methodology is also being used in Bolivia. In addition, CICAD underwrote the monitoring and evaluation of the impact achieved by the farm field schools program in Peru, which reached 5,840 farmers through 234 farm field schools over the three years of the project. The project's first phase finished in late 2008, and the ACCESO team is planning a follow-on stage of activities.

Colombia: Study on the Effects of Aerial Glyphosate Spraying

In 2005, CICAD's scientific evaluation team presented the results of an independent study, undertaken at the request of the governments of Colombia, the United States and the United Kingdom, to measure the impact of aerial spraying of coca fields in Colombia on human health and the environment. Although no association between spraying and human reproduction was found, the team proposed to carry out additional studies to identify possible risk factors associated with other human activities or the environment. The independent scientific evaluation team that CICAD hired in 2006 presented most of its findings of the follow-up study on the human heath and environmental evaluation of the aerial spraying to control coca and poppy crops in Colombia in late 2008. The completed study, which consisted of several technical articles, was submitted for consideration in the peer-reviewed scientific periodical *Journal of Human and Environmental Toxicology*, and was also to be published on the CICAD web site. The findings will also be presented to the public in Washington, DC and in Bogota in 2009.

The components of the study are the following:

- Risk to human and environmental health posed by the use of Glyphosate for the control of coca crops;
- Differences in gestation period in fertile women in five Colombian regions;
- Bio-monitoring of genotoxic risks for farm workers in five Colombian regions, considering their work exposure to Glyphosate;
- Identification of the geographic distribution of amphibian fauna exposed to the use of pesticides;
- Risk posed to amphibians due to the production and eradication of coca;
- Analysis of the drift from aerial spraying with Glyphosate and Cosmo-Flux, as employed in the Colombian eradication program; and
- Identification of the mixtures of Glyphosate and additives that might be less toxic for aquatic organisms than the one currently in use by the Government of Colombia.

Annex 123

SGS (SOCIETÉ GÉNERALE DE SURVEILLANCE, S.A) COLOMBIA S.A., "REPORT OF CONTAMINATION CONTROL FOR GLYPHOSATE APPLICATION AT THE SIERRA OF SANTA MARTA", 1987

(SGS Colombia S.A. Bogotá, *Report of Contamination Control for Glyphosate Application at the Sierra of Santa Marta,* 1987. pp. 2, 5, 6, 7, 8, 12)

[Page 2]

INTRODUCTION

This study has been undertaken for the need of the Colombian National Police to establish the effects on the jungle as a consequence of the intensive application (by means of spraying) of glyphosate used to destroy marijuana crops. In the participation of this effort, SGS has been contracted as an independent, private institution to carry out control of the current contamination resulting from the use of glyphosate. For this preliminary study, it was decided to sample some sites recently sprayed by the National Police and considered by it the most heavily sprayed with Glyphosate.

Soil, foliage, and water samples were taken in seven (7) recently sprayed sites as well as water samples from the Ciénaga Grande de Santa Marta or Puente de la Parra, and the Cordoba River downstream the sprayed areas.

[…]

[Page 5]

2. Inspection Period

Inspectors from SGS carried out the inspection on 2 and 3 February 1998. On those days, an aerial reconnaissance was made on a helicopter of the National Police. During this reconnaissance of the northern and western area of the Sierra de Santa Marta, a lot of overflights on previously sprayed sites were made, landing on the sites with the greatest spraying to take soil, foliage, and water samples.

All of the above mentioned sites (See 2 a.) were widely sprayed during the August-November 1987 period, according to the Police officers that carried out the task and to the documentation submitted) See Annex DOC 9774/5-6-7-8)

Thus, we can consider that the inspection sites with no exemption were sprayed with glyphosate in a 2 to 5 month period prior to our sampling process.

[…]

[Page 6]

4. Procedure to collect samples

Taking into account the glyphosate characteristics, a sampling scheme was designed so that it were reliable and allowed us to get representative result of contamination of the sites sprayed with glyphosate.

[…]

[Page 7]

Sampling Scheme

In every sampling site; that is, a site intensively sprayed with glyphosate, soil, foliage, and water samples were taken at random with the purpose of obtaining a representative compound soil, foliage, and water sample of each site.

The scheme is designed to determine if

-There is or there is not presence of glyphosate in soils

- There is or there is not presence of glyphosate in weeds and/or food plants that grew again in the sprayed sites.

- There is or there is not contamination in the rivers water, resulting from leaching and erosion of soils in hilly landscape.

Soil Sampling

Only the superficial horizon was sampled (A) which corresponds to the zone in contact with the glyphosate that has fallen and that due to the characteristics of the product (quick absorption) may contain contaminants.

Superficial samples were taken at few centimeters of the different types of soil found in the same site, which are made up of heterogeneous materials. They are little evolved soils coming from the high and low areas of the field given its wavy and hilly features.

[Page 8]

Water Sampling

Two 500-ml samples were taken in each sprayed site, when water was found.

A sample of no-running and a sample of running water was taken.

Water samples include colloidal particles, clay, and organic matter in suspension.

Foliage Sampling

All types of plants were collected: weed, pasture, food plants, and trees existing in the sampling sites.

To make the sample representative, small and big leaves from the said plants were taken always and only from the sprayed areas .

No aquatic flora samples were taken because they are scarce and also for the obvious reason that the aquatic zones were not sprayed.

[…]

[Page 12]

7. Conclusions

Taking into considerations the efforts made by the National Police in Magdalena [province] that helped us with transport by helicopter, as well as with the location of sites to be sampled, classified by the official pilots of the Police as the sites where the greatest amount of herbicide was applied during the August-November 1987 period.

Considering also the procedure to collect samples established by SGS so that a representative result of the contamination of sites could be obtained regarding the determination of presence of glyphosate:

-in soils
-in weed and/or food plants that grew again
-in river waters

And the results from the analyses made to the 26 samples to detect the presence of glyphosate in soil, foliage, and water samples duly collected and packed by SGS, we can certify that (see sampling and quality certificates by SGS Colombia S.A.) there is no detectable contamination with glyphosate in the sampled sites.

SGS COLOMBIA S.A.
[Signed]

Annex 124

J.P. GIESY, S. DOBSON S & K.R. SOLOMON, "ECOTOXICOLOGICAL RISK ASSESSMENT FOR ROUNDUP HERBICIDE"

(*Reviews of Environmental Contamination and Toxicology* 167: 35-120, 2000, pp. 69, 74.)

Rev Environ Contam Toxicol 167:35–120

Ecotoxicological Risk Assessment for Roundup® Herbicide

John P. Giesy, Stuart Dobson, and Keith R. Solomon

Contents

I. Introduction

Glyphosate-based weed control products are among the most widely used broad-spectrum herbicides in the world. The herbicidal properties of glyphosate were discovered in 1970, and commercial formulations for nonselective weed control were first introduced in 1974 (Franz et al. 1997). Formulations of glyphosate,

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Table 16. Acute toxicity of Roundup®, glyphosate, AMPA, and POEA to aquatic invertebrates.

Species	Test duration (days)	EC_{50} or LC_{50} (mg/L)[a]	NOEC (mg/L)[a]	Reference
Roundup®: freshwater species				
Scapholeberis kingi	0.125	61	—	Sun (1987)
Anopheles quadrimaculatus larvae (mosquito)	1	673.4	—	Holck and Meek (1987)
Chironomus plumosus	2	58.1[c]	—	Folmar et al. (1979)
Daphnia magna	2	9.7[c]	1.9[e]	Folmar et al. (1979)[f]
D. magna	2	24	7.8	EG & G Bionomics (1980f)
D. magna	2	12.9[c]	4.6[c]	EG & G Bionomics (1980e)
Daphnia pulex	2	19	—	Hartman and Martin (1984)
Gammarus pseudolimnaeus	2	42	4.4	ABC Inc. (1982b)
G. pseudolimnaeus	2	200[c]	—	Folmar et al. (1979)
D. pulex	4	25.5	—	Servizi et al. (1987)
G. pseudolimnaeus	4	138.7[c]	—	Folmar et al. (1979)
Orconectes nais	4	7	—	Mayer and Ellersieck (1986)
Procambarus clarkii	4	47.3	—	Holck and Meek (1987)
Glyphosate: freshwater species (tested as acid)				
Daphnia magna	2	780	560	ABC Inc. (1978a)
Pseudosuccinea columella	n.r.	98.9	—	Thompson (1989)
Glyphosate: freshwater species (tested as IPA salt)[b]				
D. magna	2	930	320	ABC Inc. (1981a)
Chironomus plumosus	2	55	—	Folmar et al. (1979)
Chironomus riparius	2	5600	—	Buhl and Faerber (1989)
Hyalella azteca[d]	10	>530	265	Beyers (1993)
Chrionomus tentans[d]	10	>530	265	Beyers (1993)
Glyphosate: marine species (tested as acid)				
Crassostrea virginica, eggs	2	>10	10	Bionomics (1973a)
Palaemonetes vulgaris	4	281	210	Bionomics (1973b)
Uca pugilator	4	934	650	Bionomics (1973b)
Mysidopsis bahia	4	>1000	—	EG & G Bionomics (1978c)
Tripneustese esculentes	4	>1000	1000	EG & G Bionomics (1978d)
AMPA: freshwater species				
D. magna	2	690	320	ABC Inc. (1991a)
POEA: freshwater species				
C. plumosus	2	13.0	—	Folmar et al. (1979)
D. magna	2	2.0	0.32	ABC Inc. (1980b)
D. pulex	2	4.1	—	Moore et al. (1987)
D. pulex	4	2.0	—	Servizi et al. (1987)

[a]Units are mg RU/L, mg a.e./L, mg AMPA/L, or mg POEA/L. RU, Roundup; a.e., glyphosate acid equivalents. [b]Test material was glyphosate IPA salt; LC_{50} reported as mg glyphosate IPA salt/L. [c]Value from data source corrected to mg RU/L. [d]Sediment/water test. [e]Derived from an acute EC_{50}/acute NOEC ratio of 5. [f]Reference used in setting acute toxicity reference value.

RU LC_{50} values range from 4.2 to 52 mg RU/L, compared with glyphosate values that range from 22 to >1000 mg a.e./L. The results of several studies on glyphosate appear in the literature but were not included in Table 18 because several of the criteria for inclusion were not met. One study reported glyphosate LC_{50} of 5.5 mg a.e./L for carp (*Cyprinus carpio*) and 7.9 mg a.e./L for *Tilapia* sp. (Wang et al. 1994). Fundamental water chemistry values and survival of control organisms were not reported in these studies. In another study (Wan et al. 1989), several values for glyphosate LC_{50} less than 22 mg a.e./L were reported for nonnatural waters (dechlorinated city water). These values were not included in this evaluation because it was not clear if the pH observed for the city water, and possibly other water quality parameters, were artifacts of the water treatment process. Exclusion of these glyphosate values did not affect the acute TRV because the TRV was based on RU that has greater toxicity deriving from the surfactant.

The greater aquatic toxicity of RU compared to glyphosate is attributed to POEA. For rainbow trout, the 96-hr RU LC_{50} value was 8.3 mg RU/L (2.6 mg a.e./L), whereas the glyphosate LC_{50} from the same study was 140 mg a.e./L (Folmar et al. 1979). The same authors reported a POEA 96-hr LC_{50} of 1.6 mg/L, which suggests that POEA is the main source of aquatic toxicity.

Glyphosate Chronic TRV. Glyphosate exhibited little chronic toxicity to fish (Table 19). No effects on survival, growth, or reproduction of adult fathead minnow or progeny were observed when exposed to concentrations as great as 26 mg a.e./L for up to 8 mon (EG & G Bionomics 1975). A prolonged study with RU (21 d) was conducted with rainbow trout to determine effects on growth or survival (ABC Inc. 1989d). The NOEC for that study was 2.4 mg RU/L (0.74 mg a.e./L). Because the latter NOEC is protective of all glyphosate chronic values, 0.74 mg a.e./L was selected as the chronic TRV for fish.

Table 19. Chronic toxicity of Roundup® and glyphosate to fish.

Species	Test duration (days)	NOEC[a] (mg/L)	Reference
Roundup®			
Rainbow trout, *Oncorhynchus mykiss*	21	2.4	ABC Inc. (1989d)[b]
Glyphosate			
Fathead minnow, *Pimephales promelas*	255	26	EG & G Bionomics (1975)
Rainbow trout, *O. mykiss*	21	52	ABC Inc. (1989a)

[a]Units are mg RU/L or mg a.e./L; RU, Roundup; a.e., acid equivalents.
[b]Reference used in setting toxicity reference value.

Annex 125

G. M. Williams et al., "Safety evaluation and risk assessment of the herbicide Roundup® and its active ingredient, glyphosate, for humans"

(*Regulatory Toxicology and Pharmacology* 31:117–165, 2000, pp. 117, 160.)

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Safety Evaluation and Risk Assessment of the Herbicide Roundup[1] and Its Active Ingredient, Glyphosate, for Humans

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Reviews on the safety of glyphosate and Roundup herbicide that have been conducted by several regulatory agencies and scientific institutions worldwide have concluded that there is no indication of any human health concern. Nevertheless, questions regarding their safety are periodically raised. This review was undertaken to produce a current and comprehensive safety evaluation and risk assessment for humans. It includes assessments of glyphosate, its major breakdown product [aminomethylphosphonic acid (AMPA)], its Roundup formulations, and the predominant surfactant [polyethoxylated tallow amine (POEA)] used in Roundup formulations worldwide. The studies evaluated in this review included those performed for regulatory purposes as well as published research reports. The oral absorption of glyphosate and AMPA is low, and both materials are eliminated essentially unmetabolized. Dermal penetration studies with Roundup showed very low absorption. Experimental evidence has shown that neither glyphosate nor AMPA bioaccumulates in any animal tissue. No significant toxicity occurred in acute, subchronic, and chronic studies. Direct ocular exposure to the concentrated Roundup formulation can result in transient irritation, while normal spray dilutions cause, at most, only minimal effects. The genotoxicity data for glyphosate and Roundup were assessed using a weight-of-evidence approach and standard evaluation criteria. There was no convincing evidence for direct DNA damage *in vitro* or *in vivo*, and it was concluded that Roundup and its components do not pose a risk for the production of heritable/somatic mutations in humans. Multiple lifetime feeding studies have failed to demonstrate any tumorigenic potential for glyphosate. Accordingly, it was concluded that glyphosate is noncarcinogenic. Glyphosate, AMPA, and POEA were not teratogenic or developmentally toxic. There were no effects on fertility or reproductive parameters in two multigeneration reproduction studies with glyphosate. Likewise there were no adverse effects in reproductive tissues from animals treated with glyphosate, AMPA, or POEA in chronic and/or subchronic studies. Results from standard studies with these materials also failed to show any effects indicative of endocrine modulation. Therefore, it is concluded that the use of Roundup herbicide does not result in adverse effects on development, reproduction, or endocrine systems in humans and other mammals. For purposes of risk assessment, no-observed-adverse-effect levels (NOAELs) were identified for all subchronic, chronic, developmental, and reproduction studies with glyphosate, AMPA, and POEA. Margins-of-exposure for chronic risk were calculated for each compound by dividing the lowest applicable NOAEL by worst-case estimates of chronic exposure. Acute risks were assessed by comparison of oral LD_{50} values to estimated maximum acute human exposure. It was concluded that, under present and expected conditions of use, Roundup herbicide does not pose a health risk to humans. © 2000 Academic Press

Key Words: glyphosate; Roundup; herbicide; human exposure; risk assessment.

INTRODUCTION

History of Glyphosate and General Weed Control Properties

The herbicidal properties of glyphosate were discovered by Monsanto Company scientists in 1970. Glyphosate (Fig. 1) is a nonselective herbicide that inhibits plant growth through interference with the production of essential aromatic amino acids by inhibition of the enzyme enolpyruvylshikimate phosphate synthase, which is responsible for the biosynthesis of chorismate, an intermediate in phenylalanine, tyrosine, and tryptophan biosynthesis (Fig. 2). This pathway for biosynthesis of aromatic amino acids is not shared by members of the animal kingdom, making blockage of this pathway an effective inhibitor of amino acid biosynthesis exclusive to plants. Glyphosate expresses its herbi-

[1] Roundup is a registered trademark of Monsanto.

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Acute exposure. Estimates of aggregated acute exposure in adult applicators (0.163 mg/kg body wt/day) and children (0.0911 mg/kg body wt/day) were substantially higher than those for chronic exposure. In children, this increase was primarily due to contributions from reentry exposure and, to a lesser degree, the ingestion of wild foods. The acute oral LD_{50} of POEA is approximately 1200 mg/kg. The estimated acute exposure values are 7360 to 13,200 times lower than this value.

OVERALL CONCLUSIONS AND SUMMARY STATEMENT

This assessment was conducted for adult applicators and children (age 1 to 6 years) because they have the highest potential exposures. Estimates of exposure described for these two subpopulations and used in these ri: :alculations are considered excessive compared to those likely to result in the general population from the use of Roundup herbicide. MOE analyses compare the lowest NOAELs determined from animal studies to worst-case levels of human exposure. MOEs of greater than 100 are considered by authoritative bodies to indicate confidence that no adverse health effects would occur (WHO, 1990). The MOEs for worst-case chronic exposure to glyphosate ranged from 3370 to 5420; the MOEs for AMPA ranged from greater than 269 to 83,300; and for POEA the MOEs ranged 461 to 1380. Based on these values, it is concluded that these substances do not have the potential to produce adverse effects in humans. Acute exposures to glyphosate, AMPA, and POEA were estimated to be 7360–1,730,000 times lower than the corresponding LD_{50} values, thereby demonstrating that potential acute exposure is not a health concern. Finally, under the intended conditions of herbicide use, Roundup risks to subpopulations other than those considered here would be gnificantly lower. It is concluded that, under present and expected conditions of new use, there is no potential for Roundup herbicide to pose a health risk to humans.

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Annex 126

EMBASSY OF THE UNITED STATES OF AMERICA - CLÍNICA DE TOXICOLOGÍA 'URIBE CUALLA', *ALLEGED EFFECTS OF GLYPHOSATE ON HUMAN HEALTH*, BOGOTÁ, DECEMBER 2001

(*Embajada de los Estados Unidos de América, clínica de toxicología 'Uribe Cualla'* , *Supuestos efectos del Glifosato en la salud humana,* pp. 52, 53, 54. *Archives of the Ministry of Foreign Affairs of Colombia*)

[…]

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5. CONCLUSIONS AND RECOMMENDATIONS

[Page 52]

- Despite the number of diseases observed in the Putumayo's population, there are several reasons why these cannot be attributed to a single chemical substance. The first of them corresponds to the limitations of a retrospective epidemiological environmental study, which makes it difficult to collect evidence of exposure to the substance involved. It is also the case of biomarkers presence, and the difficulty to establishing a correlation between exposure to the glyphosate and symptoms reported by people. Therefore, it is almost impossible to establish a causal relationship between exposure to the substance in question and clinical manifestations attributed to exposure. It is not feasible to make a plausible assumption in order to explain a phenomenon of morbidity attributable to the effects of the introduction of low toxic potential chemical and poor dispersion in the environment.
- To determine whether there is an increase in health problems frequency and diseases after aerial spraying with glyphosate and if this supposed increase is related to exposure, an informative epidemiological environmental study is required. However, this was not possible because this study design and implementation was made five (5) months after aerial spraying. The initial cases and controls model was ruled out, leaving the retrospective study, with the limitations entered, as the only option available.
- The information obtained by the study reflects only the demand characteristics and the use of health services offered by the Health Brigade in nine districts of three municipalities of Putumayo Province (Orito, Valle de

Guamuez and San Miguel) 13. The sample cannot be defined as random given that the people came voluntarily and in response to a call wide.

• Despite the limitations of a retrospective study, an analysis of data from the ICI, together with the morbidity data available and the toxicological information on the glyphosate, indicate that the aerial spraying with glyphosate carried out by the DIRAN [Anti-Narcotics Direction of the National Police] between December 2000 and February 2001 cannot be identified as the cause of the phenomena of disease reported by the population of Putumayo.

Within the data collected it is worthwhile to quote the following:

• Health problems encountered in the study population was similar to the prevalence rates found in the epidemiological reports of previous years at the start of PECIG, both in municipalities object of the program (e.g. La Hormiga) and in municipalities […]

[Page 53]

[…] located in provinces where the eradication of illicit crops have never been carried out, as is the case of Puerto Wilches and San Vicente de Chucurí in Santander Province. • (See Table No. 5.1). The findings are consistent with the poor health, poverty, poor supply of drinking water, inappropriate practices in the personal hygiene, precarious excrete disposal and refuse and the poor food handling in the Putumayo Province, where the percentage of unmet basic needs – UBN - was 78.7% in 2001 and the incidence of poverty was 68.9 % in 1998.

[…]

[Page 54]

[…]

The illnesses most often attributed by the study's subjects as secondary to glyphosate spraying were: gastrointestinal symptoms (diarrhea, vomit and nausea), skin symptoms (pruritus or itch, erythema or reddening, vesicles or blisters, soreness and sores), eye symptoms (soreness, reddening, pink eye, pain and pruritus), respiratory symptoms (dyspnea or fatigue, cough and croup or rhinorrhea), cephalea (headache and fever). These symptoms may originate due to multiple causes, as well as to exposure to chemical elements.

Annex 127

R.E. RAMOS C., J.P. RAMOS B., *ENVIRONMENTAL ASSESSMENT OF THE IMPACT OF COCA CROPS AND THE PROCESSING OF COCA LEAF*, UNIVERSIDAD DE LOS ANDES, BOGOTÁ, COLOMBIA, 2002

(R.E. Ramos C., J.P. Ramos B., *Evaluación Ambiental del Impacto de cultivos de coca y el procesamiento de la hoja de coca*, Universidad de los Andes, Bogotá, Colombia, 2002, pp. 1, 5, 10-11)

[Page 1]

ABSTRACT: This document analyzes environmental impacts caused by coca crops and the processing of coca leaf in the province of Norte de Santander, Tibu municipality. To determine environmental impacts, forest cover loss was analyzed using multi-temporal analysis of SPOT satellite images for the years 1999, 2000, and 2001. The cover loss due to coca crops corresponded to 30% of the total for that period. The environmental effects generated by the use of pesticides and processing laboratories were established by determining residues and pouring resulting from the processing of coca paste and their location. It, combined with the permanence of coca crops, allows to determine sites of potential chemical substances accumulation, given that coca crops use 10 time more agrochemicals compared to cocoa crops, the traditional agricultural crop in the municipality.

[…]

[Page 5]

[…]

Acid solutions are poured directly on the soil or in the nearest water course depending on the laboratory location. It is likely that the effects of pouring acid solutions alter the pH in soils and water where they deposit.
Transformation of coca leaf into coca paste and cocaine has negative environmental effects. Studies of the United States Department of State show that 10 million liters of sulfuric acid, 16 million liters of Ethyl Ether, 8 million liters of acetone, and 40 to 770 million liters of kerosene are poured every year on the soil by coca processors in the Andean Region, mainly in Colombia (Scheafer 2002).

5.2 Chemical precursors used in processing

Processing of coca leaf requires a great deal of chemical precursors and water to extract the alkaloid (DNE, 2002). According to data obtained from the Antinarcotics Police, it is estimated that every hectare of coca crops requires the use of approximately 127 kilos/ha of solid precursors, 447 litres/ha of liquid precursors and 400 litres/ha of water (DIRAN 2002).

[…]

[Page 10 and 11]

8. CONCLUSIONS

[…]

5. after establishing the types of pesticides used by coca growers, it was possible to identify 5 pesticides that due to its use intensity and toxicological classification are classified from extremely to highly toxic. These pesticides are: herbicides such as Gramaxone (A.i. paraquat), Faena (A.i. glyphosate), insecticides such as Tamaron (I.a. Metamidaphos), and fungicides such as Manzate (I.a. Mancozeb). The analysis allowed to establish that the risk of substances accumulation per environmental component and the monitoring needs are: In soils, substances that need to be monitored are Gramaxone and Faena, in underground waters, Anikilamina and Tamaron, and in superficial water sediments all these compounds must be monitored.

6. Processing of coca is made in order to extract or wash the alkaloid, which represents only 0,5 to 1,5 % of the total substances in the leaf. This extracting and purification process requires the use of acids, bases, water, and organic solvents that are added to the process along the different stages until the pure alkaloid or coca paste is obtained. Of these substances, organic solvents are recycled and acids (sulfuric acid) and bases (ammoniac), and water are dumped on the environment without any control. Likewise vegetation residues are produced. They get contaminated along the process and then are dumped. Based on analyses made, in the production of 1 kg of coca paste, **1.9 litres of sulphuric acid, 1.25 litres of ammonia, 193,75 litres of contaminated water, and 625 kg of solid waste are released into the environment**.

7. In the study zone, the following amounts of chemical substances and waste were released in the 1999-2001 analysis period. 91,962 litres of sulphuric acid or 434 tins of 55 gallons each, 60.501 liters or 286 tins of ammonia, and 9.378 m3 of contaminated water and 30 tons 0f vegetation waste were poured. Therefore, there is a great chance that of existence of these substances on superficial water and soil, which affects the populations that depend on these two components.

8. The multi-temporal analysis of coverage allowed to establish that the illicit coca crops fostered the loss forest coverage. Although between 1999 and 2001, coca crops replaced 4.501 ha of primary and secondary forest, the forest coverage loss was of 38.967 hectares, due mainly to replacement with pastures. Since coca crops are planted among the primary forest, the neighboring are intervened and become secondary forest, and later pastures and bushes.

[…]

Annex 128

O. SAAVEDRA, LABORATORIO INMUNOPHARMOS LTDA., TOXICITY STUDY ON LABORATORY ANIMALS FOR TWO CONCENTRATIONS OF GLYPHOSATE 44% + COSMOFLUX 1% + WATER 55%, BOGOTÁ, 15 FEBRUARY 2002. STUDIES: ACUTE ORAL TOXICITY LD50 (EPA GUIDELINE 870-1100), ACUTE DERMAL TOXICITY LD50 (EPA GUIDELINE 870-1200), ACUTE INHALATION TOXICITY LD50 (EPA GUIDELINE 870-1300), ACUTE EYE IRRITATION (EPA GUIDELINE 870-2400), ACUTE DERMAL IRRITATION (EPA GUIDELINE 870-2500), DERMAL SENSITIZATION (EPA GUIDELINE 870-2600)

(O. Saavedra, Laboratorio Inmunopharmos Ltda., *Toxicity Study on Laboratory Animals for two concentrations of Glyphosate 44% + Cosmoflux 1% + Water 55%,* Bogotá, 15 February 2002. Studies: Acute oral toxicity LD50 (EPA Guideline 870-1100), Acute dermal toxicity LD50 (EPA Guideline 870-1200), Acute inhalation toxicity LD50 (EPA Guideline 870-1300), Acute eye irritation (EPA Guideline 870-2400), Acute dermal irritation (EPA Guideline 870-2500), Dermal sensitization (EPA Guideline 870-2600), pp. 1, 2, 7, 13, 14, 37, 38, 45, 50, 62, 67, 74, 77, 80, 88)

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STUDY REQUIRED BY: NATIONAL NARCOTICS DIRECTORATE
PRODUCT: GLYPHOSATE 44%+COSMOFLUX 1%+WATER 55%
DOCUMENTS: 5111-001; 5121-002; 5131-003; 5141-004; 5152-005; 5161-007

TOXICITY STUDY

ON

LABORATORY ANIMALS

GLYPHOSATE 44%+COSMOFLUX 1%+WATER 55%

STUDY REQUESTED BY:

NATIONAL NARCOTICS DIRECTORATE
2002-02-15

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VERIFICATION

This study meets the requirements established EPA (Environmental Protection Agency) of the United States of America guidelines.

STUDY	GUIDELINE
ACUTE ORAL TOXICITY	(870-1100)
ACUTE DERMAL TOXICITY	(870-1200)
ACUTE INHALANT TOXICITY	(870-1300)
LOW OCULAR IRRITATION	(870-2400)
LOW DERMAL IRRITATION	(870-2500)
SKIN SENSIBILISATION	(870-2600)

And done under Good Laboratory Practices

Study Director:
Orlando Saavedra Cruz.
Veterinary
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Quality Assurance:
Javier Darío Calderón
Veterinary
Professional License NO.06643

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DOCUMENTS NUMBER: 5111-001-1216
VOLUME: 1
STUDY TITLE: ACUTE ORAL TOXICITY LD_{50}
GUIDE RECORD: EPA (870-1100)
BEGINNING DATE: 2001-12-16
ENDING DATE: 2001-12-30
STUDY DIRECTOR: ORLANDO SAAVEDRA CRUZ, VETERINARY
QUALITY ASSURANCE: JAVIER DARIO CALDERÓN, VETERINARY
LABORATORY: INMUNOPHARMOS L TOA (COTA, CUNDINAMARCA)
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RESULTS:

Mortality clinical signs: (Refer to daily observations)

Dosage of 5000 mg/kg:
With this dosage, the animals presented the following signs immediately after product administration: Groans after 10 minutes product administration, which diminished as a few hours; by the end of the first 5 hours, the animals were apparently normal, eat and drink normally.
24 hours after the study started, the animals were normal and remain so until completion of the study, that's to say 14 days.
It was no mortality with this dosage.
At the end of the study, the autopsy of the survivor animals demonstrated that the bodies are apparently normal.
The mortality was 0% for both males and females.

Dosage of 2500 mg/kg:
Normal behavior was observed throughout the study.
With this dosage, the mortality was 0% for both males and females

Dosage of 1250 mg/kg:
Normal behavior and normal fitness was observed throughout the study.
The mortality was 0% for both males and females.
(Table) Death during the test

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Necropsy: The autopsy of all animals' organs was done macroscopically: heart, lung, spleen, liver, bladder, kidney, stomach, small intestine, large intestine, reproductive organs

The oral LD_{50} based on these 3 dosages for the sample product GLYPHOSATE 44% + COSMOFLUX 1% + WATER 55 % received from the National Narcotics Directorate is:

FEMALES: More than 5000 mg/kg
MALES: More than 5000 mg/kg

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The readings were also made daily until the day 14.
The animals were observed for mortality and pharmaco-toxicity signs on the day of the implementation and then daily until the end of the study on day 14, supervising if changes in their behavior or in hair, skin, eyes and mucous membranes were presented.

BODY WEIGHT: It was taken the day of the dosage, weekly, and before slaughter.
NECROPSY: After 14 days of observation, all the survivor animals were slaughtered without suffering and they were autopsied, so as to examine the skin (site of implementation), visceral organs of the chest, abdomen and reproductive organs.

RESULTS
Clinical signs: The monitoring made to the rabbits in cage, revealed no pharmacological signs or toxic effects.

Local effects: After removing the bandage, an erythema (10/10) was observed at the site of the treated skin, which was resolved within the first 2 days of evidence. Then mild drying and peeling appeared, and the hair started to be restored on the 5th day. At the end of the study, all animals were completely in good health.

Body Weight: The animals gained weight during the trial period. Only two male animals maintained the initial weight during the first week of the study. Normal increase weight occurred during the second week.

Mortality: There was no death during the study.

Necropsy: All organs macroscopically examined were normal. The internal organs without presence of patognomonic signs and shaved skin on site implementation appeared normal.

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CONCLUSIONS

The analyzed product GLYPHOSATE 44% + COSMOFLUX 1% + WATER 55 % received from the National Narcotics Directorate didn't present mortality in animals treated with 5000 mg / kg of weight dosage.
Locally it was no signs of toxicity.
The animals presented minor injuries at the implementation site.
The lethal dermal50 dose is greater than 5000 mg/kg.

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DOCUMENTS NUMBER: 5121-002-1230
VOLUME: 1
STUDY TITLE: ACUTE INHALING TOXICITY LC_{50}
INFORMATION: EPA (870-1300)
BEGINNING DATE: 2001-12-30
ENDING DATE: 2002-01-13
STUDY DIRECTOR: ORLANDO SAAVEDRA CRUZ, VETERINARY
QUALITY ASSURANCE: JAVIER DARIO CALDERÓN, VETERINARY
LABORATORY: INMUNOPHARMOS L TDA (COTA, CUNDINAMARCA)
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RESULTS

The autopsy of the survivor animals demonstrated that the bodies were apparently normal.
No signs of damage at the tissue level on histopathological examination of the samples were notes, as heart, lungs, liver, spleen, kidney, uterus, testicles according to pathology 02 E 12 of the laboratory of histopathology at the La Salle University, Faculty of Veterinary Medicine.

Mortality in was absent in animals treated with different dosage, 20, 10 Y 5 mg/kg of weight dosage.

CONCLUSIONS

The CL 50 for females and males of the product GLYPHOSATE 44% + COSMOFLUX 1% + WATER 55 % from the NATIONAL NARCOTICS DIRECTORATE is greater than 20 mg/L of air /hour .

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DOCUMENTS NUMBER: 5141-004-0512
VOLUME: 1
STUDY TITLE: PRIMARY OCULAR IRRITATION
INFORMATION: EPA (870-2400)
BEGINNING DATE: 2001-05-12
ENDING DATE: 2001-05-19
STUDY DIRECTOR: ORLANDO SAAVEDRA CRUZ, VETERINARY
QUALITY ASSURANCE: JAVIER DARIO CALDERÓN, VETERINARY
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Observations and records: All eyes treated and controlled, were registered and measured for possible injuries on days 1, 2, 3, 4, 5, 6 and 7 using a lamp, a magnifying glass and an ophthalmoscope to facilitate the observation, and ophthalmic fluorescein to detect damage in cornea or sclera, in order to qualify the type of injury and register it.

CONCLUSIONS:

It's considered that the product GLYPHOSATE 44% + COSMOFLUX 1% + WATER 55 % received from the NATIONAL NARCOTICS DIRECTORATE produces a mildly to moderately eyes irritation in animals treated but not washed, which is discernible between first and seventh day. (See attached statistical analysis results)

It's considered that the product GLYPHOSATE 44% + COSMOFLUX 1% + WATER 55 % received from the NATIONAL NARCOTICS DIRECTORATE doesn't produce an eyes irritation in animals treated and washed 30 seconds after product implementation, which lasts from 1 to 4 days. (See attached statistical analysis results)

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DOCUMENTS NUMBER: 1512-005-0109
VOLUME: 1
STUDY TITLE: LOW OCULAR IRRITATION
INFORMATION: EPA (870-2500)
BEGINNING DATE: 2002-01-09
ENDING DATE: 2002-01-12
STUDY DIRECTOR: ORLANDO SAAVEDRA CRUZ, VETERINARY.
QUALITY ASSURANCE: JAVIER DARIO CALDERÓN, VETERINARY.
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Methods:
24 Hours before the implementation, the animals were shaved in the back, approximately 25 cm2. On exhibition day, the animals that did not have the skin intact were ruled out.

Three bandages were placed, each one with 0.5 ml of product and covered with adherent and hypoallergenic gauze. The bandages were withdrawing according to the presence or absence of irritation: The first bandage after 15 minutes, the second after one hour, and the third after 4 hours.
Observations and records:
60 minutes after cleaning the skin and after 4 hours of exposure, the reactions of each skin site were measured for erythema and edema using a modification of Draize method (see table). Readings were made 24, 48 and 72 hours after the treatment. The product is considered irritant if the low irritation rating is greater than 2.5 degrees or whether there were ulceration, laceration or necrosis producing irreversible destruction of tissue

RESULTS:
The product GLYPHOSATE 44% + COSMOFLUX 1% + WATER 55 % received from the NATIONAL NARCOTICS DIRECTORATE does not produce erythema nor edema, on shaved and intact skin of albino rabbits.

CONCLUSIONS:
The product GLYPHOSATE 44% + COSMOFLUX 1% + WATER 55 % from the NATIONAL NARCOTICS DIRECTORATE is not a primary skin irritant.

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DOCUMENTS NUMBERS: 5161-007 -1216
VOLUME: 1
STUDY TITLE: SKIN SENSIBILISATION
INFORMATION: EPA (870-2600)
BEGINNING DATE: 2001-12-16
ENDING DATE: 2002-01-15
STUDY DIRECTOR: ORLANDO SAAVEDRA CRUZ, VETERINARY
QUALITY ASSURANCE: JAVIER DARIO CALDERÓN, VETERINARY
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CONCLUSIONS

The product GLYPHOSATE 44% + COSMOFLUX 1% + WATER 55 % received from the NATIONAL NARCOTICS DIRECTORATE does not produce adverse skin reactions after several implementations, according to the method of Buehler.

The product GLYPHOSATE 44% + COSMOFLUX 1% + WATER 55 % received from the NATIONAL NARCOTICS DIRECTORATE is not a skin sensitizer, according to the Buehler method used in this study.

Annex 129

Miguel San Sebastián & Anna-Karin Hurtig, "Oil exploitation in the Amazon Basin of Ecuador: a public health emergency", Pan Am J Public Health, 15(3):205-211, 2004

(*Pan Am J Public Health,* 15(3):205-211, 2004)

Temas de actualidad / Current topics

Oil exploitation in the Amazon basin of Ecuador: a public health emergency

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Key words: petroleum, extraction and processing industry, environmental pollution, water pollution, Ecuador.

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Oil is a major source of income for Ecuador and since the 1970s has been the "engine" of the nation's economy. Before the 1970s oil price boom, Ecuador was one of the poorest countries in Latin America. Since then, oil production has been the primary cause of Ecuador's economic growth, which has averaged 7% annually. Per capita income rose from US$ 290 in 1972 to US$ 1 200 in 2000. Today, oil continues to account for 40% of the nation's export earnings and of the budget of the national Government (1, 2). Most of this oil comes from the northeastern part of the country, the Amazon basin.

The Amazon basin of Ecuador, known as *el Oriente* (the provinces of Sucumbios, Orellana, Napo, Pastaza, Morona Santiago, and Zamora-Chinchipe), consists of more than 100 000 km^2 of tropical rain forest lying at the headwaters of the Amazon river network. The region contains one of the most diverse collections of plant and animal life in the world (3). The Oriente region is also the home of some 500 000 people, or about 4.5% of the country's population. These half-million persons include eight groups of indigenous people as well as peasants who, encouraged by land policies of the national Government, moved to the area from Ecuador's coastal and highland regions in the 1970s and the 1980s (4).

In 1967 a Texaco-Gulf consortium discovered a rich field of oil beneath the rain forest, leading to an oil boom that has permanently reshaped the region. The Amazon of Ecuador now houses a vast network of roads, pipelines, and oil facilities. While the national Government has retained dominion over all mineral rights, several private foreign companies have built and operated most of the oil infrastructure.

Current oil production activities in the Oriente region span nearly one million hectares, with over 300 producing wells and 29 production camps. The country has 4.6 billion barrels of proven oil reserves, with crude production of around 390 000 barrels per day. Of this production, Petroecuador, the Government-owned company, accounts for about 55% of Ecuador's total output, with private companies accounting for the remaining 45%. Petroecuador is attempting both to attract foreign investment to the country's largest oil fields and to boost its own production from around 215 000 barrels per day today to 600 000 barrels per day by 2005 (5).

Since 1967 many different companies have been involved in the oil exploitation process. There are currently 16 companies operating in the country: Petroecuador, 3 private Ecuadorian companies, and 12 foreign companies (6). Figure 1 shows the oil companies now operating in the country and the blocks where they are located.

Since the beginning of oil exploitation, foreign oil companies and Petroecuador have extracted more than two billion barrels of crude oil from the Ecuadorian Amazon. However, in this development process, billions of gallons (1 gallon = 3.7853 liters) of untreated wastes, gas, and crude oil have been released into the environment (7).

This paper examines the environmental and health impacts brought about by the oil development process in the Amazon region of Ecuador.

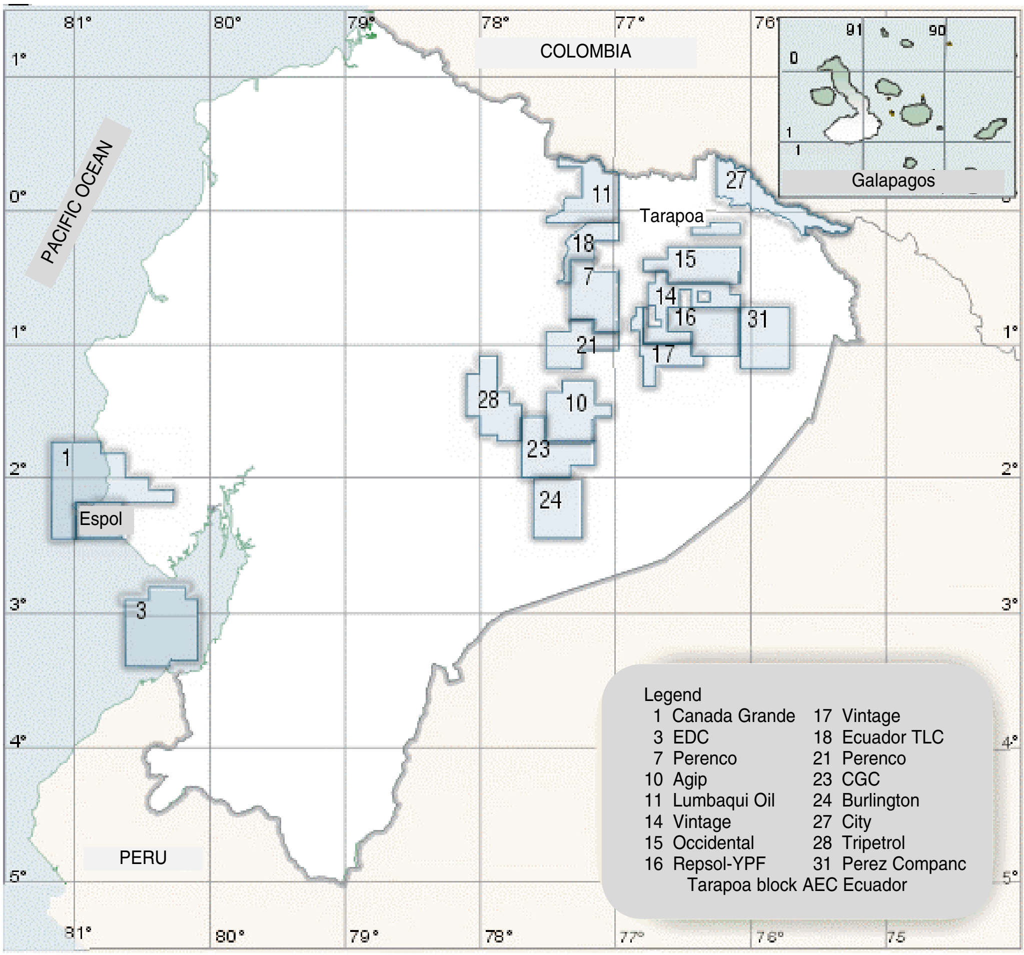
THE ENVIRONMENTAL EXPOSURE

Source and extent of pollution

Oil development activities include several contaminating processes. The extent of these polluting processes depends mainly on the environmental practices and technology used by oil companies. In Ecuador these practices have repeatedly been questioned (8–10).

Deep below the earth's surface, oil is usually mixed with natural gas and "formation water," which contains hydrocarbons, heavy metals, and a high concentration of salts. In the Amazon basin of

FIGURE 1. Oil blocks operated by oil companies, Ecuador, 2003



Source: Petroecuador (http://petroecuador.com.ec/donde.htm). Used with permission.

Ecuador, each exploratory well that is drilled produces an average of 4 000 cubic meters of drilling wastes, including formation water and drilling muds (which are used as lubricants and sealants). These wastes were frequently deposited into open, unlined pits called separation ponds, from which they were either directly discharged into the environment or they leached out as the pits degraded or overflowed from rainwater (7, 8). Although some companies have modified this practice in the last 10 years by building protected ponds, these practices still occur. There are currently nearly 200 open ponds in the Amazon region (11).

If commercial quantities of oil are found, the production stage starts. During production, oil is extracted in a mixture with formation water and gas and then separated in a central facility. At each facility, over 4.3 million gallons (16.3 million liters) of liquid wastes are generated every day and discharged without treatment into pits. Roughly 53 million cubic feet (1.5 million cubic meters) of "waste" gas from the separation process is burned daily without temperature or emissions controls. Air contamination can also be generated at pits and oil spills by hydrocarbons coming from standing oil slicks (1, 7).

Routine maintenance activities at over 300 producing wells discharge an estimated five million gallons (18.9 million liters) of untreated toxic wastes into the environment every year. Leaks from wells and spills from tanks have been common (12). According to a study conducted by the Government of Ecuador in 1989, spills from the flowlines that connect the wells to the stations were dumping an estimated 20 000 gallons (75 800 liters) of oil every two weeks (13).

Spills from the main and secondary pipelines, which connect the separation stations to the refinery in the coastal region, are also common. In 1992 the Ecuadorian Government recorded approximately 30 major spills, with an estimated loss of 16.8 million gallons (63.6 million liters) of crude oil (7). In 1989 a spill of at least 294 000 gallons (1.1 million liters) of crude oil caused the Napo River, which has a width of one km, to run black for a week; the same thing happened in 1992, when there was a spill of about 275 000 gallons (1.0 million liters) of crude oil (12). It was estimated in 2002 that two big spills per week were occurring from the main oil fields in the Oriente region (14).

Overall, during the period of 1972 through 1993, more than 30 billion gallons (114 billion liters) of toxic wastes and crude oil were discharged into the land and waterways of the Oriente (7). This compares to the 10.8 million gallons (40.9 million liters) spilled in the *Exxon Valdez* tanker disaster in 1989 in Alaska, one of the largest sea oil spills that has ever occurred.

Environmental analysis

Numerous reports have indicated that the contamination has occurred since the beginning of the oil exploration in the Ecuadorian Amazon (8–10, 15) even though longitudinal data on the levels of population exposure over time do not exist.

A study in 1987 by the Ecuadorian Government found elevated levels of oil and grease in all of the 36 samples taken from rivers and streams near productions sites. That study also found that a shortage of dissolved oxygen in the majority of water samples had seriously harmed the aquatic ecosystem (16). In 1989 another Ecuadorian Government study of 187 wells found that crude oil was regularly dumped into the forests and into bodies of water (13).

In 1994 a study carried out by the Ecuadorian environmental and human rights organization *Centro de Derechos Económicos y Sociales* (the Center for Economic and Social Rights) also found highly elevated levels of oil pollutants in the streams and rivers of the Oriente area. Concentrations of polynuclear aromatic hydrocarbons were 10 to 10 000 times greater than the levels recommended by the Environmental Protection Agency of the United States of America (9).

In 1998 an independent local laboratory that is frequently used by the oil companies surveyed 46 streams in the Oriente region (17). The laboratory found contamination by total petroleum hydrocarbons (TPH) in areas of oil activities, while no water contamination was found in areas without such activities.

In 1999 the *Instituto de Epidemiología y Salud Comunitaria "Manuel Amunárriz"* ("Manuel Amunárriz" Institute of Epidemiology and Community Health), a local nongovernmental organization concerned with health issues, undertook water analyses for TPH in communities near oil fields and also in communities far away from the fields. Those analyses showed high levels of TPH concentrations in rivers used by the communities that were close to the oil fields. In some streams, hydrocarbon concentrations exceeded by more than 100 times the limit permitted by European Community regulation (18).

Since 1999 the oil companies have been required by law to regularly monitor the level of pollution in the environment and to send reports to the national Government of Ecuador. This information is not open for public scrutiny. However, in 1999, when one of these reports was presented to a community that had made several complaints to the Ministry of Environment, it showed that streams in the community had concentrations of TPH that were over 500 times the limit permitted by European Community regulations (19). Nevertheless, the oil company and a representative of the Ecuadorian Government insisted that the levels that had been found were acceptable.

For the Amazon basin of Ecuador, there is a lack of data on soil pollution and its possible impact, and no study has been conducted on the impact that oil development has had on fish and fishing. However, studies from the Amazon basin of Peru found, after an oil spill in the Marañon River, high concentrations of TPH in the stomach and muscles of fish (20).

THE HEALTH EFFECTS

Several studies have focused on residents exposed to major coastal oil spills from tankers (21–23). However, there are few epidemiological studies concerning persons who live in communities that are near oil fields and who are exposed to acute and/or long-term contamination (24).

For many years residents of the oil-producing areas of the Ecuadorian Amazon have raised concerns over pollution related to oil development. Both peasants and indigenous people have reported that many local streams and rivers, once rich in fish, now support little or no aquatic life; further, cattle are reported to be dying from drinking from contaminated streams and rivers. These are typically the same waters that people use for drinking, cooking, and bathing. Residents have also reported that bathing in the river waters causes skin rashes, especially after heavy rains, which accelerate the flow of wastes from nearby pits into the streams (25).

In 1993 a community health workers association in the Ecuadorian Amazon conducted a descriptive study in its communities. The study suggested that, compared to communities free from oil exploitation, communities in oil-producing areas had elevated morbidity rates, with a higher occurrence of abortion, dermatitis, skin mycosis, and malnutrition, as well as higher mortality rates (26).

In 1994 the Center for Economic and Social Rights released a study reporting skin problems (dermatosis) in the population in the Ecuadorian Amazon, apparently related to crude oil contamination of local rivers (9).

In recent years the "Manuel Amunárriz" Institute of Epidemiology and Community Health has been involved in a research process to assess the potential health impact of oil pollution in communities near oil fields. In the first of these studies, women living in communities near oil fields reported higher rates of various physical symptoms than did women in control areas. These symptoms included skin mycosis, tiredness, itchy nose, sore throat, headache, red eyes, ear pain, diarrhea, and gastritis. After adjustment for possible confounding factors, the symptoms significantly associated with exposure were those expected from known toxicological effects of oil (27). Another study found that the risk of spontaneous abortions was 2.5 times as high in women living in the proximity of oil fields (28).

Research done in 1998 found an excess of cancers among males in a village located in an oil-producing area in the Oriente region (29). Another study, from 2000, examined the differences in cancer incidences over the period of 1985 to 1998 in the Amazon region of Ecuador. This study found a significantly higher overall incidence of cancer in both men and women in the *cantones* ("counties," or divisions of provinces) where oil exploitation had been going on for at least 20 years. Significantly elevated levels were observed for cancers of the stomach, rectum, skin melanoma, soft tissue, and kidney in men and for cancers of the cervix and lymph nodes in women. An increase in hematopoietic cancers was observed in children (30).

GOVERNMENT RESPONSES

Peasants and indigenous people from the Amazon have presented their complaints to various administrations of the national Government of Ecuador. The inhabitants of the Ecuadorian Amazon have asked for a better quality of life and for technical assistance; that electricity, water, health services, and other basic services be provided; and, above all, that the oil pollution be remediated. Through their own organizations and with support from national environmental groups, Oriente residents have demanded that the companies clean up the environmental pollution and compensate them for damages caused by oil-related contamination. The measures adopted so far by oil companies and the various administrations of the national Government have been described as "patches," such as covering some waste pits, building some schools, and constructing roads, all without facing the root causes of the problem (10, 31, 32).

Various administrations of the national Government of Ecuador have declared the essential importance of oil to Ecuador's development. However, despite the oil revenues, improvements in socioeconomic conditions in the country have fallen short of expectations. Ecuador now has the highest per capita debt of any country in South America, nearly US$ 1 100 per person (1). In the period from 1970 to 2002 the unemployment rate rose from 6.0% to 7.7%, and the percentage of people living in poverty climbed from 47.0% to 61.3% (2, 33). The ratio of the income received by the poorest 5% of the population and by the richest 5% changed from 1:109 in 1988 to 1:206 in 1999 (34). The Amazon region has the worst infrastructure and the lowest socioeconomic and health indicators in the country (35).

In response to the nearly $16 billion in external debt that Ecuador has, one of the main economic strategies of the national Government and the International Monetary Fund has been to expand the oil exploitation in the country. The national Government's proposals include opening two million hectares of pristine rain forest in the south of the Amazon to oil exploitation and constructing a new heavy crude oil pipeline in the north of the Amazon, to allow further oil exploitation in that area (36, 37).

WHAT NEEDS TO BE DONE

Modern oil and gas development, if compatible with sustainable development and the well-being of Amazonian peoples, must be based on comprehensive environmental planning that fully considers the cumulative impact of ongoing and planned oil exploitation throughout the region. Strict environmental controls and careful long-term monitoring of oil activities—with both of those firmly grounded in the rule of law and broad participation by local communities, local governments, and nongovernmental groups—are necessary in order to prevent further negative environmental and health impacts in the Oriente region (38). Five interrelated actions are urgently needed:

- The Ecuadorian Government should conduct an evaluation of the environmental situation in the Oriente region. It is also necessary to develop and oversee the implementation of a plan to repair the damage that has already occurred and to limit further destruction. While oil pollution persists, the health of the population of the Oriente area and other populations in similar situations will remain at risk. Some indigenous and environmental groups have called for the application of the precautionary principle. (The precautionary principle has been defined as "when an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically" (39)). That principle has been developed by scientists in the face of scientific uncertainty, and it is a strong call for prevention of potential harm and for caution in actions taken. Those indigenous and environmental groups have also asked the national Government for a moratorium on oil and gas development in new areas of the Amazon. Such development alternatives as ecotourism and rain forest conservation have been proposed, and they should be seriously considered (40, 41).
- Oil companies operating in the Ecuadorian Amazon should change their practices to minimize environmental impacts and to build partnerships with local communities so that local residents benefit from development. Environmental protection standards and environmental management plans should be accessible to and appropriately discussed with communities and independent environmental groups. Without such basic information, these groups are left unaware of potential risks, they cannot participate meaningfully in formulating public policy, and they cannot hold companies accountable for their actions. In addition, an environmental monitoring system should be established, with the involvement of the affected communities. As a minimum, this system should include regular detailed chemical sampling of the environment and reporting on the emissions and effluent controls.
- Oil development policies have an impact on health, and the consequences of those policies need to be assessed and taken into account. The Ecuadorian Government should acknowledge the need for health impact assessments as an integral feature of policy development and evaluation. Community consultation and participation are essential in assessing impacts on the environment and health (42).
- Ecuador enacted a new constitution in 1998. That document acknowledges the right of communities to be consulted by oil companies before the companies begin the exploratory stage of oil development. To enforce these rights, it is essential for community organizations to work with regional, national, and international environmental groups. The Ecuadorian Government has already given a commitment to develop mechanisms to enforce the laws protecting the environment and the health of their citizens, but developing those mechanisms will be difficult. This should be addressed within the context of promoting human rights, combating corruption, and strengthening democratic institutions.
- Concern has been raised around the world that globalization of trade does not bode well for the environment and for people's health (43–45). Shifting trade policies in the direction of environmental sustainability and social justice is urgently needed if environmental protection, economic security, and health benefits are to be received by the majority of the world's population.

We believe that oil exploitation in the Amazon basin of Ecuador has resulted in a public health emergency because of its adverse impact on the environment and health. So far, the Ecuadorian Government has not designed an adequate strategy to prevent further negative environmental and health impacts. The oil industry argues that it has a role to play in the development of the country (46-48), but that development should not come with the added cost of pollution and poor health.

At first, it may appear that the oil industry and public health are not related. However, we have shown that they are closely interconnected. Unfortunately, Ecuador is not the only country in Latin America to suffer the negative consequences of oil exploitation; Bolivia, Colombia, and Peru are in a similar situation (49, 50). There are already public health problems, and these problems may grow if unregulated oil exploitation continues to expand in Latin America. Preventing additional health and environmental damage will require action on a local, national, and international level.

Acknowledgments. The studies on the health impact of oil exploitation in Ecuador carried out by the "Manuel Amunárriz" Institute of Epidemiology and Community Health have been funded by the Vicariato de Aguarico (the local Catholic church) and Medicus Mundi Gipuzkoa (a Spanish nongovernmental organization).

Note on conflicts of interest. In 1993 a lawsuit was filed in the United States of America against Texaco, an oil company that had worked in Ecuador for more than 20 years. The plaintiffs—some 30 000 indigenous persons and peasants—claimed that the oil company had caused irreparable damage to the rain forest of the Amazon region of Ecuador. In 2000 the suit was dismissed in the United States and sent to Ecuador to be considered. In October 2003 one of the authors, Miguel San Sebastián, presented testimony in an Ecuadorian court on behalf of the plaintiffs; he did not receive any payment for his testimony.

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SINOPSIS

La explotación petrolera en la cuenca amazónica de Ecuador: una emergencia para la salud pública

Desde la década de 1970, el petróleo ha sido una de las principales fuentes de ingresos del Ecuador y ha servido como "motor impulsor" de la economía nacional. La mayor parte del petróleo ecuatoriano se extrae en la cuenca amazónica del nordeste del país. Desde que comenzó la explotación petrolera, compañías extranjeras y la empresa petrolera estatal Petroecuador han extraído más de dos mil millones de barriles de petróleo crudo de la Amazonía ecuatoriana. A lo largo de este proceso se han liberado al medio ambiente miles de millones de galones de desechos sin tratar, gas y petróleo crudo. Este artículo analiza el impacto ambiental y sanitario provocado por el desarrollo petrolero en la región amazónica del Ecuador. Por ejemplo, el análisis del agua de varias corrientes fluviales de la localidad ha demostrado la presencia de altas concentraciones de productos químicos derivados del petróleo en las zonas petrolíferas en explotación. Los estudios epidemiológicos han encontrado un mayor riesgo de sufrir síntomas asociados con el petróleo y abortos espontáneos en las mujeres que viven en las proximidades de los campos petroleros. También se ha encontrado una incidencia excesiva de cáncer. Se necesitan intervenciones locales, nacionales e internacionales para evitar que se empeoren los efectos negativos que ejerce sobre el medio ambiente y la salud el desarrollo petrolero. Estas intervenciones deben abarcar un sistema de monitoreo y remediación ambiental, consultas a la comunidad y participación comunitaria, mecanismos para hacer cumplir las leyes que protegen el medio ambiente y la salud de la población, y cambios en las políticas comerciales dirigidos a lograr la sostenibilidad en materia ambiental y la justicia social.

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Annex 130

K.R. SOLOMON ET AL., *A RESPONSE TO TOMÁS LEÓN SICARD* ET AL., INTER-AMERICAN DRUG ABUSE CONTROL COMMISSION (CICAD), ORGANIZATION OF AMERICAN STATES, 2005

(Available at: http://www.cicad.oas.org/Desarrollo_Alternativo/ESP/Colombia/Panel%20response%20to%20Leon%20Sicard%20et%20al.pdf (last visited 7 March 2010))

A RESPONSE TO TOMÁS LEÓN SICARD ET AL.

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Introduction

The following is a response to a Critique of a Panel Report "Environmental and Human Health Assessment of the Aerial Spray Program for Coca and Poppy Control in Colombia"(Solomon et al. 2005).

Whilst there might be some points raised in the Critique(León Sicard et al. 2005) that result from aspects of translation between English and Spanish, there are a series of critical points made by León et al. (2005) that require responses, as they are based on misunderstanding, a lack of knowledge, or possibly a less critical approach to the subject under discussion than is desirable. In the response that follows, reference to the scientific advisory team (SAT) report is noted as: (Panel, with reference to page numbers in the English version). The Report by Tomás León Sicard et al. is referred to as the Critique.

General comments

The critique was written by a team from the "Programa de Investigación en Impactos de Cultivos Ilicitos (PIAC)", from the National University of Colombia. This team is lead by a PhD and composed by two PhD candidates but the areas they are working on are not stated. In addition, the team has an architect, a zootechnologist, a civil engineer, and a topographic engineer. There are no members of the team with any apparent expertise in human health, epidemiology, medicine, public health, or ecotoxicology. Clearly, some of the comments in the Critique would not have been necessary if the team had included expertise in these critical areas.

As a general observation, the comments in the Critique were not well referenced to the primary scientific literature. There are 17 references in the bibliography of the Critique but many of them can not be easily found. For example the reference of de Luengas (2005) can not be is only listed by the title. The reference of Maldonado (2003) was not listed in the bibliography and Nivia 2001 etc. on page 4 are also not properly referenced. This is in contrast with more than 350 updated references reviewed by the panel to work on the assessment.

Content, layout, objectivity, and Monsanto

First, there are a number of expectations noted in the Critique that were not met by the report. A point made several times is that the study by the SAT Panel did not encompass social, economic and political aspects of the issue. The Independent Panel (we are not "the OEA experts" and were specifically requested to be independent) took the view that a purely scientific risk assessment was a valid, indeed essential, contribution to make to a topic already clouded with misinformation. In a situation where allegation is compounded by rumour and even deceit, an appropriate response is to take an independent view of the known facts. The example of alleged effects of deposition of herbicide within Ecuador resulting from the aerial spray programme in Colombia is a case in point. There is a 5 km-wide no-spray buffer zone along the border in Colombia. The alleged incidents were 10 km within Ecuador, 15 km away. Given the characteristics of the spray droplets, the nature of the application, knowledge off-target deposition in the actual spray areas in Colombia, and other locations where similar equipment is used, deposition sufficient to cause effects in plants, the most sensitive organisms, would not be possible over this distance. There is no scientific evidence to support the allegation that significant spray drift occurs over a distance of 15 km

The Critique makes the point that the eradication programme and its effects are in the domain of sociology, politics and economics, not forgetting ecology and human health. The report clearly states that its focus was on the human health and biological science only. As such, the report contributes factual scientific information to the debate. But, by the same token, so does this Critique and its authors should be very careful in the content and manner of their writing.

The Panel's risk assessment contributed to an evaluation of the eradication programme. It is not the whole part of such an evaluation, nor was it meant to be. Similarly, the eradication programme is only a part of the whole approach to controlling illicit crops in Colombia. By design, politics and socioeconomic issues were not part of the considerations of the Panel. These issues are for the nation of Colombia and its institutions. Whilst it might be gratifying to have been expected to provide an absolute and comprehensive answer the problem of illicit crops in Colombia in a12-month study, that was never our aim. The Critique observes that the report will be used for political ends whatever. That is no excuse for subjectivity or poor science on the part of the Critique. We attempted to be as clear and as objective as we could, allowing that there were aspects of the risk assessment that would rely on expert judgement. It is therefore disappointing to have our objectivity questioned (p.3 et seq.), instead of offering a reasoned scientific argument rebutting our interpretations.

There is also an implication that we have not properly consulted the rich literature on glyphosate, or that we have been selective in our use of it. This is not so. The bibliography of the report cites about 350 references from the scientific literature as well as documents and reports known or obtained by the Panel because of their expertise and knowledge of the research and academic community in their fields. There have been a number of recent extensive reviews of the literature, including Giesy et al. (2000), Williams et al., (2000), and Solomon and Thompson (2003). We took these reviews as a good starting point, so that most of our bibliography is more recent than 2003. To dismiss the review by Williams et al. on the basis that it was commissioned by Monsanto is to ignore the fact that it was published in the peer-review literature and also ignores the reviews by national regulatory agencies in several countries (US EPA, Australian NRA, and many other countries) and international groups such as the EU and the World Health Organization. More insidiously, it implies that the Panel were somehow influenced by or in the pay of the Monsanto Company. The authors of the Critique seem unaware that glyphosate has been off-patent for some years and most of the herbicide used around the world is not sold by Monsanto.

The Critique notes that the report is not in the form of a scientific paper or report, with sections on Introduction, Methods, Results and Discussion. The difficulty in finding details of methodological approaches is alluded to. In the opening sentences of the Preface, it is clearly stated that the report is a formal risk assessment. Thus, the report is not written in the classical scientific study format, but one that takes the form appropriate to an evaluation of risks to health and the environment such as is widely used in the regulatory arena and in the literature. The writers of the Critique seem to be unaware of structure of formal risk assessments.

What is a risk assessment of a pesticide? What should it contain? Why does it not cover, for example, 8000 recorded complaints about the eradication programme?

The framework of a formal risk assessment of a pesticide, as used by regulatory authorities across the globe, characterizes, a) toxicity and, b) exposure and evaluates the likely risks with margins of safety between these. More simply, it asks - what the likely effects of a pesticide are at realistic exposures? Currently, with much greater interest in non-target effects, there are formal means of calculating toxicity-exposure ratios (TERs), based on exposures causing toxic responses in test populations, with appropriate consideration of uncertainty factors. This was the approach used by the panel and is consistent with state of art risk assessments procedures. The Panel used exposure scenarios calculated from the literature as appropriate for conditions in Colombia and toxicity values both from the literature and from tests conducted specifically for the study.

Is a risk assessment an end in itself? No. Risk assessments should be re-evaluated regularly, in the light of new information. This is, in fact one of the recommendations of the Panel. The Panel would modify their assessments, if further information becomes available, for example in mammalian neurotoxicology, ecology, etc.

Section 2 (p.4) of the Critique suggests that a major deficiency of the report is that no account has been taken of the many complaints received by the Defensoria del Pueblo, either directly in terms of their content, or in framing the work of the Panel. The Panel was aware of this dataset and welcomes its existence. It is alleged that the data are well-supported and that 87% of complaints refer to effects on vegetation and just short of 7% refer to health effects. This is undoubtedly the case, but the Panel needed to take a judgement on the likelihood of ascribing the true, rather than alleged, causality for the complaints received. The information given to the Panel was that, of all the complaints received only seven cases of damage to crops were proven and compensation provided. For the human health cases, the Panel required well-documented cases where the exposures and symptoms were clearly characterized. As glyphosate is excreted from the body in a few days, it is not possible to quantify exposure unless samples of urine or blood are taken shortly after exposure. This means that a robust biomarker of exposure is not available to allow causality of effects to be unequivocally ascribed to glyphosate. Bearing in mind that an unknown proportion of complaints are likely to be mischievous, the Panel took the view that work based on the complaints would be unsound and a more objective approach, given our timescale, would be to conduct a properly controlled epidemiology study. That is not to say that these complaints should not be evaluated. We would encourage a detailed investigation of all complaints but recognize that the assignment of causality may difficult to accomplish.

Further, the Critique states that "the study did not consider, or if so it was only by the side, direct and indirect risks on ecosystems and agroecosystems…." This is incorrect - the assessment of the panel also considered the effects of the entire cycle of production of illicit crops on erosion, loss of biodiversity, deforestation, and human health. The major focus was on glyphosate but these other effects were also considered.

Detailed comments by section

Section 2:

The Critique, apart from referring to the 8000 complaints (see above), also notes that there are aspects of the Panel's work on human health that are questionable. Specifically, the timescale of effects on human health would be longer than the actual study and that we did not consider aspects of genetic impacts. Both these points are ill-founded. First, time to first pregnancy (TTP) has been well validated in the literature as an indicator of fertility and was used to examine a sample time of 5 years In other words, the data integrates exposure impacts over a significant time period prior to the study and included the years of major eradication spraying. We agree that this does not address all aspects of human health, but is does investigate a key aspect of human reproduction that can reflect exposures to threats from within the local environment. Second, the Panel Report quotes data from the published literature and that provided for registration which indicates that glyphosate is not genotoxic, mutagenic, nor carcinogenic. It is not teratogenic or developmentally toxic, except at high doses that are overtly toxic to the mother and extremely unlikely to result from the spray program (p.51). The lowest no-effect level for the purposes of risk characterization for adults is the NOEL of 175 mg/kg/bw/day, value based on the maternal toxicity at the highest dosage tested of 350 mg/kg bw/day. We trust the meaning of this in relation to glyphosate is clear. Other pesticides such as those used agriculture and also in the production of coca and poppy may be more toxic than glyphosate, however, they were not included in the this review.

The Critique questions whether the panel should be concerned regarding herbicide exposure amongst the spray mixers and operators. The panel was concerned with **all** aspects of exposure and these were addressed. To consider otherwise might be interpreted as reflecting a particular agenda, rather than an impartial scientific approach.

This section closes with a final thought, that health should also encompass mental as well as physical health and proposes, in a bizarre statement, that witnessing crop spray planes accompanied by military helicopters operating on a criminal enterprise may have adverse impacts. One might well ask the same question about the effects of cocaine or heroin addiction on family members of victims of the drug trade. As both of these are social issues, they were excluded from the assessment.

Section 3. Planning

It is alleged that the purpose of the report is not clearly stated, that the questions asked are not obvious and that the procedures followed are ambiguous. As noted above, the report is a formal risk assessment and follows a commonly used and widely recognized framework for conducting such assessments.

The Critique is also contradictory as, on the one hand it recommends that questions should be concrete and obvious, while also asking for wider and nebulous questions such as the economic and social effects of the glyphosate to be addressed.

Section 4. Methods

As there is no chapter on methods, the Critique notes that it is difficult to comprehend the approaches. It is claimed that the Panel did not examine the areas where effects were most likely to be found, but concentrated where effects were less likely. The main criticism is that the report does not address effects on plants and it is suggested that the conclusion would have been very different if effects on plant biodiversity had been studied.

As the Critique notes (p.6), glyphosate is a broad-spectrum herbicide. One of the basic assumptions in the Panel report is that glyphosate kills all plant species, if a sufficient dose is received. This is nearly true, though certain species show degrees of resistance (Panel: pp. 71; 109). The assumption, therefore, is that glyphosate kills all plants in the target area, so it becomes a trivial question to ask what are the effects on plants in the coca fields – it kills them all. It is not a trivial question to ask what happens to plants outside the target area. This was approached in the Report in terms of likely drift and off-target deposition.

The section then makes some remarks regarding the lack of study of the process of adsorption of glyphosate on to clay in soils. Whilst this is not developed in the Panel report, the science of this process is relatively well-documented and referenced to in the Report. The Critique then introduces the important topic of soil erosion, noting that loss rates of between 15 and 25 tonnes ha-1 year-1 occur. It is not clear to us if the Critique implies that glyphosate adsorption to clay particles in soil affects erosion. This seems most unlikely, considering the rates of application compared with soil bulk density. However, it is well-understood that removal of forest cover, such as is done when planting coca or poppy, causes erosion and this is noted in the Panel report (Panel: p. 79).

The Critique makes a valuable suggestion that it would be really interesting to know the range of erosion rates in Colombia a) in virgin sites, b) in sites cleared for coca production and c) coca sites that have been sprayed with glyphosate from the air. The Panel would encourage the Institute to approach the appropriate research funding agencies to support such a project. The opinion of the Panel, based on the literature, is that erosion rates of a) are lowest and those in b) and c) would be the same, but significantly higher than a).

Section 5. Target environment

The Panel are entirely aware that extensive areas of Colombia contain significant amounts of the world's plant diversity and that there is overlap between coca and poppy production areas. This is clearly stated in the report (Panel: p. 9 - "much of the production takes place in remote areas that are close to or part of the Andean Biodiversity Hotspot"). The point made earlier is that the proportion of land area involved is relatively small.

Section 6. Off-target deposition

In the Critique, there is some confusion between results of the assessment of glyphosate use in the Canadian Forest Service (Payne et al. 1990) and the estimates of off-target damage in the eradication programme in Colombia reported by Helling (2003) (Panel: p. 33). The Canadian experience is highly relevant; nevertheless there is some confusion in the interpretation of data here. We accept that the Helling studies, which are conducted on an annual basis, present a relatively small sample of fields. A greater sampling size might be appropriate, but we also proposed that an experimental approach to measure drift should also be conducted. But to imply that 22.6% of spray sites have non-target effects is misleading. The key question is what is the likely area of non-target damage? Is it 1 m^2 or is it thousands of hectares? A single site out of 200 that has non-target drift damage of hundreds of hectares could be classified, according to the Critique, as less than 1% of spray sites with drift damage. Aerial application, even with safety limits built into calculated spray paths, is more prone to drift than ground application. The upper and lower estimates of observed areas of damage (Panel: Table 5) were applied to the total area of aerial applications in each year. This provides an estimated range of the area likely to be damaged by glyphosate drift. In the last sentence of this section the Critique states that 7.1% of Colombia's area has coca crops. This number is incorrect.

Section 7. Risk scoring

The Critique questions the use of 5-point scoring systems in Figures 11 and 12, used to calculate overall measures of risk. How were the scores derived? Did the group come to a consensus?

The risk frameworks are explained in the text (Panel: pp. 34, 35). All operations associated with growing and processing coca carry some risk to humans and the environment. Sowing and fertiliser are considered in human and environmental risk frameworks, both for completeness and because there is potential for health effects, e.g. physical injury from tools or machinery. The risk scenarios were agreed to by all Panel members as a means of presenting relative risks.

When it is reported that a number of highly toxic pesticides have been seized in anti-narcotic operations by the police, the Critique asks if the relatively low scores for pesticides (2) and recovery time of (0.5 of a year) are appropriate. Impact score is based on the additional impact to the clear-cut and burn and recovery is based on the need for repeated use of these products in pest management. If one were to increase the impact of pesticides to a score of 5 and increase the longevity of effect to one year, the impact score would still only be 5 and the percentage impact would only be 1%. Bearing in mind that this approach is only to evaluate relative risks over an annual cycle, the scoring system is relatively robust. This highlights an important area of risk the Panel are aware of – the use of banned pesticides in the illicit production of drugs. The discovery of the banned insecticide endosulfan in the surface water samples (Panel: p. 46, 47) means the product is being used. Our concerns have been reported to CICAD, but please note that our task was an evaluation of the use of glyphosate in the eradication programme, not the use of banned chemicals in an illegal activity.

The Critique concludes this section with the observation that POEA is not discussed and that the Panel have ignored dioxins, which are apparently impurities in the pesticides. In regard to POEA (polyethoxylate dethoxylated tallow amine), the effects of this surfactant, the main surfactant in previous formulations of the glyphosate product Roundup®, on toxicity are extensively discussed in the report (Panel: pp.53, 66, 67). The Critique seems to ignore the highly significant data summarised in Figure 17. This presents toxicity data for technical glyphosate (with no surfactants), glyphosate as Roundup® (data including POEA formulations) and glyphosate plus Cosmoflux® (as used in Colombia). There are no dioxins in glyphosate or Roundup®. Nothing in the process of its manufacture or the manufacture of the surfactants would lead to the formation of dioxins. The authors of the Critique may be confused by a historical reference to the use of dioxane, a totally different chemical, in the manufacture of components of the formulation. It is troubling that the authors of the Critique have raised the topic of dioxins without any validation or reference. What are Leon et al. attempting? If, by innuendo, they wish to raise the issue of use of 2,4,5-T more than 30 years ago in Vietnam, then their motives may not be honourable. In so doing, they also conveniently overlook the fact that more that 86% of the glyphosate used in Colombia is in legitimate operations by agricultural and other workers in the field, rather than in the eradication programme. In addition, other surfactants such as CosmoFlux® are also used. Additionally, glyphosate is widely used in almost every other country on the planet.

Section 8. Characterising exposure

The Critique raises valid questions in regard to basing estimates of exposure to glyphosate on the literature. It may be of interest that the Panel proposed an experimental study of direct exposure to the spray, using volunteers in Colombia. Unfortunately, the experiment could not be conducted at the time because of concerns expressed by the Approval Board in Colombia. However, it is well known that there is little penetration of glyphosate through human skin. Even if exposures to the skin were greater, this would not have increased total exposures to a level of concern, even for chronic risks. The Critique points out that mixer-loaders use protective clothing. This is standard operating procedure for many pesticides and is done because these individual may be exposed to concentrated material. People exposed to spray in the field are exposed to diluted product which has lower hazard. However, the likelihood of this occurring is small as, according to standard operating procedures, fields are not sprayed if people are observed to be present.

The Critique implies that exposure is estimated on the basis of a single person, which is incorrect. Exposure was estimated in terms of the effects on a person, but is the same for however many people may be present in the field and are contaminated. The point is raised that the environmental conditions – temperature, humidity – and the health of the coca growers may be very different from those considered in the literature. Whilst the environmental conditions may impact exposure and uptake, no assumptions regarding health are made in estimating exposure as these were already included in the uncertainty factors incorporated into the reference dose to which the exposures were compared. As is pointed out in the Report, these are made even more conservative because acute exposures, such as would occur from the spray program, are compared to chronic reference doses.

The Critique alludes to the 8000 complaints and the need to design studies to investigate these. As was pointed out above, for almost all of these cases it is logistically impossible to collect confirmatory exposure data and, in many cases, the reported effects are inconsistent with those needed to establish causality. Given immediate and free access to these situations and better infrastructure, such investigation would be possible. However, the toxicity data on the sprayed formulation and experience in other regions suggests that effects, if any, would be minor and temporary.

Section 9. Environmental exposure

There are criticisms that the approach to evaluating the presence of glyphosate and its breakdown product AMPA in the environment taken by the Panel is too small a sample and that the site conditions are not described for sound conclusions. A series of questions are posed, highlighting perceived deficiencies in the work.

Whilst, as an ecologist, one might have sympathy for a number of the points raised and a desire to see a comprehensive monitoring programme for pesticides in surface waters in Colombia, it is appropriate to focus on what the aims of the task were. This exercise had two objectives: first, to determine if glyphosate was present and secondly to test whether its presence might be influenced by the eradication programme.

The Critique suggests that the methods in the epidemiological study were not clearly described. The Panel report does describe how the epidemiological study was carried out, why the places were chosen, what field work was conducted, and what analyses were conducted for assessing the association between glyphosate and TTP. The site descriptions are available in separate reports. The sites were selected as representing different land uses, though with similar environments. A number of sites were explored as potential locations for the water and sediment sampling as well as for the epidemiological study of TTP. Important factors in the final selection were accessibility and safety for the staff involved. Ultimately the sites differed in a number of ways, some of which we do not understand, as illustrated by the TTP results. Nevertheless, a detailed protocol (*note: all sampling and analytical protocols are available for inspection*) was followed, over a 22 week period with fortnightly sampling, involving the use of sample blanks and spiked samples, so that both contamination and analytical recoveries were monitored.

A valid question is: what can the data tell us? Returning to the objectives, the data clearly tell us that glyphosate is not found often in surface waters. Only two samples out of 86 contained the herbicide and then only at concentrations just above the limit of detection. On the basis that the molecule is rapidly adsorbed by soils, this is consistent with the properties of glyphosate and with observations in other locations such as were reviewed in the Panel Report.

The second objective was to test whether there was evidence that the eradication programme was influencing amounts of the herbicide in the environment away from the application areas. On the basis of the available data, there was no evidence to show this. Nevertheless, the Panel has recommended that the environmental monitoring programme is expanded in Colombia.

The Critique then proposes that there is no evidence for rapid recolonization of sprayed plots and that because there were no measurements of residues in soils, we cannot conclude lack of effects. The information on rapid replanting of coca in sprayed fields and recolonization from Helling (2003) is compelling and our own observations in the field cannot be refuted. Similarly, there is very wide experience of lack of residual activity of glyphosate in agricultural uses, a fact that the authors of the Critique were apparently ignorant of. Leon et al. (2005) should be aware that a key factor is whether the herbicide residues in soil have biological effects. Repeated applications of glyphosate to soils may result in an increase in residue that can be found, if soils are extracted with techniques involving strong acids. However, this tells little about its biological activity in soils which, from extensive use in agriculture, is known to be minimal. The review of Racke et al. (1997) (Panel: pp. 22, 23) also indicates generally more rapid dissipation of pesticides in tropical soils.

Section 10. Effects characterisation

It is a shame that the Critique takes on a patronising tone at this point, implying that the Panel have been partisan, rather than exercising critical judgement. The authors of the Critique seem to be happy to accept the validity of articles that are not in the peer-reviewed scientific press, which is to be regretted. When we write that a risk assessment contains uncertainties, the Critique betrays a non-scientific approach in its comments, compounded by not understanding that potential cancer and neurological effects are different.

Section 11. Effects on non-target organisms

There is a lack of objectivity in the comments made here. If the authors are unhappy with the judgements made in regard to individual papers, then they should advance an alternative scientific argument, backed up with suitable references. The effects on amphibians we note is not "finally admitted", but clearly stated and developed in relation to shallow water bodies and likely contamination effects from overspray (see Figure 19). I would also refer to one of the specific recommendations (Panel: p. 95) that toxicity measures be made on amphibians, which are clearly more sensitive than other organisms to some formulations of glyphosate. The Critique refers to a report by Bigwood, not peer-reviewed, that reviews "effectos nocivos" of glyphosate. From the title alone, one would question the balance inherent in such a report.

The paper by Relyea (2005) is referenced and discussed fully in the panel report (Panel: pp. 67, 111). To quote "*The rate of application was equivalent to 16 kg/ha, a value that is unrealistic and probably the result of an error in the methods. At this concentration, glyphosate formulated with POEA would be expected to be lethal to tadpoles.*" Further, the Relyea study suffered from poor experimental design and the wild speculations regarding amphibian declines contained therein were not justified by the data.

Section 12. Effects on mammals

The Critique makes some wild statements in regard to testing effects of pesticides on mammals, betraying a lack of understanding of regulatory, experimental, and ethical issues. Perhaps León et al. (2005) might like to explain the alternative. It is the practice across the globe to evaluate chemicals, pharmaceuticals, foods, and cosmetics on laboratory mammals, including mice, rats, rabbits, and guinea pigs. The Critique asks, is a slight to moderate eye irritant a risk to human health? The answer is, it is a risk, but so is getting soap in one's eye when washing. A little balance is required – there are a large number of substances in the home, in agriculture, and industry that are eye irritants and can be safely used.

Section 13. In summary

- The risk assessment draws sound and defensible conclusions from the literature, from field assessments, from specially conducted toxicity testing, interviews of nearly 3000 women and not least from a sound understanding of the subject.

- The peer-reviewed scientific literature was consulted exhaustively by the Panel. To suggest otherwise is disingenuous.

- The Panel have assumed that if there is spray drift, there are impacts on plant biodiversity, as glyphosate kills all plants. There is drift, so there are effects, although to a limited area. However, effort has been placed on the less obvious impacts, including human exposure and non-target organisms.

- The Critique suggests that the report should include social, political and economic aspects to the environment. In the totality of the issue, these are potentially important factors, but they do not help in providing a science-based risk assessment of a pesticide and have been intentionally not addressed, in order to improve the objectivity of the Panel Report. Should a modification to the title be appropriate, the work "risk" could be added, but no other change is necessary.

- The illicit drug problem is undoubtedly complex and it is one that is faced by a number of countries, including Colombia and Afghanistan. However, to base an evaluation on lists of complaints about an eradication programme, some of which are genuine, but which also include specious representations and even some perhaps made under duress, seems somewhat naïve. A risk assessment of part of the illicit crop control programme is entirely justified and hopefully will shed some light on the actual practices on the ground, both good and bad.

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Annex 131

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Guest Editors: Keith R. Solomon and E. J. P. Marshall

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K.R. SOLOMON ET AL., "HUMAN HEALTH AND ENVIRONMENTAL RISKS FROM THE USE OF GLYPHOSATE FORMULATIONS TO CONTROL THE PRODUCTION OF COCA IN COLOMBIA: OVERVIEW AND CONCLUSIONS"

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Human Health and Environmental Risks from the Use of Glyphosate Formulations to Control the Production of Coca in Colombia: Overview and Conclusions

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Much of the world's cocaine originates in Latin America with the majority of the supply coming from Colombia. The control of the coca plants from which cocaine is produced (*Erythroxylum coca* and *E. novogranatense*) has been the focus of considerable effort and expenditure. As part of the supply control effort that started in the 1970s, an aerial spraying eradication program in Colombia was started in 1997 using the herbicide glyphosate. The total area planted with coca was 99,000 ha and the cumulative area of coca sprayed with glyphosate was 153,134 ha in 2007, 11% less than in 2006 (UNODC 2008).

The potential human and environmental risks related to the use of glyphosate for controlling coca plants have generated considerable interest and attention in Colombia and other countries. At the request of the Organization of American States (OAS), an independent scientific review of this issue was completed in 2005 by an expert panel (Solomon et al., 2005). This review, published in the scientific literature in 2007, noted that, at the time, knowledge of the toxicity of glyphosate and its formulated products did not suggest significant risks to humans or most wildlife (Solomon et al., 2007b). In addition to assessing the toxicological effects of the eradication spray program, the review pointed out that some of the chemicals used in the production and refining of the final product, cocaine hydrochloride, presented potential hazards to humans and the environment (CICAD/OAS 2004, 2005; Solomon et al., 2007a). However, the primary review noted that there were several outstanding questions and issues. Key environmental issues that were identified included the influence of spray procedures and conditions on spray drift and the toxicity of the spray mixture to amphibians, with ancillary questions related to alternative products and mixtures that would pose less risk to amphibians and the distributions of amphibians in relation coca production and the spray program (Solomon et al., 2007b). Other questions have also been raised, such as in a recent report in the literature of effects of glyphosate use on humans (Paz-y-Miño et al., 2007), which suggested that drift of spray was affecting humans at distances of several km from areas of application.

As a result of these questions, several studies were initiated to collect data and to test specific hypotheses. These studies have been completed and are published as a series of articles in this issue of *Journal of Toxicology and Environmental Health*. This article is an overview of the results of these studies which places them in the context of other recent publications on the spray program and the effects of glyphosate on the environment and on human health. As is common for all risk assessments (U.S. EPA, 1998), this overview addresses both exposures and effects and draws on the data in these articles to integrate these observations into a risk assessment and overview.

EXPOSURES IN THE ENVIRONMENT

As exposure is the primary driver of risks, the first article in the series relates to spray drift (Hewitt et al., 2009). One of the primary questions addressed in this article was the effect of spray conditions on droplet size and the potential for spray drift. Until recently, the aircraft currently used for eradication spraying in Colombia were the OV-10 and the AT 802; however, the only one in current use is the AT 802 (National Police, Colombia, personal communication, September 2008). The speed during spray application is 333 km/h for the OV-10 and 274 km/h for the AT-802, both in excess of the speeds used in conventional agricultural spray applications (approximately 200 km/h). The greater speed of these aircraft, necessitated by the need to avoid hazards such as gunfire from the growers of illicit crops, would be expected to increase velocity of air and shear at the spray nozzles. This, in turn, would increase the

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formation of small droplets with a greater propensity for drift and offsite damage. Currently, exposure characterization is conducted by using models such as AGDISP (Bilanin et al., 1989) and AgDRIFT (Hewitt et al., 2001) for predicting on- and off-target deposition of aerially applied sprays of pesticides. However, data on droplet size under spray conditions in Colombia to input into the models were lacking.

Data on droplet size spectra were measured in a unique wind tunnel facility in Australia where the appropriate velocity of air could be achieved, and these data were then used to model spray drift in relation to sensitive organisms (Hewitt et al., 2009). These results showed that the tank mix of Glyphos and Cosmo-Flux, as used in the eradication spraying in Colombia, produced droplets of median diameter ($D_{v0.5}$) of 128 to 140 μm, which are classified as very fine to fine sprays. Modeling of spray drift using AgDRIFT showed that the spray droplets would not evaporate as rapidly as most similarly sized agricultural sprays because of the large proportion of nonvolatile components (active and inert adjuvant ingredients). Thus, even under worst-case conditions of a cross-wind of 9.3 km/h, the potential for longer range drift was small and most drift that might occur would deposit relatively close to the application swath. In addition, drift only occurs downwind and with winds of velocity less than the modeled maximum the drift distance would be less. Based on worst-case spray drift at various distances from the application swath, exposures of plants and organisms in shallow water (15 cm deep) were estimated and compared to species sensitivity distributions of toxicity values for formulations of glyphosate in plants and amphibians, the most sensitive group of animals.

Based on modeled drift and 5th centile concentrations, which would be protective of 95% of plants, appropriate no-spray buffer zones (distance from the end of the spray boom as recorded electronically ±5%) were 50 m to 120 m for coca spraying. These buffers are additionally protective of plants, as it was shown that, at small rates of application, glyphosate stimulates plant growth (Velini et al., 2008), which, even in the long term, does not reduce yields (Cedergreen, 2008).

The equivalent buffer zone for protection of amphibia in shallow water was 5 m, which, as discussed later, is conservative because adsorption of glyphosate and formulants in the mixture to sediments and particulate matter further reduces exposures and therefore, risk. The low toxicity of glyphosate and its formulations to mammals (Williams et al., 2000; Solomon et al., 2007b) suggests that these aerial applications are not a concern to bystanders, even those close to the spray swath. The assertion that spray drift over long distances was adversely affecting humans (Paz-y-Miño et al., 2007) is not supported by these observations, as exposures would be extremely small. For example, at 1 km from the spray swath, deposition would be between 1 and 0.1 g glyphosate acid equivalents (a.e.)/ha, which is equivalent to between 0.57 and 0.06 μg/kg body weight (bw), assuming a total exposed skin area for a naked 70-kg human of 2 m^2 and 2% penetration (Solomon et al., 2007b). This is between 175- and 1750-fold less than the chronic reference dose of 100 μg/kg/day as determined by the U.S. Environmental Protection Agency (EPA) (2008) and between 3500- and 58,000-fold less than the acceptable operator exposure level (AOEL) of 200 μg/kg/d (IUPAC, 2009).

EFFECTS IN THE ENVIRONMENT

With regard to effects on organisms in the environment, the initial review (Solomon et al., 2007b) noted that amphibians appeared to be relatively more sensitive to formulations of glyphosate than other aquatic animals, however, there were no data for the mixture of Glyphos and Cosmo-Flux as used for coca eradication in Colombia. It was also noted that many other pesticides were used in the production of coca and that these could present significant risks to humans and non-target organisms in the environment (Solomon et al., 2007a). Based on a worst-case exposure scenario, and a quotient based on the reference dose, some of the chemicals used by growers, particularly the organophosphorus insecticides, had hazard quotients for humans 2000-fold greater than that for the eradication spray (Solomon et al., 2007a). Similarly, hazards to all aquatic organisms were up to 20,000-fold greater (for endosulfan) than the eradication spray mixture (Solomon et al., 2007a). A refinement of this approach that focused on amphibians (Brain & Solomon, 2009) is published in this issue and confirmed the greater hazards to amphibians of the chemicals used to produce coca. For some species of larval amphibians, sensitivity to several pesticides (mainly insecticides) was 10- to 1000-fold greater than estimated worst-case exposures and hazards were much greater than those for the eradication spray mixture. In addition, habitat destruction, such as clear-cutting forests for production of coca or food crops, was identified as another major threat to amphibians (Brain & Solomon, 2009; Lynch & Arroyo, 2009).

As there were no data on the susceptibility of amphibians to the mixture of Glyphos and Cosmo-Flux used in the eradication sprays, this was also a focus in the collection of additional data. An initial lab study with the African clawed frog, *Xenopus laevis* (Wildlife International, 2006a, 2006b), showed that the mixture was somewhat less toxic than reported values for other formulations of glyphosate. The LC50 for the mixture as used on coca was the equivalent of 1100 (95% CI; 560-2,300) μg glyphosate a.e./L, while the lowest LC50 previously reported for formulated glyphosate (Vision) in the same species of frog was 800 μg a.e./L (Edginton et al., 2004). This then raised two questions; the first was whether there were alternative formulations of glyphosate that were potentially less toxic to frogs but as effective as the currently used mixture for the control of coca and, second, were Colombian frogs generally more or less sensitive to formulated glyphosate than other species tested in other regions?

To investigate the efficacy of other formulations of glyphosate on coca, field trials were conducted in Tolima Department, Colombia (Marshall et al., 2009). Coca plants (*E. coca*) were grown from seedlings to 75 cm height and then sprayed with a range of glyphosate formulations and different adjuvants using an experimental ground sprayer. Assessments were made of plant vigor, height, and above-ground standing crop (fresh weight) 3 wk after application. Resprouting of plants was assessed at 9 wk after treatment. Even mixed with adjutants, unformulated glyphosate applied as the product Rodeo gave poorer control of coca than two formulated products, Roundup Biactive (from Europe) and the formulation currently used in eradication spraying, Glyphos. In general, these latter two products performed well without added adjuvants, giving control similar to that of the mixture of Glyphos and Cosmo-Flux as currently used in Colombia. There was some evidence that addition of the adjuvant Silwet L-77 and, to a lesser extent, Mixture B (from the United Kingdom) resulted in the earlier appearance of symptoms of injury. There were also indications that glyphosate rates of less than 3.7 kg a.e./ha provided control in the range of 95%. When also considering that glyphosate appears to inhibit the production of cocaine in coca plants (Casale & Lydon, 2007), effective control of drug production may be possible with lower rates of application. These results also illustrate that there are potential alternatives to currently used products, one of which, Roundup Biactive, was shown to be less toxic to amphibians (Mann et al., 2003). Before using these products, field testing to assess the influence of different environmental conditions, varieties of coca, and aerial application procedures needs to be conducted. Should a different adjuvant be required, Silwet L-77 and Mixture B would be good candidates for further evaluation, including toxicity to nontarget organisms.

To address the question of sensitivity of Colombian species of frogs to formulated glyphosate, a series of toxicity bioassays was conducted on tadpoles under laboratory conditions (Bernal et al., 2009a). Laboratory studies were conducted in glass containers and in the absence of sediments and particulate matter. LC50 values for the 8 species tested (Gosner stage-25 tadpoles of *Scinax ruber, Dendrosophus microcephalus, Hypsiboas crepitans, Rhinella granulosa, R. marina, R. typhonius, Centrolene prosoblepon,* and *Engystomops pustulosus*) ranged from 1200 to 2780 μg glyphosate a.e./L. These values suggest that sensitivity to Roundup-type formulations of glyphosate in these species is similar to that observed in other tropical and temperate species of frogs for which data have been published in the literature. The toxicity of the mixture of Glyphos and Cosmo-Flux as used to spray coca was likely driven by the surfactant in the Glyphos, as the addition of Cosmo-Flux did not increase toxicity above those values reported in other frogs for studies using both Vision and Roundup, two similar formulations used in North America (discussed earlier). Cosmo-Flux is of low toxicity to fish with an LC50 of 4417 mg formulation/L (Rondon-Barragan et al., 2007). That tropical frog species were of similar sensitivity to those from temperate regions is also consistent with observations with other pesticides and other organisms (Maltby et al., 2005) and therefore allows the combination of Colombian data with those from other regions for the purposes of risk assessment.

In contrast to laboratory observations, toxicity studies conducted on Gosner stage 25 tadpoles under field conditions in 15-cm deep microcosms containing a 3-cm layer of sediment showed reduced sensitivity (Bernal et al., 2009b). Microcosms were sprayed with the mixture of Glyphos and Cosmo-Flux as used in eradication spraying. Mortality >50% was only observed in the tested species when the application rates were >2-fold the normal application rate of 3.69 kg glyphosate a.e./ha. LC50 values were between 8.9 and 10.9 kg glyphosate a.e./ha (equivalent to initial nominal concentrations of 5963 to 7303 μg glyphosate a.e./L in the microcosms. These results show that toxicity of the spray mixture is reduced in the presence of sediments and particulates in the water column. Although it was not possible to measure concentrations of glyphosate in these systems, the reduction in toxicity was similar to that observed by others (Tsui & Chu, 2003, 2004, 2008; Tsui et al., 2005) for the formulated product and also for the POEA surfactant, which contributes the greatest to the toxicity of the formulation (Wang et al., 2005). In these studies, reductions in toxicity were attributed to reductions in exposure as a result of absorption to sediments and/or breakdown by microbes. Thus, risks to larval frogs (representing sensitive aquatic organisms) from the eradication sprays as used in Colombia would be reduced by adsorption to sediments under field conditions and, even with direct overspray, amphibians in shallow water systems (~15 cm deep and theoretically the most vulnerable) would be at low risk.

In bioassays where terrestrial stages of frogs (juveniles and adults) were exposed to a direct overspray of the Glyphos–Cosmo-Flux mixture, LC50 values ranged between 4.5 and 22.8 kg a.e./ha, all of which were above the application rate of 3.7 kg a.e./ha for eradication spraying. These studies were conducted under realistic conditions with soil and leaf litter present in the bottom of the exposure chambers, a different exposure system from that used in other studies that claimed high toxicity of formulated glyphosate (Relyea, 2005). The observations of Relyea (2005) on adult frogs may have been the result of the presence of formulants specific to the product used (Dinehart et al. 2009) or incorrect calculation of exposures as the results reported by Bernal et al. (2009a) are consistent with those of Mann and Bidwell (1999), who observed that adult and juvenile terrestrial stages of the Australian frog, *Crinia insignifera* were less sensitive to Roundup than tadpoles. The overall conclusions of the studies on Colombian frogs are that, under worst-case exposure conditions, the mixture of Glyphos and Cosmo-Flux used for control of coca in Colombia is of low or negligible risk to aquatic and juvenile terrestrial stages of frogs.

To provide background information on amphibians and their distribution in relation to coca production and aerial eradication spraying in Colombia, data on the more than 53,000 records of amphibians in the Instituto de Ciencias Naturales

(ICN) (Bogotá) were characterized (Lynch & Arroyo, 2009). Analyses were based on the proximities of actual museum records to localities in which illegal crops are being grown and the subset of those that have been sprayed with glyphosate. ARC MAP software was used so that direct distance separating of collection locations for frogs, known coca fields, and areas where aerial spraying was being conducted could be measured (Lynch & Arroyo, 2009).

Based on data for the location of amphibians collected in Colombia, records existed of 193 species (28% of the national diversity) of frogs and toads from localities within 10 km of areas where coca is grown. Records in or near coca fields included records for 13 of the 15 families of frogs and toads known for Colombia. Only Ceratophryidae and Pipidae were not reported from these locations and would not be at risk. For eight species (*Dendrobates truncatus*, *Craugastor raniformis*, *Pristimantis gaigeae, Smilisca phaeota, Elachistocleis ovale, Hypsiboas crepitans, Trachycephalus venulosus*, and *Pseudis paradoxa*) selected to represent several coca-associated habitat preferences and lifecycle strategies, large areas of their distributions lie outside coca production regions and the populations as a whole are at low risk of exposure. For a limited number of species that barely enter Colombian territory, the consequences of coca production may be more serious and may have placed several species of frogs at risk. These include *Ameerega bilingua, Dendropsophus bifurcus, Eleutherodactylus colomai, E. degener, E. diadematus, E. quaquaversus, E. variablis,* and *Trachycephalus jordani.* Other species may be at risk, but exact numbers are unknown because little investigation occurred in these areas during the past 30 yr. As these species are found in Ecuador, it is assumed that healthy populations persist there.

Overall, the risks from pesticide used for eradication spraying must be placed in the context of the greater toxicity of other products used by growers (Brain & Solomon, 2009) and the sensitivity of frogs from Colombia to the mixture of glyphosate and Cosmo-Flux as used in the aerial eradication spraying. Laboratory-based toxicity studies showed that aquatic larval stages of Colombian species are not differently sensitive as compared with frogs from other locations (Bernal et al., 2009b). When tested under realistic conditions—in shallow water (15 cm deep) in the presence of sediment and particulates that will absorb glyphosate and the more toxic surfactant—toxicity was reduced (Bernal et al., 2009b), resulting in lower risk. In contrast, some of the products used by growers may be more bioavailable in the environment and risks to these may not be mitigated. Terrestrial stages were less susceptible than aquatic stages (Bernal et al., 2009b). Modeling of spray drift from the aerial eradication spraying (Hewitt et al., 2009) showed small downwind exposures to the mixture of glyphosate and Cosmo-Flux at distances beyond 30 m. Based on laboratory toxicity data, larval stages of frogs would only be at risk if they were in shallow water within 5 m of the spray swath. However, under conditions of exposure in the field, interception by foliage and adsorption to soils and sediments reduce exposures still further, and risks, even to a direct mixtures of the eradication mixtures, are small to negligible.

EFFECTS IN HUMANS

In previous reviews of the risk of glyphosate to humans, it was concluded that both the active ingredient and the formulated product (Roundup) present low risks to humans whether used in agricultural or vegetation management (Williams et al., 2000) or as used in the eradication of coca in Colombia (Solomon et al., 2007b). The first article in this series on the potential human health effects of the use of Glyphos and Cosmo-Flux for the eradication of coca addressed the issue of possible reproductive effects of the spray program in Colombia (Sanin et al., 2009). This issue was identified as a possible response by earlier reports of associations between pesticides and reproductive outcomes. Arbuckle et al. (2001) reported moderate increases in the risk of early abortion when preconception self-reported exposures to phenoxy acetic acid herbicides were present and for late abortions and self-reported preconception exposure to glyphosate was associated with higher risks. In another study, Curtis et al. (1999) showed a positive association (decrease in fecundability of 20% or more) measured through time to pregnancy (TTP) when both spouses reported exposure to pesticide-related activities, one of which was glyphosate.

The study in Colombia was to test whether there was an association between the use of glyphosate when applied by aerial spray for the eradication of illicit crops eradication (cocaine and poppy) and time to pregnancy (TTP) among fertile women. The study was a retrospective cohort study with an ecological exposure index related to areas of residence with different uses of glyphosate. First pregnancies in 2592 fertile women from 5 regions were included in the study and the women were interviewed regarding potential reproductive, lifestyle and work history predictors of TTP. The results showed that there were differences in TTP between regions. Boyacá, a region with traditional crops without glyphosate eradication spraying (manual eradication), had the minimal risk and was the reference region. Sierra Nevada, a control area with organic agriculture and no pesticide use; Putumayo, where illicit crops are grown and with an intensive eradication spray program; and Valle del Cauca, a sugar cane region where glyphosate and others chemicals have been used for more than 30 yr, had greater risk of longer TTP, with the highest risk for Valle del Cauca (Sanin et al., 2009).

Classification of exposure in the study was by location of residence. Nonexposed participants were those who lived in the region where organic crops were produced and who, in addition, did not report any use of pesticides in the interview. In the other four departments, there was exposure not only to glyphosate, but also to other herbicides and pesticides. Although place of residence is not an accurate surrogate for exposure to pesticides and may generate misclassification (Arbuckle et al., 2004), this ecological assessment was useful to explore, at the population level, whether an association existed between the putative exposure (aerial spraying of glyphosate) and outcome (Ritter et al., 2006). Pesticides in general are likely not the cause of observed differences either. Large differences in TTP were found between two regions of high to moderate pesticide use, Valle del Cauca and Boyacá. The observed ecological differences remain unexplained, but may be produced by varying exposures to environmental factors, history of contraceptive programs in the region, or psychological distress. Future studies examining these alternative causes are needed.

Epidemiological studies have not shown consistent or strong relationships between glyphosate exposures and health outcomes. Glyphosate and its formulations have been extensively investigated for potential adverse effects in humans (Williams et al., 2000). They have been reported to exert a low acute toxicity to different animal species. Chronic feeding studies have not shown evidence of carcinogenicity or any other relevant long-term effect (U.S. EPA, 1993; World Health Organization International Program on Chemical Safety, 1994). Glyphosate AI and Roundup were extensively tested for genotoxicity in a wide range of in vitro and in vivo systems evaluating different genetic endpoints (gene mutation, chromosome mutation, DNA damage and repair) using bacteria and mammalian somatic cells (Williams et al., 2000). Although effects were reported in some in vitro studies, it was concluded that, in vivo, glyphosate and its formulations were not genotoxic (Williams et al., 2000). Several in vitro and in vivo studies with parallel testing of glyphosate AI and Roundup showed that only the commercial formulation was genotoxic (Rank et al., 1993; Bolognesi et al., 1997; Gebel et al., 1997; Grisolia 2002), in general agreement with the observation that adjutants in the formulation may be more toxic to animals than glyphosate itself (Giesy et al., 2000; Williams et al., 2000; Richard et al., 2005).

Evidence of DNA damage in peripheral lymphocytes from a small group of subjects potentially exposed to glyphosate was reported in a recent article (Paz-y-Miño et al., 2007). Problems with the study design, such as the small number of subjects (21 control and 24 exposed) and the fact that random selection produced 23 females and 1 male in the exposed group, do not allow conclusions to be drawn; however, this article did raise concerns about possible effects and a study was carried out using the micronucleus (MN) response in peripheral lymphocytes as a biomarker (Bolognesi et al., 2009).

This study was carried out in volunteers from five Colombian regions, characterized by different exposure to glyphosate and other pesticides. The epidemiological design was a prospective cohort study but, for logistical reasons, without exposure biomonitoring. A large sample, 274 persons comprising 137 women of reproductive age (15–49 yr of age) and their spouses (137), were included in the study. Participants were interviewed to obtain relevant details about health status, history, lifestyle, past and current occupational exposure to pesticides, and factors known to be associated with increased frequency of micronuclei. In regions where glyphosate was being sprayed, blood samples were taken prior to spraying, 5 d after spraying, and 4 mo after spraying. Lymphocytes were cultured and MN analysis performed using standardized techniques on binucleated lymphocytes (BN) with preserved cytoplasm.

The frequency of binucleated lymphocytes with micronuclei (BNMN) was smallest in Santa Marta, where organic coffee is grown without pesticides. Compared with Santa Marta, the pre-spray baseline frequency of BNMN was significantly greater in subjects from the other four regions. The highest frequency of BNMN was in Boyacá, where no aerial eradication spraying of glyphosate was carried out, and Valle del Cauca, where glyphosate was used for maturation of sugar cane. Boyacá and Valle showed significantly higher frequency on BNMN than Nariño and Putumayo, where aerial spraying was carried out. Region, gender, and older age (≥35 yr) were the only variables associated with the frequency of BNMN measured before spraying. A significant increase in frequency of BNMN between first and second sampling was observed in Valle, Putumayo, and Nariño immediately (<5 d) after spraying. Four months after spraying in Nariño, there was a statistically significant decrease in the mean frequency of BNMN compared with the second sampling, but in Valle del Cauca the decrease was not significant nor was the increase in Putumayo.

There was no significant association between self-reported direct contact with eradication sprays and frequency of BNMN. The frequency of BNMN in participants who self-reported that they were exposed to glyphosate because they entered the field immediately after spraying (to pick the coca leaves), felt spray drops in their skin, or they thought they were exposed because they had contact with the chemical in the air, was not significantly greater than in subjects living in the same areas but who were not present during spraying. Overall, these results suggest that genotoxic damage associated with glyphosate spraying, as evidenced by the MN test, is small and appears to be transient. The frequencies of BNMN in Nariño and Putumayo during the second and the third sampling fell within the range of values observed in Boyacá, an area where people were exposed to a complex mixture of different pesticides (including glyphosate). A greater increase in frequency of BNMN was observed in Valle del Cauca, but it cannot be attributed only to the glyphosate exposure, because the application rate of the herbicide in this area was one-third compared with that in Nariño and Putumayo. There was no association between self-reported direct contact with eradication sprays and frequency of BNMN. Overall it was concluded that the genotoxic risk potentially associated with exposure of humans to glyphosate in the areas of Colombia where the herbicide is applied for coca and poppy eradication is of low biological relevance. When these conclusions are combined with the lack of significant spray drift (Hewitt et al., 2009), there is no support for the earlier conclusion (Paz-y-Miño et al., 2007) that eradication spraying is producing adverse effects in humans.

OVERALL CONCLUSIONS

The study started out with three questions related to the risks to the environment and human health of the use of glyphosate for eradication of coca (and poppy) in Colombia. These questions were related to spray drift, effects on sensitive wildlife such as amphibians, and effects on humans. On the basis of the results of the series of studies reported in this issue and other observations reported in the literature, several overall conclusions were reached. In terms of spray drift, new data showed that drift from eradication spraying is minimal and that relatively small buffer zones, ranging from 5 to 120 m, are protective of sensitive aquatic animals and, the target organisms, plants, respectively.

Laboratory and field tests on amphibians showed that Colombian species were of similar sensitivity to species tested in other locations and that they were not especially sensitive to glyphosate formulations. Tests on larvae stages of amphibians under realistic conditions showed that toxicity was reduced, most likely because of the rapid absorption of glyphosate and its adjuvants to sediments and particulate matter. Terrestrial stages of frogs showed a range of sensitivity, but all had LC50 values less than the application rate used for eradication of coca. Given interception by foliage, risks to aquatic and terrestrial stages of frogs from Colombia, even from direct exposure to aerial eradication sprays, are judged to be small to negligible. The study of the large distribution of large diversity of frog species in Colombia in relation to coca production and eradication spraying showed that there were only a few species of frogs potentially at risk because of their location in southwest Colombia. As these species are also found in Ecuador, the likely small risks are to populations in Colombia, not the species as a whole. A much greater risk to frogs in Colombia is from the other pesticides used by the growers of coca (and poppy) and particularly the deforestation that precedes the planting of these crops.

In terms of effects on humans, an epidemiological study did not provide evidence of effects on reproductive function in terms of TTP. In a study on potential genotoxicity that combined epidemiological surveys with biological monitoring of the frequency of MN in white blood cells, differences in the baseline frequency were observed in relation to region sampled. In those regions where spraying of glyphosate was being carried out for agricultural and eradication purposes, frequency of MN rose after spraying but these increases were not related to the rate of application or to self-reported exposures to the spray. In some regions the frequency decreased after spraying but in one, it did not. These observations do not fulfill all of the criteria for causality, suggesting that if glyphosate spraying has any influence on MN, this is small and not of biological significance.

Overall, the risks to sensitive wildlife and human health from the use of glyphosate in the control of coca (and poppy) production in Colombia are small to negligible, especially when compared to the risks to wildlife and humans that result from the entire process of the production of cocaine (and heroin) in Colombia.

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Annex 131-B

HEWITT ET AL., "SPRAY DROPLET SIZE, DRIFT POTENTIAL, AND RISKS TO NONTARGET ORGANISMS FROM AERIALLY APPLIED GLYPHOSATE FOR COCA CONTROL IN COLOMBIA"

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Spray Droplet Size, Drift Potential, and Risks to Nontarget Organisms from Aerially Applied Glyphosate for Coca Control in Colombia

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A wind tunnel atomization study was conducted to measure the emission droplet size spectra for water and Glyphos (a glyphosate formulation sold in Colombia)+Cosmo-flux sprays for aerial application to control coca and poppy crops in Colombia. The droplet size spectra were measured in a wind tunnel for an Accu-Flo nozzle (with 16 size 0.085 [2.16 mm] orifices), under appropriate simulated aircraft speeds (up to 333 km/h), using a laser diffraction instrument covering a dynamic size range for droplets of 0.5 to 3,500 μm. The spray drift potential of the glyphosate was modeled using the AGDISP spray application and drift model, using input parameters representative of those occurring in Colombia for typical aerial application operations. The droplet size spectra for tank mixes containing glyphosate and Cosmo-Flux were considerably finer than water and became finer with higher aircraft speeds. The tank mix with 44% glyphosate had a $D_{v0.5}$ of 128 μm, while the value at the 4.9% glyphosate rate was 140 μm. These are classified as very fine to fine sprays. Despite being relatively fine, modeling showed that the droplets would not evaporate as rapidly as most similarly sized agricultural sprays because the nonvolatile proportion of the tank mix (active and inert adjuvant ingredients) was large. Thus, longer range drift is small and most drift that does occur will deposit relatively close to the application area. Drift will only occur downwind and, with winds of velocity less than the modeled maximum of 9 km/h, the drift distance would be substantially reduced. Spray drift potential might be additionally reduced through various practices such as the selection of nozzles, tank mix adjuvants, aircraft speeds, and spray pressures that would produce coarser sprays. Species sensitivity distributions to glyphosate were constructed for plants and amphibians. Based on modeled drift and 5th centile concentrations, appropriate no-spray buffer zones (distance from the end of the spray boom as recorded electronically ±5%) for protection of sensitive plants were 50–120 m for coca spray scenarios and considerably lower for poppy spray scenarios. The equivalent buffer zone for amphibia was 5 m. The low toxicity of glyphosate to humans suggests that these aerial applications are not a concern for human health.

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Aerial applications of glyphosate to control illicit coca and poppy crops have been made in Colombia since 1997. The area of coca sprayed with glyphosate has shown a steady increase over recent years, reaching approximately 153,000 ha in 2007 (personal communication, National Police of Colombia, Bogotá, December, 2007). Concerns have been raised as to the possible environmental and human health effects of the aerial spray program (International Court of Justice, 2008).

The aerial application of herbicides involves release of spray liquid over a target area using appropriate equipment (aircraft, nozzles, boom setup, etc.) and directing the spray toward the target, considering any cross-wind, vertical wind, or other meteorological effects. Many studies examined the effects of application, meteorological, chemical, and canopy parameters that may influence deposition of the spray and thus efficacy and potential off-target spray drift. Studies by the Spray Drift Task Force (Hewitt et al., 2002) and others have led to the development and validation of accurate models such as AGDISP (Bilanin et al., 1989) and AgDRIFT (Hewitt et al., 2001) for predicting on- and off-target deposition of aerially applied sprays. Originally developed by the U.S. Forest Service, NASA, U.S. Army, and other organizations around the world, this model has been extensively validated for use in spray drift exposure assessments for aerial applications of herbicides such as glyphosate. The U.S. Environmental Protection Agency (EPA) has been a key participant in the development of these modeling tools (Bird et al., 2002), and routinely uses them for risk assessments involving pesticide drift. One of the most important factors affecting spray application and environmental fate modeling is the droplet size spectrum applied by the aircraft or sprayer (Hewitt 1997).

This article describes a wind tunnel atomization study to measure the emission droplet size spectra for water alone and the herbicide glyphosate (Glyphos) plus the adjuvant Cosmo-Flux sprays applied under simulated conditions for aerial application to control coca and poppy crops in Colombia. The droplet size spectra were measured in a wind tunnel for the same Accu-Flo nozzles that are used in the field spray applications, under appropriate simulated aircraft speeds (up to 333 km/h), using a laser diffraction instrument covering a dynamic size range for droplets of 0.5 to 3500 μm. The nozzle size was 0.085 (2.16 mm) with 16 discharge orifices. The spray pressure was 2.4 bar at the nozzle. Using the droplet spectrum data from the wind tunnel study, the spray drift potential of the glyphosate spray mixture was modeled using the AGDISP model with application and meteorological input parameters representative of those occurring in typical aerial application for control of coca and poppy in Colombia. Based on model predictions, and in combination with data on the potential environmental effects of glyphosate and the adjuvant Cosmo-Flux (Solomon et al., 2007; Brain & Solomon, 2009), studies were undertaken to assess the risk to plants and the environment associated with the potential for off-target spray drift under the conditions of use in Colombia.

MATERIALS AND METHODS

A Sympatec HELOS VARIO laser diffraction particle size analyzer was used to measure the emission droplet size spectra for Accu-Flo and solid-stream nozzles in a wind tunnel. All measurements were made using a 2000-mm focal length lens which measured droplets in the size range 0.5 to 3,500 μm. Data and results were obtained using model-independent analysis (MIA) and Windox software. MIA is the usual analysis method used by other liquid spray researchers in the Spray Drift Task Force (Hewitt, 1994). The wind tunnel, a straight-through blower design used for such studies (Foster & French, 1992), was set to deliver airstream velocities up to 333 km/h (92.6 m/s; 207 miles/h), measured using Pitot and hot wire anemometer probes. The end fans were also operated to draw air through the filter section of the wind tunnel and ensured uniform air velocities while sampling the sprays. All measurements were made for atomized droplets of spray, i.e., beyond the initial ligament breakup distance (with the laser 1.5 m downwind of the nozzle). All measurements were replicated to provide two or three measurements per treatment, which were statistically averaged and characterized. The spray pressure was measured using a calibrated pressure gauge connected to a capillary at the nozzle tip, and set to approximately 2.4 bar (35 psi) for most of the applications.

Droplets contained in the spray clouds produced by the nozzles in the present study were not spatially uniform. Droplet size varied across the spray plume (for example, larger droplets typically occurred at the edge of the plume, and smaller droplets in the center). It was therefore important to ensure that a cross-sectional average spray sample was obtained at a given axial location that was representative of the spray plume under evaluation (Dodge, 1988; Snyder et al., 1989). Cross-section averages were obtained in this study by traversing the nozzle vertically down across the laser beam while spraying.

Volumetric and cumulative volumetric droplet size spectra as well as the $D_{v0.5}$ value were calculated for water as a standard control and two different spray mixtures containing Glyphos and Cosmo-Flux. The $D_{v0.5}$, or volume median diameter, is the droplet diameter (μm) at which 50% of the total spray volume is contained in droplets with larger and smaller diameter. Droplet parameter size values were calculated by the particle size analyzer in compliance with ASTM Standard E799-87 (ASTM, 1987). In this study, there was interest in the spray volume contained in relatively small droplets, i.e., those with diameter below 150 μm. This represents the finer droplets in the spray, which might present more of an exposure risk for downwind spray drift under unfavorable conditions.

Experimental runs were conducted using either (a) water alone, (b) water, 44% Glyphos, 1% Cosmo-Flux as used for treatment of coca crops, or (c) water, 4.9% Glyphos, 0.5% Cosmo-Flux as used for treatment of poppy crops. Glyphos and Cosmo-Flux were the exact same products used in Colombia for aerial application. Aerial application rates of glyphosate for coca are 3.69 kg a.e./ha. In order to maximize penetration and effectiveness of the spray formulation, Glyphos is tank-mixed with an adjuvant product (Cosmo-Flux 411F; Cosmoagro, Bogotá). Cosmo-Flux is an agricultural adjuvant containing nonionic surfactants (a mixture of linear and aryl polyethoxylates: 17% w/v) and isoparaffins (83% v/v). These tank mixes were prepared by mixing the components on a volumetric basis using graduated measuring cylinders. The mixtures were stirred thoroughly and placed into 20-L pressurized containers. Compressed air was used to displace the products from the spray tanks through the nozzles for sampling the droplet size spectra in the wind tunnel. Applications of each tank mix were made through the Accu-Flo nozzle (0.085 [2.16 mm] with 16 orifices, as used in Colombia) and an alternative D10 nozzle type at simulated aircraft speeds of 259, 296, and 333 km/h. The Accu-Flo nozzle was also tested in a prototype reverse Venturi chamber (supplied by Russ Stocker, Woodland) to see if such devices used to reduce air shear effects on liquid atomization could increase droplet size.

Spray Drift Modeling

Assessments of spray drift and deposition were conducted using the AGDISP model. This model was developed and validated by NASA, the U.S. Forest Service, U.S. Army, Spray Drift Task Force, and others over several decades for aerial forestry (Bilanin et al., 1989) and agricultural spray applications (Hewitt et al., 2002). The AGDISP model was run using the following inputs:

- Droplet size data measured from the wind tunnel tests, specified in 32 size classes by spray volume.
- For OV-10 and AT-802, 60 Accu-Flo nozzles (maximum allowed by AGDISP model); for Ayres Turbo Thrush (ATT-65), 35 Accu-Flo nozzles, regularly spaced on the boom, spaced at equivalent of 74 nozzles at 114 mm for OV-10; and 96 nozzles at 140 mm for AT-802 and 35 nozzles at 152 mm for ATT-65.
- Aircraft types from the library to include Ayres Turbo Thrush 65, Bronco OV-10, and Air Tractor 802 with characteristic configurations, vortex patterns, and default settings except operational flight speed.
- Aircraft flight speeds of 333 km/h for OV-10, 274 km/h for AT-802, and 226 km/h for ATT-65.
- Tank mix compositions to represent water with 4.992 or 1.2 kg/ha glyphosate isopropylamine salt (as appropriate for modeling each application scenario), of which it is assumed the acid equivalents (a.e.) rate was 75%. Nonvolatile rate set to assume that all of the glyphosate and Cosmo-Flux molecules were nonvolatile. Spray volume rate of 10.4 L/ha (1.11 gallon/acre) total tank mix for coca sprays.
- Aircraft height above ground 30.48 m.
- Canopy (tree) height 25.91 m.
- One flight line (i.e., single swath applications as used operationally in Colombia).
- An 18.3-m effective swath width.
- 2.57 m/s (9.3 km/h) wind speed at 90º to aircraft flight direction (i.e., perpendicular cross-wind).
- 35ºC air temperature and 70% relative humidity.
- Weak atmospheric stability (weak solar insolation equivalent to partial or full cloud cover).
- Evaporation rate 37 μm^2/ºC/s (representative of glyphosate products).

All other model input values were the model default settings.

Risk Assessment

Amphibians had been identified as aquatic organisms at greatest risk from a direct overspray in a previous risk assessment (Solomon & Thompson, 2003; Solomon et al., 2007) and, as glyphosate is a herbicide for the control of plants, plants would be potentially at risk from direct overspray (the desired outcome) as well as from spray drift. As the human health risks of exposures to a direct overspray of glyphosate–Cosmo-Flux mixture were judged to be negligible in previous studies (Solomon et al., 2007), any exposures from drift would also be negligible. A deterministic risk value for amphibians and plants was calculated from the intercept of the 5th centile toxicity values and the drift deposition values from the AGDISP model.

Toxicity data were obtained for plants and the most sensitive aquatic species, amphibians. The toxicity data for plants were taken from the U.S. EPA Ecotox database (U.S. EPA, 2001) for effects of glyphosate on plants. The values were the EC25 from tests for plants sprayed with formulated glyphosate (mostly Roundup). These values were converted to units of g/ha a.e. to allow for a common basis for comparison. It is recognized that Cosmo-Flux may increase potency of the mixture for plants; however, there were no data for sensitivity to the mixture in plants other than coca, where there was little difference between Glyphos alone or in combination with Cosmo-Flux (Marshall et al., 2009). The plant data were fitted to a log-normal distribution to create a species sensitivity distribution (SSD; Solomon & Takacs, 2002). In doing this, the test plants were used as surrogates for other plants in the environment, a normal process for assessing risks using SSD. For amphibians, the toxicity data for formulated glyphosate were taken from literature as summarized elsewhere (Brain & Solomon, 2009). These data are for formulated glyphosate without the addition of Cosmo-Flux, but toxicity tests on the spray mixture with the most sensitive frog species (*Xenopus laevis*) (Wildlife International, 2006) showed no increased sensitivity over previously published values (Edginton et al., 2004). The 5th centile of the distribution was calculated using the transformed values for the slope and intercept of the regression line of the SSD. The 5th centile of the amphibian SSD was calculated as already described and converted from a concentration to a rate per hectare under the worst-case assumption that the concentration resulted from direct overspray of a 15-cm-deep pool with no exposure reduction via adsorption to sediments and organic matter, and no interception by surrounding plants.

RESULTS

Droplet Size Spectra

The droplet size from the Accu-Flo nozzle became smaller as the aircraft speed increased, due to higher air shear at the point of liquid atomization (Table 1). For example, for the coca spraying tank mix, as aircraft speed increased from 259 to 296 to 333 km/h, the $D_{v0.5}$ (volume median diameter droplet size) value of the sprays decreased from 219 to 173 to 128 μm, respectively, and the fine spray volume in droplets with diameter below 150 μm increased from 35 to 44 to 57%.

The water sprays were much coarser than tank mixes containing glyphosate and Cosmo-Flux. Examples for the two active ingredient tank mixes at 333 km/h (180 knots) aircraft speed are shown in Figures 1 and 2. There was less difference in droplet size between the two active ingredient tank mixes, with both being considerably finer than water sprays. An example of the effect of tank mix composition on droplet size is given as follows, for applications through the Accu-Flo

TABLE 1
Volume Median Diameter Droplet Size ($D_{v0.5}$) and Fine Spray Volume in Droplets Below 150 µm, for Water and the Tank Mixes for Coca and Poppy Control for Accu-Flo and D10 Nozzle Types

		Accu-Flo (0.085-16) nozzle		D10 nozzle	
Spray solution	Speed (km/h)	$D_{v0.5}$ (µm)	Percent volume <150 µm	$D_{v0.5}$ (µm)	Percent volume <150 µm
Water	259	253	29	329	17
	296	250	31	–	–
	333	217	37	225	31
Coca spray:	259	219	35	229	30
44% glyphosate	296	173	44	179	41
+1% Cosmo-Flux	333	128	57	147	51
Poppy spray:	259	194	39	–	–
4.9% glyphosate	296	178	43	–	–
+0.5% Cosmo-Flux	333	139	53	167	45

Note. Data are the means of three runs each.

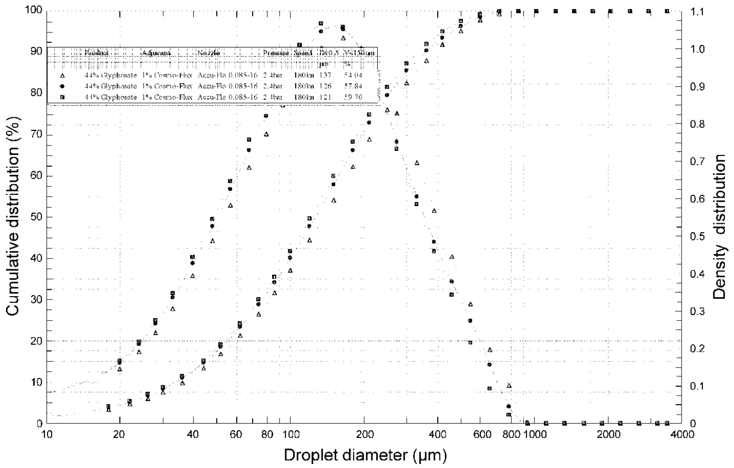

FIG. 1. Volumetric droplet size spectra for coca control spray mixture at 333 km/h (180 knots) aircraft speed with the Accu-Flo nozzle.

nozzle at an aircraft speed of 296 km/h. The water spray had a $D_{v0.5}$ value of 250 µm and 31% spray volume in droplets <150 µm. The tank mixes containing glyphosate and Cosmo-Flux were much finer, with $D_{v0.5}$ values around 175 µm and 44% spray volume in droplets <150 µm (Table 1). There was a clear approximately linear relationship ($r^2 \geq .996$) between droplet size and effective aircraft speed within the range tested in this study for the coca sprays (Figure 3), which allows extrapolation of droplet size for additional aircraft speeds for the Accu-Flo nozzle.

The study included assessments of alternative application systems to the Accu-Flo nozzles currently in use. Accu-Flo nozzles are effective at increasing droplet size for spray applications by rotary wing (helicopter) aircraft, but with their relatively small orifice diameter are less effective at very high aircraft speeds. Large orifice solid stream nozzles such as the D10 (named for its 10/64 in [4 mm] diameter orifice) provide a viable alternative, especially if used at high spray pressures to increase the spray breakup length. At the same spray pressure (2.4 bar), this nozzle increased the $D_{v0.5}$ at 333 km/h from 139 to 168 µm, with a proportional approximate 15% decrease in droplets <150 µm relative to the Accu-Flo nozzle (Table 1). The use of higher spray pressures would probably produce even coarser

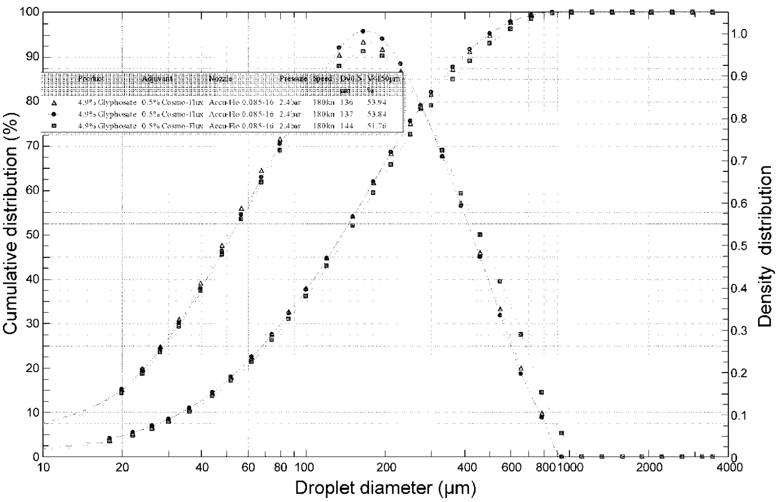

FIG. 2. Volumetric droplet size spectra for poppy control spray mixture at 333 km/h (180 knots) aircraft speed with the Accu-Flo nozzle.

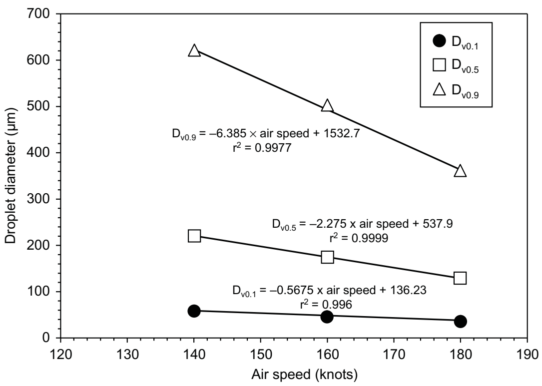

FIG. 3. Droplet size parameter values ($D_{v0.1}$, $D_{v0.5}$, and $D_{v0.9}$) at different aircraft speeds for the Accu-Flo nozzle with fitted regression lines.

sprays with this nozzle, based on previous research observations with narrow-angle, large-orifice (e.g., large solid stream) nozzles on high-speed aircraft.

Tests with the prototype reverse Venturi chamber showed that increases in droplet size, especially for the "fines" in the spray, can be achieved (Figure 4). For example, there was a decrease in "fines" from 31 to 25% at an aircraft speed of 296 km/h.

Spray Drift Modeling

The AGDISP model showed that the spray drift potential for these applications was equivalent to that of fine to very fine sprays. However, the high proportion of the tank mix contained in nonvolatile materials (the active ingredient product and inert adjuvant) and the high relative humidity (70%) of the air during these applications reduced evaporation rates significantly compared to similar agricultural applications. In addition, the tree canopy and adjacent vegetation are effective at intercepting spray and reduce the availability of droplets for off-target drift where these trees and vegetation are present (AgDRIFT, 2008).

The model-predicted off-swath spray deposition rates for glyphosate (a.e.) using each of the three simulated aircraft types is shown in Figure 5. Mean deposition rates for the most concentrated application rate, i.e., the coca spray, on the target spray block were between 3030 and 3260 g/ha, which is close to the target rate of 3690 g/ha of active product. Spray drift potential was related to the speed of the aircraft and was similar for the AT-802 and OV-10, but less for the slower ATT-65 where lower air shear at the nozzles produced coarser sprays.

Because the relative humidity (RH) of the air exerts an influence on spray drift, particularly for smaller droplets, additional modeling was conducted to characterize spray drift at an RH of 90%, which is more typical of the conditions that occur in the Nariño and Putamayo areas in the SW part of Colombia. The modeling data (Figure 6) demonstrate that the majority of the active ingredient (>90%) deposits within 100 m of the swath edge. Under higher humidity conditions, comparatively lower deposition of active ingredient occurs at downwind distance, with the differential being most pronounced at distances beyond 200 m downwind. This pattern reflects the disproportional influence of relative humidity on smaller droplets (<150 μm),

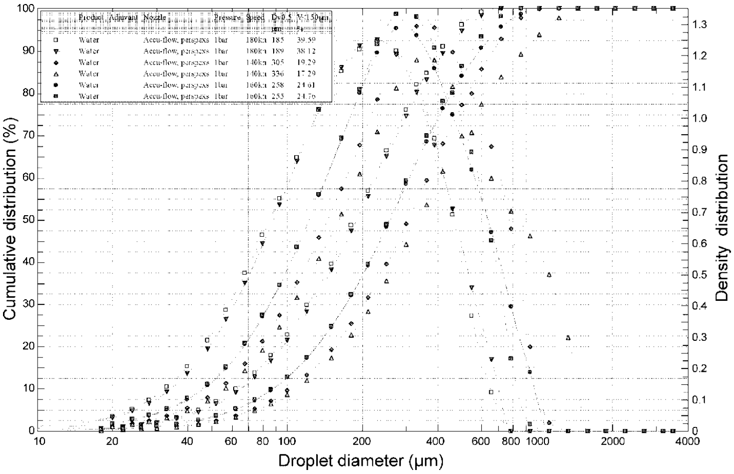

FIG. 4. Droplet size distribution from the Accu-Flo nozzle in the reverse Venturi chamber. VMD for water only at 259, 296, and 333 km/h (140, 160, and 180 knots) were 321, 257, and 187 μm, respectively.

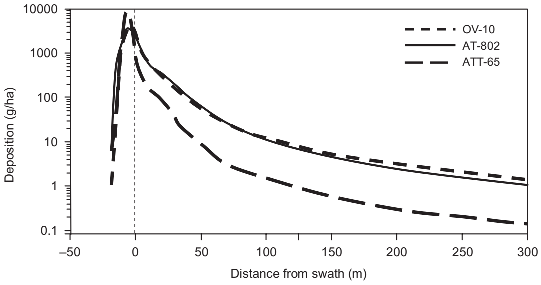

FIG. 5. AGDISP-predicted deposition of glyphosate (g/ha on a log scale) for different aircraft types at representative flight speeds. Negative distances represent deposition within the target area; 0 m represents downwind edge of spray block.

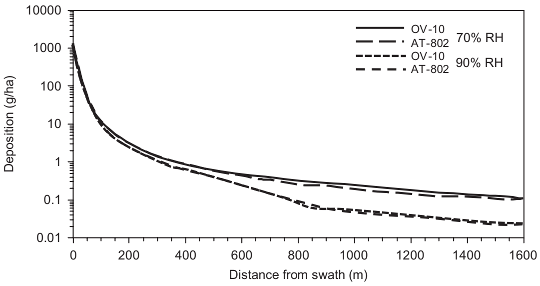

FIG. 6. Influence of relative humidity on spray drift potential of the glyphosate–Cosmo-Flux mixture as used to spray coca. The RH of 90% is more typical of the southwest region of Colombia. Note that the *y* axis is a log scale to better show that the effect of RH on spray drift is most pronounced at deposition rates of less than 10 g/ha.

which are primarily responsible for drift, but which also carry a small proportion of the total amount of active ingredient released into the air. The effect of evaporation is due to the loss of water, which is important because even the most concentrated tank mix included approximately 50% by volume of water. This means that at least half of the droplet volume could potentially be lost through evaporation.

Airborne spray volumes decreased rapidly, with the majority of the spray predicted to deposit within 30 s after release from the aircraft.

Toxicity Data

Toxicity data were obtained for plants and the most sensitive aquatic species, amphibians. The toxicity data for plants were taken from the U.S. EPA Ecotox database (U.S. EPA, 2001) for effects of glyphosate on plants. The values were the EC25 from tests for plants sprayed with formulated glyphosate. These values were converted to units of g a.e./ha to allow for a common basis for comparison (Table 2).

The most sensitive plant in the data set was *Brassica rapa* and the least sensitive was *Magnoliaphyta* spp. The plant data were fitted to a log-normal distribution to create a species sensitivity distribution (SSD, Figure 7) using standard methods (Solomon & Takacs, 2002). In doing this, the test plants were used as surrogates for other plants in the environment, a normal process for assessing risks using SSDs. The datum for *Magnoliaphyta* spp. is plotted on the SSD but was not used in the regression as this datum was judged to be an outlier. The 5th centile of the distribution

TABLE 2
Toxicity Data for Formulated Glyphosate in Plants

Species scientific name	Species common name	EC25 (g/ha)	Effect	Exposure duration (days)
Brassica rapa-rapa	Turnip	36	Development	28
Raphanus sativus	Radish	44	Growth	21
Cucumis sativus	Cucumber	60	Development	28
Glycine max	Soybean	76	Growth	28
Triticum aestivum	Bread wheat	78	Growth	28
Helianthus annuus	Sunflower	78	Development	21
Sorghum bicolor	Broomcorn	78	Growth	21
Beta vulgaris	Beet	87	Growth	28
Abelmoschus esculentus	Okra	90	Growth	28
Raphanus sativus	Radish	100	Development	28
Beta vulgaris	Beet	103	Development	21
Triticum aestivum	Bread wheat	108	Growth	21
Lactuca sativa	Lettuce	111	Growth	28
Zea mays	Corn	117	Development	336
Avena sativa	Common oat	120	Development	28
Allium cepa	Common onion	137	Development	21
Glycine max	Soybean	157	Growth	21
Cucumis sativus	Cucumber	220	Development	21
Cyperus rotundus	Purple nutsedge	372	Growth	28
Pisum sativum	Pea	436	Development	21
Magnoliophyta	Angiosperm	1958	Development	28

Note. Data from (U.S. EPA, 2001).

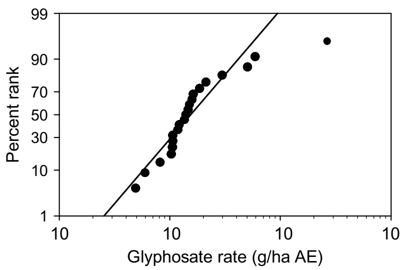

FIG. 7. Species sensitivity distribution (SSD) of glyphosate in plants.

TABLE 3
Regression Coefficients and Intercepts for the Toxicity Data Distributions for Acute Exposures of Plants and Frogs to Formulated Glyphosate

			$y = ax + b$		Centile intercepts (a.e.)	
Data source	n	r^2	a	b	5%	Units
Plants	21	0.90	2.96	–6.47	43	g/ha
Amphibians	11	0.90	3.68	–12.53	917	μg/L (= 1368 g/ha in water 15 cm deep)

was calculated using the transformed values for the slope and intercept of the regression line of the SSD (Table 3).

For amphibians, the toxicity data for formulated glyphosate were taken from literature as summarized in a companion paper (Brain & Solomon, 2009). These data are for formulated glyphosate without the addition of Cosmo-Flux, but toxicity tests on the spray mixture with the most sensitive frog species (*Xenopus laevis*) (Wildlife International, 2006) showed no change in sensitivity over previously published values (Edginton et al., 2004). The 5th centile of the amphibian SSD was calculated as already described (Table 3) and converted from a concentration to a rate per hectare on the assumption that the concentration resulted from direct overspray of a 15-cm-deep pool with no exposure reduction via adsorption to sediments and organic matter.

Environmental Risk

Deterministic risk values for amphibians and plants were determined from intercept of the 5th centile toxicity

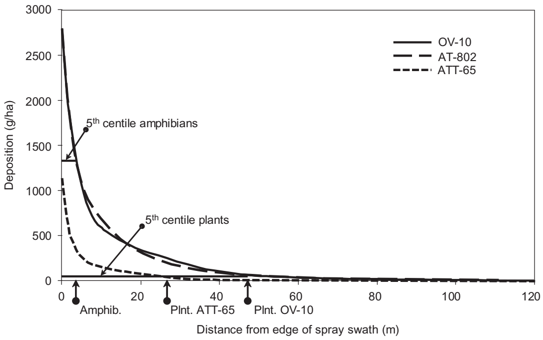

FIG. 8. Modeled drift deposition values for glyphosate plus Cosmo-Flux overlaid with the 5th centile toxicity values for plants and amphibians. The distances from the edge of the spray swath where sensitive plants and amphibians may be at risk are shown by the arrows on the *x* axis.

values (given earlier) and the drift deposition values from Figure 5. These values are shown in Figure 8. These data show that, for the ATT-65 aircraft, the worst-case spray drift will be such that the 5th centile toxicity value for amphibians will not be exceeded in the off-swath area. This is indicative of negligible risk to amphibians located in 15-cm-deep pools located off-field for this type of aircraft.

For worst-case spray drift from the AT-802 and the OV-10, the model predicts that the 5th centile toxicity value for amphibians may be exceeded in 15-cm-deep pools located within 5 m of the edge of the field. Thus amphibians could be at risk in locations where pools containing larvae of sensitive species were in the coca field or were within 5 m of the downwind edge of the spray swath. Studies in field microcosms show that toxicity to larval amphibians is reduced in the presence of natural sediments and that amphibian larvae would not be at risk, even from a direct overspray at twice the normal rate of application (Thompson et al., 2004; Wojtaszek et al., 2004; Bernal et al., 2009).

For plants, which are the most sensitive to glyphosate, the risks from the worst-case modeled spray drift are greater. For spray drift from the ATT-65, sensitive plants within 30 m of the edge of the field may be affected. For spray drift from the AT-802 and OV-10 aircraft, sensitive plants within 50 m of the spray swath may be affected. Adverse effects beyond that distance are unlikely, especially as glyphosate were shown to stimulate the growth of the several species of plants, such as maize, soybean, eucalyptus (*Eucalyptus grandis*), pine (*Pinus caribea*), and tropical spiderwort (*Commelina benghalensis*), at rates ranging from 1.8 to 36 g glyphosate a.e./ha (Velini et al., 2008).

DISCUSSION AND CONCLUSIONS

Effective decision making in aerial applications of pesticides can be assisted through the use of appropriate risk assessment and modeling information and tools. The present study assessed spray drift exposure risk in aerial field applications of glyphosate sprays for control of poppy and coca crops in Colombia. The droplet size spectra generated when the tank mixes in this study were applied through Accu-Flo nozzles under the simulated aircraft speeds relative to field applications were classified as very fine to fine sprays. The droplet size, application, herbicide tank mix, and meteorological and canopy/terrain characteristics for Colombian conditions were input to a spray drift exposure risk model, AGDISP, to assess off-target spray drift potential and on-target spray performance. The results predicted that most of the spray safely deposits within the target area or a few hundreds of meters downwind of the application. An appropriate no-spray buffer to protect sensitive plants from spray drift exposure would be 50 to 120 m for the coca spray. This is proposed to be a directional buffer because drift only occurs in the downwind direction, and not upwind.

The extensive vegetation of the forest canopy and environment around the area where the coca and poppy plants are sprayed in Colombia will afford excellent reductions in spray drift potential by interception of droplets with leaf and other surfaces (Raupach et al., 2001). This will greatly reduce the spray drift exposure risk from the values reported in this study by 50–90% (AgDRIFT, 2008). The present study showed that the product tank mixes produced up to 50% more small, driftable droplets than water alone. This is due largely to the relatively low dynamic surface tension and extensional viscosity of the tank mix when these active and inert materials are added. Tests could be conducted to evaluate the effectiveness of alternative adjuvants in increasing droplet size, or even alternative glyphosate products with lower surfactant loading or more favorable physical property and atomization characteristics. Candidate emulsion/ polymer adjuvants for possible screening could include invert suspension agents, esterified seed oils, polyacrylamide, and/or guar gum with ammonium sulfate and adjuvants containing lecithin.

Because a direct overspray of humans with glyphosate plus Cosmo-Flux was a negligible health risk to humans (Solomon et al., 2007), exposure to spray drift downwind of the spray presents an even smaller risk. Amphibians in shallow pools within 5 m downwind of the edge of the field may be at risk under worst-case conditions but field microcosm experiments demonstrated that this is not the case where natural sediments are present. As a broad-spectrum translocated herbicide, application of glyphosate may pose a risk to the most sensitive plant species in areas within 30–50 m downwind of spray targets. However, drift deposition will only occur downwind and be reduced at lower wind speeds. Further, droplet capture by adjacent trees and shrubs may reduce drift from the modeled worst-case figures.

In sensitive, high-biodiversity environments, risk to nontarget plant species may be reduced by a number of mitigation measures. A primary approach would be to use spray nozzles that produce larger drops, notably the D10 solid stream nozzle. This will significantly reduce spray drift. No-spray buffer zones or reduced spray target areas, particularly downwind, can also be implemented to protect sensitive areas. This approach is regularly used for ground application machinery adjacent to for example watercourses. Other approaches could be to use drift control adjuvants, though these are reported to exert little effect on lethal or injury drift distances with glyphosate, when compared with reductions in drift from alternative nozzle types (Johnson et al., 2006).

Long-distance transport of spray drift particles is small and not an issue for humans or the environment beyond 50 m downwind at the maximum permitted wind velocity of 9 km/h for spraying operations. Long-distance movement of glyphosate is negligible if appropriate no-spray buffers are used and nonexistent if the wind direction during spraying is away from the areas of concern.

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Annex 131-C

E.J.P. MARSHALL ET AL, "COCA (*ERYTHROXYLUM COCA*) CONTROL IS AFFECTED BY GLYPHOSATE FORMULATIONS AND ADJUVANTS"

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Coca (*Erythroxylum coca*) Control is Affected by Glyphosate Formulations and Adjuvants

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The aerial spray program for the eradication of coca in Colombia uses Glyphos, a local formulation of glyphosate tank-mixed with an adjuvant product, Cosmo-Flux. There are some potential risks to amphibians from direct overspraying of shallow waters. In order to evaluate potential alternative mixtures, a field experiment was conducted at the Center of National Training of Police Operations in Tolima province, Colombia. Plants of coca were established with irrigation and grown to 75 cm tall. A randomized split-plot design experiment was laid out and sprayed with a range of glyphosate formulations and different adjuvants using an experimental ground sprayer. Assessments were made of plant vigor, height, and above-ground standing crop (fresh weight) 3 wk after application. Resprouting of plants was assessed at 9 wk after treatment. Unformulated glyphosate applied as the product Rodeo gave poorer control of coca than two formulated products, Roundup Biactive (from Europe) and Colombian Glyphos. In general, these products performed well without added adjuvants, giving control similar to that of the eradication mixture with Cosmo-Flux. There was some evidence that addition of the adjuvant Silwet L-77 and to a lesser extent Mixture B (from the United Kingdom) gave more rapid herbicide symptoms. There were also indications that glyphosate rates of less than 3.69 kg acid equivalents (a.e.)/ha could give control in the range of 95%. Depending on the environmental risk requirements, the experiment indicates that, should other spray mixtures be required, there are potential alternatives. These would require extensive field testing to cover different environmental conditions, different coca varieties, and particularly aerial application, prior to a recommendation. Should the glyphosate product require changing, Roundup Biactive may be considered. Should the adjuvant require changing, then on the basis of this research, Silwet L-77 and Mixture B would be good candidates for further evaluation.

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The control of the drug plant *Erythroxylum coca* Lam. and the closely related *E. novogranatense* (coca), the sources of cocaine, is the focus of considerable effort and expenditure in a number of South American countries. Authorities are targeting the removal of the plant and are also engaged in rural development projects to replace the illicit cultivation of this crop. As well as controlling supplies of the drugs, there are also efforts to reduce global demand for the drug. The illicit cocaine industry has an estimated production that reached the streets of 600 tonnes in 2007 with a retail value of approximately $934 million. Retail prices are $2200/kg in Colombia, $10,200/kg in the United States, and $85,000/kg in the streets of Europe (UNODC, 2007). As part of the supply control effort that started in the 1970s, an aerial spraying eradication program in Colombia was started in 1997 using the herbicide glyphosate. The area of coca sprayed with glyphosate has shown a steady increase over recent years, reaching 153,000 ha in 2007 (personal communication, National Police of Colombia, Bogotá, December 2007).

The aerial spray program is conducted with two types of commercial crop-spraying aircraft fitted with Accu-Flo air-induction nozzles. The spray planes, Air Tractor 802 (Air Tractor Inc., Olney, TX) and Rockwell OV-10, are equipped with high-resolution tracking equipment and positional data recorders that display position, provide directional guidance, and store data for later analysis (Solomon et al., 2007).

Glyphosate used for the aerial eradication program in Colombia is the Glyphos product containing 354 g acid equivalents (a.e.)/L sold for agricultural use. Glyphosate was found to be effective at controlling both species of coca, *E. coca* and *E.*

novogranatense (Ferreira et al., 1997). The aerial application rate of glyphosate is 3.69 kg a.e./ha in Colombia. To maximize penetration and effectiveness of the spray formulation, glyphosate is tank-mixed with an adjuvant product (CosmoFlux 411F; Cosmoagro, Bogotá). The inclusion of the adjuvant follows the studies of Collins and Helling (2002), who demonstrated a fourfold increase in glyphosate efficacy by including suitable adjuvant mixtures in the spray.

Surfactants, such as the polyethoxylates in Cosmo-Flux, enhance efficacy through (1) increasing target surface adherence, (2) promoting better droplet spread, (3) better dispersion, (4) prevention of aggregation, and (5) enhanced penetration of herbicides into target plant tissues through the reduction of surface tension on plants. Surfactants also disrupt the water-insoluble wax cuticle, thus increasing the penetration of herbicide active ingredient. Base oils, such as the isoparaffins in Cosmo-Flux, are another class of adjuvants used in pesticide formulations to primarily aid foliar absorption of the pesticide by disrupting the waxy cuticle on the outer surface of foliage, which increases permeability (Solomon et al., 2007).

Environmental risk assessments of the aerial eradication program indicated that the relative impact of the glyphosate mixture is small in comparison with the impacts of forest clearance for cropping (Solomon et al., 2007). Nevertheless, there could be some impact on amphibian species in shallow waters (<30 cm deep) that are directly oversprayed. Such effects are unlikely to be due to glyphosate, but to the adjuvants present in the spray mixture. Further ecotoxicological tests were conducted with the spray mix as used in Colombia (Bernal et al., 2009a, 2009b). Developments in adjuvant research indicate that it may be possible to identify an adjuvant mixture or mixtures as effective as the current mixture, but with less risk to native amphibians.

The field experiment described here was conducted as an initial step to evaluate the efficacy of a range of glyphosate formulations mixed with different adjuvants. It was postulated that alternative combinations might give as good or better control of coca than the formulation currently used in the aerial eradication program. As noted earlier, reduced toxicity of the spray mixture may have environmental benefits, plus there is potential for reducing the application rate of glyphosate when mixed with different adjuvants used in the aerial eradication program. With approximately 153,000 ha sprayed in Colombia in 2007, there would be considerable cost savings if a reduced rate gave as good control as current practice.

MATERIALS AND METHODS

Site

The field site was located on a *finca* (ranch) in County San Luis in the Department of Tolima, Colombia. The area is to the west of Bogotá between the eastern and central mountain ranges of the Andes, located at N 04º 15.971, W 75º 01.373, and at 517 m above sea level (a.s.l.). The soils are valley alluvia. The selected area was initially covered with grasses, sedges, and low shrubs. This was mown with a tractor-mounted bush cutter, then sprayed with glyphosate and ploughed. The site was cultivated and the plants were hand planted in rows 1 m apart on 1-m spacings in plots of 60 plants, with each plot arranged with 6 rows of 10 plants. The planting and agronomy of the plants match much of the pattern of illicit growing, where pesticides (permethrin and mancozeb) and fertilizer are used to promote crop production. Irrigation was applied approximately twice per week, to enhance survival and growth.

Plant Material

Cuttings of *E. coca* variety Pajarito were obtained from the Department of Cauca, in the southwest of Colombia. Cuttings were initially maintained in a shade house in December 2006, treated as necessary with fertilizer, fungicide, and insecticide and then planted out on 15 January and 20 January 2007. Plants that did not survive were replaced. Plants were allowed to grow to approximately 75 cm tall. Two weeks prior to spray treatment, taller plants were trimmed to 75 cm.

Design Layout and Treatments

There were 49 plots of 60 plants, of which 36 were selected for experimental use on the basis of good shrub growth. These plots, each representing a main plot, were grouped into three blocks across the experimental area. Main plots (60 plants) were allocated to 1 of 12 glyphosate/adjuvant treatments at random. Three glyphosate formulations were used: Colombian Glyphos (354 g a.e./L, Monsanto), Roundup Biactive (360 g a.e./L, Monsanto Europe), and Rodeo® (479 g a.e./L, Dow AgroSciences). Glyphos is formulated with adjuvants based on polyethoxylated tallowamines (POEA) for agricultural use. Roundup Biactive, a European product, uses a patented blend of surfactants less dependent on tallowamines for use in or near water. Rodeo is an unformulated glyphosate product, lacking adjuvants. Five adjuvants were also used: Cosmo-Flux, Intake, Mixture B, Silwet L-77, and LI-700. Cosmo-Flux is an agricultural adjuvant containing nonionic surfactants (a mixture of linear and aryl polyethoxylates: 17% w/v) and isoparaffins (83% v/v) (Cosmoagro 2004). Intake (Headland Agrochemicals Ltd., Great Chesterford, United Kingdom) is an agricultural penetrant containing 40% (w/w) propionic acid. Mixture B (AmegA Sciences, Daventry, United Kingdom) is 50% (w/v) nonylphenol ethylene oxide condensate and 50% (w/v) primary alcohol ethylene oxide condensate. Silwet L-77 (GE Silicones, Wilton, CT) is 99.5% (w/w) polyalkyleneoxide modified heptamethyltrisiloxane, a nonionic organosilicone. LI-700 (Nufarm Agriculture, Inc., Calgary, Canada) is a penetrant and acidifier composed of phosphatidylcholine, methylacetic acid, and alkyl polyoxyethylene ether.

A split-plot design was created by dividing each main plot into three subplots, each of two adjacent rows of coca bushes (20 plants). Subplots were randomly ascribed to receive one of three rates of glyphosate (all rates as a.e.): 1 kg/ha, 2 kg/ha, and 4 kg/ha. Aerial application rates of glyphosate are 3.69 kg/ha in Colombia, but 2 lower rates were selected for field testing, in order to evaluate efficacy and survival at lower application rates.

Herbicide and adjuvant treatments were applied with a three-nozzle plot sprayer, mounted with 8002 Teejet nozzles (Spraying Systems Co., Wheaton, IL) 50 cm above the canopy. Calibrations showed the sprayer delivered a volume rate of 200 L/ha at 3 bar (40 psi) boom pressure at the calibrated forward speed. These treatments were ground applied, so necessarily the volume applied was higher than that used in the aerial application. This facilitated accurate small plot studies of a manageable size. Windshields were placed between subplots to prevent any drift between treatments. Applications were made on 1 and 2 August 2007 with air temperatures increasing during the day from 25 to 33ºC and relative humidities declining from 80% to 40% at midday.

Assessments

Prior to treatment, the maximum height and two widths (maximum and at 90º; Diameter-A, Diameter-B) of each coca bush were measured, allowing the calculation of bush area based on an ellipse:

$$\text{Ellipse area} = \Pi(\text{Diameter-A}/2)(\text{Diameter-B}/2) \qquad (1)$$

and bush volume:

$$\text{Bush volume} = \text{ellipse area} \times \text{height} \qquad (2)$$

Heights, ellipse area, and volume could be used as covariates in univariate analyses.

Plant symptoms were scored on a 5-point scale (Table 1) for individual bushes 1 wk (8 August 2007) and 3 wk after spraying (21 August 2007). At the same time, maximum bush heights were recorded. All bushes were harvested at ground level 3 wk after treatment (22 August 2007) and total fresh weight for each subplot was determined. Six weeks after harvesting (9 wk after spraying) on 5 October 2007, numbers of sprouts per stem were counted to measure plant recovery. These data were used to give a survival rate out of 20 plants per subplot.

TABLE 1
Symptom Scores for Coca Plant Health

Score	Effect	Symptoms
1	None	Leaves green, healthy
2	Slight	A few leaves yellowing, brown edges; healthy new growth
3	Moderate	Half the leaves yellow or brown; some recovery
4	Strong	Most leaves yellow, brown or fallen; no recovery
5	Killed	All leaves brown or fallen

Statistical Analysis

Data were analyzed using analysis of variance (ANOVA) of a split-plot design. Data were transformed as necessary to comply with the need for normality, following examination of residuals; square root or $\log_{10}$ transformations (n +0.05) were used. Plant heights were analyzed using initial bush heights as a covariate. Vigor scores were analyzed using bush ellipse area as a covariate, reflecting potential herbicide coverage and therefore dose per bush. The Genstat 9th edition package (VSN International, Hemel Hempstead, UK) was used for analyses and data transformations. There were two spraying errors, so the four affected subplots were treated as missing values in the analyses.

RESULTS

Plant Height and Bush Size

Analysis of the initial bush heights prior to treatment (mean height 80 cm) indicated there were some significant differences between treatments. Analysis of the ellipse area of each bush also indicated some initial and systematic differences across the experiment, despite arranging the plots into blocks. Plots to receive treatments 4 and 8 (Glyphosate + Intake; Roundup Biactive + Silwet L-77) had the smallest bushes, while plots with treatments 6 and 11 (Glyphosate + Silwet L-77; Rodeo + Silwet L-77) had the largest plants. These results confirmed that it was necessary to use covariates representing plant size at treatment in statistical analyses.

Three weeks after treatment, on 21 August 2007, plant heights were measured. Analysis using bush volume as a covariate indicated that treatments and application rate were significant factors, but there was no interaction. Higher rates of glyphosate gave shorter plants. Plant heights were not significantly shorter than untreated controls on plots that had been treated with Glyphos + Silwet L-77 and Rodeo + LI-700 (Figure 1). The shortest plants were found on plots treated with Glyphos + Intake, Roundup Biactive alone, and Roundup Biactive + Silwet L-77.

Symptom Scores

One week after treatment, symptoms of glyphosate were developing on treated plants. There were significant differences

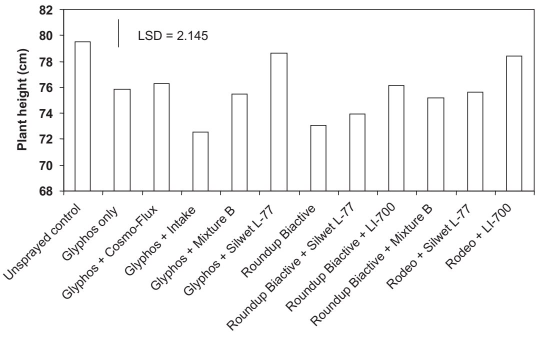

FIG. 1. Mean coca plant height (cm) on plots treated with different glyphosate formulations and adjuvants 3 wk previously. (SED = 1.094; df = 2041).

between treatments and rates of glyphosate (Table 2). All treatments, apart from the low rate of Roundup Biactive + LI-700 were significantly different from the controls and higher scores were found at the higher rates of the herbicide. At the lowest rate of glyphosate (1 kg/ha), the treatments with the products Glyphos and Roundup Biactive with Silwet L-77 had higher scores than other adjuvants. The treatment with Roundup Biactive + Mixture B also showed good activity. At 2 kg/ha, Glyphos with Silwet L-77 and Glyphos alone had highest activity, with Roundup Biactive alone or with Mixture B also showing good activity.

Three weeks after treatment, on 21 August 2007, glyphosate symptoms were well developed, with plants clearly dying and leaves dropping. Statistical analyses again showed significant treatment and rate effects and an interaction. All treatments showed glyphosate effects (Table 3) compared with the controls. At the lowest rate of glyphosate, the highest symptom scores and therefore the most activity were shown with Glyphos + Intake and Roundup Biactive with Silwet L-77 and Mixture B. At 2 kg /ha, the greatest activity was shown by Glyphos alone, Roundup Biactive alone, Glyphos with Silwet L-77 or Mixture B, and Roundup Biactive with Mixture B. At the highest rate of 4 kg /ha, the poorest treatment was Rodeo + LI-700. When comparing the glyphosate formulations, Rodeo gave lower vigor scores than Glyphos or Roundup Biactive across the adjuvant treatments, indicating less overall activity. There was a trend for Roundup Biactive to give higher scores at the lowest rate, in comparison with the other formulations.

Fresh Weights

The fresh weights of coca were not significantly different to controls on only 6 treatments (coefficient of variation = 21%), all at the 1-kg/ha rate of glyphosate. These treatments were Glyphos alone, Glyphos with Cosmo-Flux, Mixture B, or Silwet L-77, and the two mixtures of LI-700 with Roundup Biactive and Rodeo. At 2 kg/ha, the lowest standing crop was found on plots treated with Glyphos and Silwet L-77 or Mixture B (1.62 kg). Interestingly, the only 2-kg/ha treatments that were statistically greater than this were the two other Silwet L-77 treatments and the control. At 4 kg /ha, lowest standing crop was found with the Glyphos + Cosmo-Flux treatment, but none of the plots were statistically different from each other. Only Rodeo + LI-700 plots had fresh weights statistically different from the Glyphos + Cosmo-Flux at this rate.

TABLE 2
Symptom Scores (0–5) for Coca Plants 1 wk after Treatment with Different Glyphosate Formulations and Adjuvants and Three Rates of Glyphosate (SED = 0.11; df = 2041)

	Adjuvant		Glyphosate rate		
Glyphosate product	Name	Concentration (%v/v)	1 kg/ha	2 kg/ha	4 kg/ha
None	Water control	–	2.2	2.2	2.0
Glyphos	–	–	2.6	3.2	3.3
Glyphos	Cosmo-Flux	2.3	2.7	3.0	3.7
Glyphos	Intake	0.5	2.8	2.7	3.2
Glyphos	Mixture B	2	2.5	3.0	3.2
Glyphos	Silwet L-77	1	3.2	3.3	3.5
Roundup Biactive	–	–	2.7	3.1	2.8
Roundup Biactive	Silwet L-77	1	3.0	2.9	3.3
Roundup Biactive	LI-700	0.5	2.3	2.9	3.2
Roundup Biactive	Mixture B	2	3.1	3.1	3.3
Rodeo	Silwet L-77	1	2.9	3.0	3.1
Rodeo	LI-700	1	2.5	2.6	2.6

Overall LSD (p = .05) = 0.21.

TABLE 3
Symptom Scores (0–5) for Coca Plants 3 wk after Treatment with Different Glyphosate Formulations and Adjuvants and Three Rates of Glyphosate (SED = 0.12; df = 2041)

	Adjuvant		Glyphosate rate		
Glyphosate product	Name	Concentration (%v/v)	1 kg/ha	2 kg/ha	4 kg/ha
None	Water control	–	2.2	2.4	2.2
Glyphos	–	–	2.5	4.1	4.2
Glyphos	Cosmo-Flux	2.3	2.5	3.5	4.4
Glyphos	Intake	0.5	3.2	3.3	4.3
Glyphos	Mixture B	2	2.7	3.7	4.5
Glyphos	Silwet L-77	1	3.1	3.8	4.5
Roundup Biactive	–	–	3.1	3.8	4.1
Roundup Biactive	Silwet L-77	1	3.3	3.4	4.4
Roundup Biactive	LI-700	0.5	2.7	3.3	4.0
Roundup Biactive	Mixture B	2	3.2	3.7	4.3
Rodeo	Silwet L-77	1	2.8	3.2	3.9
Rodeo	LI-700	1	2.7	3.1	3.4

Overall LSD (p = .05) = 0.23.

Recovery

After all coca bushes had been cut, the plots were left to recover, with occasional watering. On 5 October 2007, the numbers of sprouts per bush showed that most glyphosate treatments gave good control, but these data (not shown) were rather variable (coefficient of variation >50%). Only the low rate of Glyphos + Mixture B was similar to untreated control plots. The Rodeo formulation was less active than other formulations tested. There were indications that at the 2- and 4-kg/ha rates of glyphosate, the Glyphos formulation was as efficacious alone, compared with mixtures with adjuvants. At 2 kg/ha, the best mixtures were Glyphos and Roundup Biactive with the adjuvants Silwet L-77 and Mixture B.

In terms of the numbers of surviving plants 9 wk after treatment, only half of the control plants were actively growing (Figure 2). In terms of survival, glyphosate activity was poor in the Rodeo formulation, relative to other treatments. The Glyphos formulation worked well at the 2- and 4-kg/ha rates. Roundup Biactive gave slightly higher survival overall, but at the 4-kg/ha rate, control was equivalent to the Glyphos formulation, across adjuvants. The standard eradication program treatment is Glyphos + Cosmo-Flux, so comparison with this is appropriate. Glyphos + Silwet L-77 performed the same as the Cosmo-Flux across doses. Roundup Biactive gave similar control at the two higher doses, when mixed with Silwet L-77 or Mixture B.

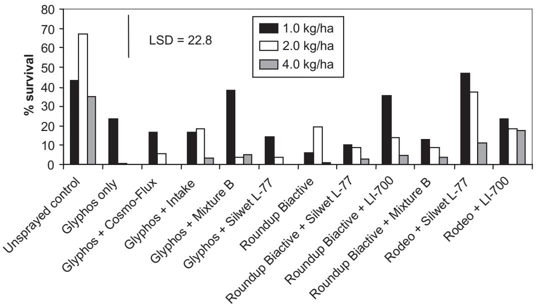

FIG. 2. Percentage survival of coca bushes after treatment with different glyphosate formulations and adjuvants and three rates of glyphosate. Data collected 9 wk after application and 6 wk after plants were cut to the ground.

DISCUSSION

In terms of treatment efficacy, there are a number of factors to consider. Outright plant kill, interpreted from the survival data, is one measure. However, speed of effect is another factor to consider. This may be evaluated from vigor at 1 and 3 wk after treatment and standing crop at 3 wk. The survival data (Figure 2) show that the unformulated Rodeo glyphosate did not work as well as the other two products. The standard eradication program treatment of Glyphos + Cosmo-Flux and Glyphos + Silwet L-77 yielded reliable control at 2- and 4-kg/ha rates. Equivalent control was also given by Roundup Biactive when mixed with Silwet L-77 or Mixture B at these rates. There were no great advantages in adding extra adjuvants to the standard Glyphos formulation. The adjuvant LI-700 was not particularly effective in enhancing glyphosate activity. These patterns were repeated in the numbers of sprouts per plant.

Assessments of plant vigor 1 wk after treatment indicated that the addition of Silwet L-77 to Glyphos and of Silwet L-77 and Mixture B to Roundup Biactive resulted in greater symptoms of herbicide damage to coca plants (Table 2) compared with other treatments. At spraying, the behavior of Silwet L-77 was noticeably different to other treatments. The spray mixture formed an even film over sprayed leaves, rather than a pattern of spreading droplets.

After 3 wk, scores were quantitatively higher (plant vigor was lower) on Glyphos + Silwet L-77 plots compared with Glyphos alone or the standard with Cosmo-Flux at the 4-kg/ha rate. The advantages of adding adjuvants to the formulated glyphosate products were marginal, in terms of the observed glyphosate activity at this stage. The weights of coca bushes 3 wk after application also indicated that the activity of glyphosate was modified only quantitatively by the addition of adjuvants to the formulated products (Table 4).

Extensive studies on the interactions between glyphosate and adjuvants were reported elsewhere (Collins & Helling, 2002). Addition of adjuvants might increase the toxicity of glyphosate to coca by a factor of 4, compared with unformulated glyphosate. Collins and Helling (2002) indicated best results with two glyphosate-surfactant systems, one being a mixture of crop-oil concentrate and the organosilicone Silwet L-77, and the other a mixture of cationic surfactant and anionic surfactants. Collins and Helling (2002) noted that the eradication program in Colombia was modified successfully in the light of their studies.

The results here indicate that the unformulated glyphosate (Rodeo), even with added adjuvants, did not yield adequate control of coca. In aiming for total control of coca, the rate of 4 kg/ha of glyphosate gave more consistent effects; total control was only recorded for Glyphos alone or with Cosmo-Flux or Silwet L-77. Nevertheless, 95% control might also be achieved by Roundup Biactive alone or mixed with Silwet L-77 or Mixture B. In terms of herbicide efficacy, the results indicate that the advantages of adding alternative adjuvants to the two formulated glyphosate products are not significant. Indeed, there appeared to be little advantage in adding Cosmo-Flux to the Glyphos product in this study. This may reflect the conservative results of this trial with higher volume spray rates, compared with the work of Collins and Helling (2002). However, in terms of reducing environmental risk from the aerial eradication program, the results provide useful data.

There needs to be careful evaluation of the relative environmental risks posed by the different components of the glyphosate formulations and the added adjuvants in the aerial eradication program. If the greatest risk is presented by Cosmo-Flux, then alternatives for mixing with Glyphos that may go for further testing are Silwet L-77 and Mixture B. If there are risks associated with formulated Glyphos, then Roundup Biactive gives similar levels of control, either alone or in mixture with Silwet L-77 or Mixture B. This product is sold in Europe by Monsanto Europe S.A., where it is also cleared for use on floating and emerged aquatic weeds (Monsanto Europe, 2007).

Although the results of our research are informative, they represent only a single trial, in one year, at one site. Further, the treatments were applied using relatively precise experimental ground-spraying equipment. The results provide indications of where further development work can be directed, but extrapolation to aerial application conditions would be premature. Herbicide behavior can change with volume rate; studies comparing glyphosate applications at 23, 47, 94, or 190 L/ha

TABLE 4

Fresh Weight (kg) of 20 Coca Bushes Treated with Different Formulations of Glyphosate and Adjuvants and Three Rates of Glyphosate, for Plants Harvested on 22 August 2007, 3 wk after Treatment (SED = 0.44; df = 64)

	Adjuvant		Glyphosate rate		
Glyphosate product	Name	Concentration (%v/v)	1 kg/ha	2 kg/ha	4 kg/ha
None	Water control	–	3.84	3.63	3.99
Glyphos	–	–	3.64	1.84	1.68
Glyphos	Cosmo-Flux	2.3	3.12	1.83	1.20
Glyphos	Intake	0.5	2.38	2.15	1.48
Glyphos	Mixture B	2	3.02	1.62	1.38
Glyphos	Silwet L-77	1	3.02	1.62	1.48
Roundup Biactive	–	–	2.59	1.74	1.66
Roundup Biactive	Silwet L-77	1	2.59	2.48	1.59
Roundup Biactive	LI-700	0.5	3.27	1.96	1.21
Roundup Biactive	Mixture B	2	2.24	1.89	1.55
Rodeo	Silwet L-77	1	2.81	2.76	1.65
Rodeo	LI-700	1	3.47	2.25	2.23

Overall LSD ($p = .05$) = 0.874.

showed best control of grasses at low volumes (Ramsdale et al., 2003). Low volumes apparently maximize glyphosate efficacy, mainly via high herbicide concentration in the spray deposit. Higher coca control might therefore be expected at volume rates typical of aerial application and the differences between adjuvants may be enhanced. Only one variety of coca was grown and tested; other varieties might be more or less susceptible to the tested formulations.

Based on this single field trial, there appears to be some scope for reducing the rate of glyphosate in the aerial eradication program from the current 3.69 kg/ha. Further testing would be required to evaluate this point and to evaluate any other changes to the current eradication treatment. Such tests would comprise field evaluations in different locations and with different coca varieties, followed by aerial application experiments. The behavior of the adjuvant mixtures when applied through raindrop nozzles may be different from that from ground application machinery, so further testing would be essential.

Conclusions and Recommendations

- Addition of the adjuvants Silwet L-77 or LI-700 to unformulated glyphosate (Rodeo) was not sufficient to give acceptable control of coca.
- Roundup Biactive would be a suitable formulation of glyphosate to use, if the Colombian Glyphos were to be replaced.
- Should Cosmo-Flux need to be replaced, then the adjuvants Silwet L-77 and Mixture B might provide suitable replacements.

The current aerial eradication treatments are working well in the field. Before any recommendations to change the spray mixture are made, there needs to be at least a two-stage process that (a) evaluates the components that drive the key risks within the current formulation, followed by (b) setting up suitable field trials of alternatives applied from the air.

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Annex 131-D

R.A. Brain et al., "Comparison of the Hazards Posed to Amphibians by the Glyphosate Spray Control Program Versus the Chemical and Physical Activities of Coca Production in Colombia"

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Comparison of the Hazards Posed to Amphibians by the Glyphosate Spray Control Program Versus the Chemical and Physical Activities of Coca Production in Colombia

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This study evaluates the cumulative multifactorial physical and chemical impacts resulting from coca production on amphibian populations in comparison with the potential impacts produced by the herbicide glyphosate (Glyphos), which, mixed with the surfactant Cosmo-Flux, is used in the spray control program for illicit crops in Colombia. Using similar worst-case assumptions for exposure, several other pesticides used for coca production, including mancozeb, lambda cyhalothrin, endosulfan, diazinon, malathion, and chlorpyrifos, were up to 10- to 100-fold more toxic to frogs than the Glyphos–Cosmo-Flux mixture. Comparing hazard quotients based on application rates, several of these compounds demonstrated hazards 3–383 times that of formulated glyphosate. Secondary effects, particularly of insecticides, are also a concern, as these agents selectively target the primary food source of amphibians, which may indirectly impact growth and development. Although the potential chemical impacts by other pesticides are considerable, physical activities associated with coca production, particularly deforestation of primary forests for new coca plots, portend the greatest hazard to amphibian populations. The entire production cycle of cocaine has been linked to ecosystem degradation. The clearing of pristine forests for coca propagation in Colombia is well documented, and some of these regions coincide with those that contain exceptional amphibian biodiversity. This is particularly problematic as coca production encroaches more deeply into more remote areas of tropical rain forest. Transportation of disease, including the chitrid fungus, to these remote regions via human intrusion may also adversely affect amphibian populations. Therefore, the cumulative impacts of coca production, through habitat destruction, application of agrochemicals, and potential transmission of disease, are judged to pose greater risks to amphibian populations in coca-growing regions than the glyphosate spray control program.

Coca production is a national security issue in Colombia that has motivated extensive enforcement measures. Currently the herbicide glyphosate is used to control coca (*Erythroxyum coca*) production through a spray eradication program facilitated by the Antinarcoticos Directorate of the Colombian National Police (DIRAN-CNP). The effort is further supported through data gathering by other nations in both North America and Europe (Solomon et al., 2007). Several concerns have been raised regarding the spray control program, ranging from peripheral crop damage to adverse environmental and human health effects. The government of Colombia has responded by appointing an independent environmental auditor to review the program (Solomon et al., 2007). In conjunction with DIRAN-CNP the spray and no-spray areas are reviewed, and spray results through field checks and data analysis are regularly monitored. Additionally, three detailed reviews on the substances used for cocaine production have been conducted for the Inter-American Drug Abuse Control Commission (CICAD) section of the Organization of American States (OAS) (Solomon et al., 2007). Of particular concern, and identified through this review, is the potential toxicity of several formulations of glyphosate to amphibians.

In order to appropriately assess the potential adverse effects of glyphosate on frogs and other amphibians, hazards need be evaluated in the context of the effects of other pesticides and activities associated with the production of coca on these organisms. Several other pesticides and substances are used in the production of coca, and many of these are hazardous to aquatic organisms if the products are applied over water at the recommended field application

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rates (CICAD/OAS, 2005). This assessment specifically considers hazards presented by these other pesticides to the aquatic stages of amphibians and on their indirect effects on the food organisms used by adult amphibians. In addition, the destructive physical activities associated with coca production are considered. The effects of habitat alteration on amphibian populations are well documented (Becker et al., 2007), and the clear-cutting and burning of tropical forests, such as occur when new coca fields are established, exert profound adverse effects on these organisms, both directly and indirectly (Hedges, 1993; Viña et al., 2004). Since habitat alteration is considered to be the greatest factor responsible for global amphibian declines (Hedges, 1993), the extensive loss of tropical rain forest in Colombia due to coca production is of paramount concern, since these areas of deforestation typically coincide with or are close to areas containing exceptional amphibian biodiversity (Myers et al., 2000; Etter et al., 2006). Other human activities may also contribute to adverse effects on frogs. Diseases have been associated with several frog extinctions, and the potential adverse effects of a newly identified fungal disease of frogs, chytridiomycosis, are also considered. This virulent disease is easily spread by human activity and may be carried into new areas of coca production. Since this disease has caused the extinction of several species of frogs (Berger et al., 1998; Speare, 2001), its presence and spread within Colombia may have serious implications for amphibians that will be exacerbated by expansion of coca production into new undeveloped areas.

DIRECT EFFECTS OF OTHER PESTICIDES USED IN COCA PRODUCTION ON AMPHIBIANS

Several pesticides are used in the production of coca in Colombia (CICAD/OAS, 2005). To assess hazards to amphibians, the ECOTOX database (U.S. EPA, 2001) and primary and secondary literature were extensively searched to obtain comprehensive and comparable data on the toxicity of these pesticides to aquatic stages of amphibians. Mortality values were the primary data compiled for the purposes of comparison, where common acute mortality data was available for the vast majority of pesticides considered (Table 1). Data for a single species were selected for inclusion based on exposure time. For example, toxicity data from 96-h exposures were selected over 48 h, etc. When multiple values were reported, the smallest value (most toxic) was selected. In cases where multiple values were reported for a given exposure time, a geometric mean was calculated. Hazard quotients (HQs) were calculated for multiple amphibian species for each pesticide according to the following equation: HQ = PEC/LC50, where PEC is the predicted environmental concentration and LC50 is the median lethal concentration. Values >1 indicate potential hazard. Due to an absence of measured exposure data, PECs were calculated assuming worst-case circumstance; direct overspray of surface water (15 cm deep) with rapid mixing, no absorption to sediments, and no flow. A depth of 15 cm was used based on assumptions of forest pools in Canada, and similar assumptions made by the U.S. EPA regarding wetlands (Urban & Cook, 1986). These data were compared to the toxicity of formulated glyphosate (mostly Roundup and Vision) and the Glyphos–Cosmo-Flux mixture as used in Colombia (CICAD/OAS, 2006). The toxicity data are summarized in Figure 1 and Table 1, comparatively illustrating the toxicity data with associated margins of safety (MOS) and outlining HQs, respectively. A number of additional endpoints were reported in the literature. However, because many of these endpoints are nonstandardized, they were not included in the hazard assessment.

Several of the pesticides used in the production of coca are inherently as toxic as or more toxic to amphibians than the Glyphos–Cosmo-Flux® mixture used in Colombia (Table 1.). Both mancozeb and lambda cyhalothrin were inherently more toxic than formulated glyphosate. Endosulfan, diazinon, malathion, and chlorpyrifos were 10- to 100-fold more toxic to frogs than the Glyphos–Cosmo-Flux mixture. The toxicity of endosulfan is particularly relevant because of the detection of endosulfan in surface waters from coca-growing regions in Colombia where it is being used illegally (Solomon et al., 2007). Endosulfan is not registered for use in Colombia.

Comparison of the worst-case exposure that would result from overspray of surface waters 15 cm deep at a typical rate of application (CICAD/OAS, 2006) (Figure 1) shows that concentrations in surface waters in, or adjoining, coca fields are predicted to be greater than the LC50 concentrations for mancozeb, diazinon, endosulfan, chlorpyrifos, and malathion. Comparing HQ values based on application rates, these compounds presented 3.2-, 4.3-, 251-, 271-, and 383-fold higher maximum hazard than formulated glyphosate. Lambda cyhalothrin and paraquat also demonstrated hazard under these worst-case circumstances. This suggests that these particular pesticides may exert adverse direct effects on amphibians through their use in the protection of coca from pest infestations. Reports from the literature provide support for the possible adverse effects of these insecticides on frogs. For example, analysis of historical pesticide application data has linked organophosphorus (OP) and carbamate insecticides with the declines of four Californian amphibians (Davidson, 2004). Toxicity values for amphibians were not available in the literature for several of the other pesticides used in coca production, such as monocrotophos. These may also present direct hazards to amphibians in or close to coca fields but can not be assessed in the absence of data. Several other pesticides used in coca production were less toxic to amphibians and present a smaller hazard (Figure 1 and Table 1). These included

TABLE 1
Toxicity Data and Hazard Auotients (HQs) for Amphibians Exposed to Various Pesticides

Common name	Scientific name	Life stage	Exposure time (h)	Concentration (µg/L)	Exposure ytype	Reference	PEC (µg/L)	HQ
Glyphosate formulated[a]								
American toad	*Bufo americanus*	Larvae	96	1700	Renewal	(Edginton et al., 2004)	2473	1.5
Sign-bearing froglet	*Crinia insignifera*	Tadpole	48	3600	Renewal	(Mann and Bidwell, 1999)	2473	0.7
Moaning frog	*Heleioporus eyrei*	Tadpole	48	6300	Renewal	(Mann and Bidwell, 1999)	2473	0.4
Western green tree frog	*Litoria moorei*	Tadpole	48	2487	Renewal	(Mann and Bidwell, 1999)	2473	1.0
Pobble-bonk frog	*Lymnodynastes dorsalis*	Tadpole	48	2548	Renewal	(Mann and Bidwell, 1999)	2473	1.0
Bull frog	*Rana catesbeiana*	?	24	2072	Static	(Clements et al., 1997)	2473	1.2
Green frog	*Rana clamitans*	Larvae	96	1400	Renewal	(Edginton et al., 2004)	2473	1.8
Leopard frog	*Rana pipiens*	Larvae	96	1100	Renewal	(Edginton et al., 2004)	2473	2.2
Wood frog	*Rana sylvatica*	Gosner 25	96	5100	Static	(Howe et al., 2004)	2473	0.5
African clawed frog	*Xenopus laevis*	Larvae	96	670	Renewal	(Edginton et al., 2004)	2473	3.7
Snouted treefrog	*Scinax nasicus*	?	96	815	Renewal	(Lajmanovich et al., 2003)	2473	3.0
2,4-D								
Common Indian toad	*Bufo melanostictus*	Larvae	96	8050	Static	(Vardia et al., 1984)	1541	0.2
Frog	*Pseudacris triseriata*	Tadpole	96	100,000	Static	(Johnson, 1976)	1541	0.02
Frog	*Adelotus brevis*	Tadpole	96	200,000	Static	(Johnson, 1976)	1541	0.008
Frog	*Limnodynastes peroni*	Tadpole	96	287,000	Static	(Johnson, 1976)	1541	0.005
Cane toad	*Bufo marinus*	Tadpole	96	288,000	Static	(Johnson, 1976)	1541	0.005
Atrazine								
American toad	*Bufo americanus*	Larvae	96	10,700	Renewal	(Howe et al., 1998)	871	0.08
Leopard frog	*Rana pipiens*	Larvae	96	14,500	Renewal	(Howe et al., 1998)	871	0.06
Carbendazim								
Toad	*Bufo bufo japonicus*	Tadpole	96	3500	Static	(Nishiuchi and Yoshida, 1974)	402	0.1
Frog	*Rana hexadactyla*	Tadpole	96	16,020	Renewal	(Khangarot et al., 1985)	402	0.03
Bog frog	*Rana limnocharis*	Tadpole	48	173,786	NR	(Pan and Liang, 1993)	402	0.002
Carbofuran								
Bog frog	*Rana limnocharis*	Tadpole	48	11,226	NR	(Pan and Liang, 1993)	670	0.06
Frog	*Microhyla ornata*	Tadpole	96	13,470	Renewal	(Pawar and Matdare, 1984)	670	0.05
Frog	*Rana hexadactyla*	Tadpole	96	112,700	Renewal	(Khangarot et al., 1985)	670	0.006

(*Continued*)

TABLE 1
(*Continued*)

Common name	Scientific name	Life stage	Exposure time (h)	Concentration (µg/L)	Exposure ytype	Reference	PEC (µg/L)	HQ
Carbaryl								
African clawed frog	*Xenopus laevis*	Tadpoles	96	1730	Static	(Zaga et al., 1998)	1340	0.8
Gray tree frog	*Hyla versicolor*	Tadpoles	96	2470	Static	(Zaga et al., 1998)	1340	0.5
Tiger Frog	*Rana tigrina*	Tadpole	96	6200	Static	(Marian et al., 1983)	1340	0.2
Toad	*Bufo bufo japonicus*	Tadpole	48	7200	Static	(Hashimoto and Nishiuchi, 1981)	1340	0.2
Green frog	*Rana clamitans*	Tadpole	96	11,320	Static	(Boone and Bridges, 1999)	1340	0.1
Tiger Frog	*Rana tigrina*	Tadpole	96	11,700	Static	(Marian et al., 1983)	1340	0.1
Frog	*Rana hexadactyla*	Tadpole	96	55,340	Renewal	(Khangarot et al., 1985)	1340	0.02
Chlorpyrifos								
American Toad	*Bufo americanus*	Tadpole	96	1	NR	(Cowman and Mazanti, 2000)	1005	1005
Marbled salamander	*Ambystoma opacum*	Tadpole	NR	325	NR	(Sheffield, 2000)	1005	3.1
African clawed frog	*Xenopus laevis*	Tadpole	NR	390	NR	(Sheffield, 2000)	1005	2.6
Grey tree frog	*Hyla chrysoscelis*	Tadpole	NR	760	NR	(Sheffield, 2000)	1005	1.3
Southern leopard frog	*Rana utricularia*	Tadpole	NR	1000	NR	(Sheffield, 2000)	1005	1.0
Bog frog	*Rana limnocharis*	Tadpole	48	2401	NR	(Pan and Liang, 1993)	1005	0.4
Leopard frog	*Rana pipiens*	Tadpole	96	3000	NR	(Cowman and Mazanti, 2000)	1005	0.3
cis-Cypermethrin[b]								
Leopard frog	*Rana pipiens*	Frog	24	0.16 (µg/g)	Subcutaneous injection	(Cole and Casida, 1983)	—	—
Leopard frog	*Rana pipiens*	Tadpole	24	0.04 (µg/g)	Subcutaneous injection	(Cole and Casida, 1983)	—	—
trans-Cypermethrin[b]								
Leopard frog	*Rana pipiens*	Tadpole	24	0.2 (µg/g)	Subcutaneous injection	(Cole and Casida, 1983)	—	—
Leopard frog	*Rana pipiens*	Frog	24	0.65 (µg/g)	Subcutaneous injection	(Cole and Casida, 1983)	—	—
Diazinon								
Green frog	*Rana clamitans*	Embryos - Tadpoles	96	25	Renewal	(Harris et al., 1998)	402	16
Bog frog	*Rana limnocharis*	Tadpole	48	4477	NR	(Pan and Liang, 1993)	402	0.09
Toad	*Bufo bufo japonicus*	Tadpole	48	14,000	Static	(Hashimoto and Nishiuchi, 1981)	402	0.03
Endosulfan								
Indian bullfrog	*Rana tigrina*	Tadpole	96	1.8	NR	(U.S. EPA, 2001)	1675	931
Bog frog	*Rana limnocharis*	Tadpole	48	12	NR	(U.S. EPA, 2001)	1675	140
Common Indian toad	*Bufo melanostictus*	Tadpole	96	123	NR	(U.S. EPA, 2001)	1675	14

Toad	*Bufo vulgaris formosus*	Tadpole	24	1946	NR	(U.S. EPA, 2001)	1675	0.9
Green frog	*Rana clamitans*	Tadpole	96	7431	NR	(U.S. EPA, 2001)	1675	0.2
Toad	*Bufo bufo japonicus*	Tadpole	48	9000	Static	(Hashimoto and Nishiuchi, 1981)	1675	0.2
lambda-Cyhalothrin								
African clawed frog	*Xenopus laevis*	Tadpoles	168	4	Renewal	(Aydin et al., 2005)	13.4	3.4
Malathion								
Frog	*Rana hexadactyla*	Tadpole	96	0.59	Renewal	(Khangarot et al., 1985)	838	1420
Striped, Northern chorus frog	*Pseudacris triseriata*	Tadpole	96	200	Static	(U.S. EPA, 2001)	838	4.2
Western chorus frog	*Pseudacris triseriata triseria*	Tadpole	96	200	Static	(Sanders, 1970)	838	4.2
Fowler's toad	*Bufo woodhousei fowleri*	Tadpole	96	420	Static	(Mayer and Ellersieck, 1986)	838	2.0
Bog frog	*Rana limnocharis*	Tadpole	48	2271	NR	(Pan and Liang, 1993)	838	0.4
Toad	*Bufo arenarum*	Larvae	NR	19,200	Renewal	(Venturino et al., 1992)	838	0.04
Mancozeb								
Leopard frog	*Rana pipiens*	Embryos	96	200	Renewal	(Harris et al., 2000)	2412	12
American toad	*Bufo americanus*	Embryos	96	1400	Renewal	(Harris et al., 2000)	2412	1.7
Methomyl								
Toad	*Bufo vulgaris formosus*	NR	24	23,000	NR	(Nishiuchi, 1980b)	670	0.03
Bog frog	*Rana limnocharis*	Tadpole	48	27,161	NR	(U.S. EPA, 2001)	670	0.02
Toad	*Bufo bufo japonicus*	Tadpole	48	40,000	Static	(Hashimoto and Nishiuchi, 1981)	670	0.02
Methyl parathion								
Striped, Northern chorus frog	*Pseudacris triseriata*	Tadpole	96	3700	Static	(Mayer and Ellersieck, 1986)	670	0.2
Tiger frog, indian bullfrog	*Rana tigrina*	Tadpole	96	9500	Static	(Alam and Shafi, 1991)	670	0.07
Bog frog	*Rana limnocharis*	Tadpole	48	11,482	NR	(Pan and Liang, 1993)	670	0.06
Paraquat								
Leopard frog	*Rana pipiens*	Embryo	96	500	Renewal	(Linder et al., 1990)	670	1.3
Toad	*Bufo bufo japonicus*	NR	24	2500	Static	(Nishiuchi, 1980a)	670	0.3
Clawed toad	*Xenopus laevis*	Embryo	96	8100	Renewal	(Linder et al., 1990)	670	0.08
Fowler's toad	*Bufo woodhousei fowleri*	Tadpole	96	15,000	Static	(Mayer and Ellersieck, 1986)	670	0.04
Frog	*Scinax nasica*	Tadpole	96	21,990	Renewal	(Lajmanovich et al., 1998)	670	0.03
Striped, Northern chorus frog	*Pseudacris triseriata*	Tadpole	96	28,000	Static	(Mayer and Ellersieck, 1986)	670	0.02
Western chorus frog	*Pseudacris triseriata triseria*	Tadpole	96	28,000	Static	(Sanders, 1970)	670	0.02
Brown Striped Marsh Frog	*Limnodynastes peroni*	Tadpole	96	100,000	Static	(Johnson 1976)	670	0.007
Tusked frog	*Adelotus brevis*	Tadpole	96	262,000	Static	(Johnson 1976)	670	0.003

Note. Data represent LC50 (median lethal concentration) values. Only the smallest values (greatest toxicity) are reported. Hazard quotients were calculated as the ratio of the predicted environmental concentration (PEC) and the LC50, where values >1 indicate potential hazard.

[a]All concentrations of formulated glyphosate are expressed as acid equivalent (AE).

[b]Data reported as the LD_{50} in µg/g.

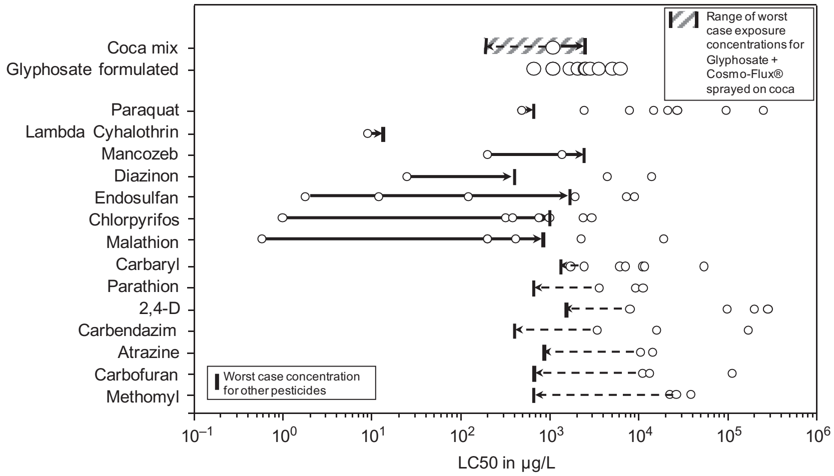

FIG. 1. Toxicity to amphibians of Glyphos and Cosmo-Flux spray mixture, formulated glyphosate (mostly Roundup and Vision), and other pesticides used in the production of coca. The data for the mixture of Glyphos and Cosmo-Flux (coca mix) are from tests on *Xenopus laevis*. Each point on the graph represents a different species of amphibian. Glyphosate data are all normalized to acid equivalents (a.e.); other data are given as active ingredient (AI). Horizontal dashed arrows pointing to the left indicate margins of safety between LC50 concentrations for *X. laevis* (Glyphos plus Cosmo-Flux) or the most sensitive species (other products) and estimated exposure; solid arrows pointing to the right indicate a hazard.

2,4-D, atrazine, carbaryl, carbendazim, carbofuran, methomyl, and parathion.

Davidson (2004) found a strong association between upwind pesticide use and amphibian declines in montane areas of California, which was consistent across a number of different species representing at least three independent ranges. For four ranid frogs, pesticides were the single strongest explanatory variable in model simulations and the relationship between declines and upwind pesticide use was consistent (Davidson, 2004). In the analysis of pesticide classes, acetylcholinesterase (AChE)-inhibiting pesticides emerged as most strongly associated with declines (Davidson, 2004). Reduced AChE levels were found in the non-declining Pacific tree frog (*Hyla regilla*) in the Sierra Nevada (downwind from California's heavily agricultural Central Valley) compared with the Coast Range (low pesticide exposure), suggesting that lower AChE levels in Sierra Nevada treefrogs may be due to exposure AChE-inhibiting pesticides (Sparling et al., 2001).

Lips (1998) conducted surveys of amphibian fauna at Las Tablas, Puntarenas Province, Costa Rica from 1991 to 1996 and found declining trends or "atypical" fluctuations in frog and salamander populations, where species with both aquatic eggs and larvae were most affected. Environmental contamination was suggested as a primary factor associated with these declines, particularly agrochemicals, some of which have been banned in the United States and Europe but are still in widespread use throughout developing countries of the tropics (Lips, 1998). Lips (1998) noted unusual female-biased sex ratios in *Atelopus chiriquiensis* and *Hyla calypsa* frog populations in 1996, where, incidentally, of the three common chemicals sprayed on the apple orchards at Las Tablas, two (mancozeb and benomyl) are suspected of having reproductive and endocrine-disrupting effects. Different species likely exhibit different symptoms and susceptibility upon exposure to a variety of pesticides, since these parameters vary markedly in amphibians (Berrill et al., 1994).

INDIRECT EFFECTS OF OTHER PESTICIDES

Many of the pesticides used in the production of coca are insecticides (CICAD/OAS, 2004, 2005). Use of these insecticides to protect coca from insect damage may inadvertently kill insects that are also food items for adult frogs that utilize the coca fields and their margins as habitat. Thus, while some of the insecticides exert little direct toxicity to the frogs (Figure 1), they may have adverse effects through reducing the availability of food. However, the indirect effects of food supply on amphibian population abundance, produced by pesticides, are poorly studied. Westerman et al. (2003) classify reduced or altered food supply as a biological stressor, defined as a reduction or change of food supply, such as reduction of insects due to pesticide application or reduction of algae due to aquatic herbicide application. Elimination of food base is considered to be a primary affect of herbicides and insecticides by Henry (2000), though no examples are provided. A small number of studies document impacts of pesticides on larval stages (Boone & Semlitsch, 2001) through indirect modification of food sources; however, there is virtually no information available with respect to the effects of pesticides on food sources for adult frogs, i.e., insects. Considering the biological target of insecticides comprises the primary diet of amphibians, particularly frogs, the lack of food-web cascade data with respect to insecticides is of concern. Indirect effects were demonstrated for the insecticide carbaryl and the herbicide atrazine on body mass, development, and survival of two anuran species (southern leopard frog, *Rana sphenocephala*; American toad, *Bufo americanus*) and two caudate species (spotted salamander, *Ambystoma maculatum*; small-mouthed salamander, *A. texanum*) reared in outdoor cattle tank mesocosms (Boone & Semlitsch, 2001). After treatment with carbaryl, zooplankton were eliminated, which likely resulted in the negative impacts found on growth and development for the spotted salamanders. If zooplankton populations are reduced or eliminated, exposure to insecticides might lead to reproductive failure and subsequent population declines for carnivorous amphibian species (Boone & Semlitsch, 2001).

TRENDS IN AMPHIBIAN DECLINES

During the late 1980s, ecologist Norman Myers established the term "biodiversity hotspots" to distinguish a global set of high-priority terrestrial ecoregions for conservation (Myers, 1988). This approach identifies an ecoregion as a "hotspot" based on the existence of exceptional concentrations of endemic species and experiencing exceptional loss of habitat (Myers, 1988). The lower montane cloud forests (at elevations of about 1300 to 2000 m) of the eastern Andes are considered a biodiversity hot spot and amongst the most threatened habitats on earth (Myers, 1988). In terms of species richness, the tropical Andes are considered to have the greatest biodiversity of total species, particularly amphibians, with 604 species of known endemic amphibians, nearly 13% of the global total (Myers, 1988). Colombia is situated in one of the world's biodiversity hotspots, containing 10% of the world's biodiversity (CICAD/OAS, 2004) and about 750 species of amphibians, half of which are endemic (J. Lynch, personal communication). Therefore, the contribution of this region to the earth's total biodiversity is substantial, but at the same time is under considerable stress due to significant anthropogenic influences, including coca production.

According to Stuart et al. (2004), 43% of global amphibian species are experiencing some form of population decline, 32.5% are threatened, 122 species are possibly extinct, and most losses have occurred since the 1980s. Declines were suggested as nonrandom in terms of ecological preferences, geographic ranges, and taxonomic associations, which are most prevalent among Neotropical montane, stream-associated species (Stuart et al., 2004). Of the 435 species listed by the World Conservation Union (IUCN) categorized as being under higher threat (rapidly declining) than in 1980, declines of 50 species are attributed to overexploitation, 183 to reduced habitat (suffering significant habitat loss), and 207 to enigmatic decline (declining, even where suitable habitat remains) for reasons that are not fully understood, although disease and climate change are commonly cited causes (Stuart et al., 2004). Surveys conducted by the Research and Analysis Network for Neotropical Amphibians (RANA) suggest that intact amphibian communities no longer exist throughout most upland (>500 m) areas of the Neotropics (Lips et al., 2005). In Latin America, 107 species of amphibian are identified as in decline, largely since the 1980s, though trends continue (Lips et al., 2005). Many extinctions and declines have taken place in seemingly pristine and often montane areas (Pounds & Crump, 1994; Pounds et al., 1997; Young et al., 2001).

EFFECTS OF DEFORESTATION FOR COCA PRODUCTION ON AMPHIBIANS

Land use change often occurs in temporal waves and in localized fronts termed "deforestation hotspots" by Myers (1993) that respond to the pulses of change in land use drivers (Etter et al., 2006). Of high concern for conservation planning is the potential for these "deforestation hotspots" to overlap "biodiversity hotspots" (Myers et al., 2000; Etter et al., 2006). The driving forces of land cover change, especially deforestation, are reported to result from the complex interaction of socio-political and economic processes (Etter et al., 2006). From the late 1980s, three main forces have driven the colonization process in Colombia: landlessness, illicit crops (largly coca), and the presence of rebel armies (Etter et al., 2006).

Deforestation and Amphibians

Habitat destruction is considered to be the single major factor responsible for the decline of the earth's amphibians and other organisms (Hedges, 1993). Deforestation (1) exposes terrestrial amphibians to severely altered microclimatic regimes, soil compaction and desiccation, (2) reduces habitat complexity, and (3) increases the amount of habitat edge, all of which decrease available moisture and elevate extreme temperatures, solar radiation, and wind disturbance compared to forest interiors (Alford & Richards, 1999; Boone et al., 2003). Because many amphibians spend all or the majority of their life in terrestrial habitats, the outcome of these changes may be the elimination of some species, alterations in abundance, or reduced individual quality of habitat (Hedges, 1993). In addition, aquatic stages of amphibians are exposed to stream environments with increased siltation and reduced woody debris (Alford & Richards, 1999). Although populations may recover as regenerating forests mature, recovery to predisturbance levels can take many years and may not occur at all if mixed forests are replaced with monocultures (Alford & Richards, 1999). Hedges (1993) indicated that approximately 65% of tropical forest was destroyed, with a likely proportional decline in the number of individuals of forest-associated amphibians. Thus far, native species survival has largely been unaffected, which, unlike the decline in individuals, is not expected to be a linear function of the decline in forest cover (Hedges, 1993). Therefore, the number of extant species may not show significant decline until forest cover levels become small, at which time extinctions may occur (Hedges, 1993). Some extinctions will occur prior to that point due to unequal rates of deforestation in different areas and stochastic effects, while those species that survive without forest cover continue to exist (Hedges, 1993). The sensitivity of forest-dwelling amphibians to changes in their environment makes them valuable indicators of forest degradation (Bishop et al., 2003).

When considering coca production as the driver, depletion of forest cover to the point of extinction in largely inaccessible montane environments may be argued as unlikely. This contention maintains that suitable habitat for refugia may be expected to remain as forest destruction does not likely occur across a broad spatial area greater than the home or migratory range potential of the species in question. However, on average, thousands of square kilometers of forest are destroyed in the montane forest regions of Colombia each year (UNODC, 2006), which are dominated by species with small ranges: only tens to hundreds of square kilometers (NatureServe, 2004). The Amazonian foothills in the Caquetá and Putumayo Departments of Columbia are reported to contain high species richness and levels of endemism; however, the average annual rate of clearing for Caquetá during 1989–2002 was 25,000 hectare (ha), with a peak of 41,000 ha during 1996–1999 (Etter et al., 2006). Furthermore, although tropical rain forests are resilient, where certain aspects can be reestablished within 65 yr, the time required to reach endemism levels is between 1000 and 4000 yr (Liebsch et al., 2008). Thus, given the regional specificity of coca production, certain areas of intense cultivation such as in the Colombian Departments of Nariño and Putumayo (UNODC, 2006) may experience deforestation levels commensurate with influencing species eradication. This prospect is enhanced when disease transmission and chemical stress associated with coca production are considered in conjunction with physical stress of altered habitat.

In Hispaniola, several species of frogs associated with streams appear to be reduced in numbers from previous years as these riparian habitats were highly altered by deforestation (Hedges, 1993). The removal of forest results in frequent flooding with intervening dry periods, and clogging of stream beds with mud and debris (Hedges, 1993). It is likely that deforestation affected these stream-associated anurans more than other species (Hedges, 1993). This may be a key aspect of potential deleterious effects in montane forests of Colombia, as the localized effect (deforestation) extends to a potentially greater area of critical habitat for stream-dependent amphibians, particularly if key requirements are for controlled low-level flow and relatively sediment-free water (e.g., to prevent washout or siltation of egg masses). In Jamaica, four species (*Eleutherodactylus cavernicola, E. fuscus, E. junori, and E. sisyphodemus*) are restricted in distribution and have not been found commonly within their - limited ranges, largely due to deforestation and human encroachment in those areas, combined with the specialized habitat requirements of the species (Hedges, 1993).

In Guatemala, there are an estimated 74 threatened species of amphibians, which are considered to be primarily impacted by the effects of deforestation (NatureServe, 2004). In Brazil, habitat loss is the most visible, and probably the main threat to amphibians (Silvano & Segalla, 2005; Becker et al., 2007). Deforestation, the advance of the agricultural frontier, mining, wildfires, and development projects are the main causes of habitat loss. Although varying in extent, all Brazilian biomes are now severely affected, especially the Atlantic Forest, where fragmented forest remnants constitute the 8% that currently remains (Silvano & Segalla 2005).

Development of agriculture and other activities can be controlled and restricted to areas that are not key amphibian habitat. In contrast, it is clear that the uncontrolled deforestation for the production of illicit crops such as coca will have a major effect on amphibians in Colombia through habitat alteration.

Deforestation and Armed Conflict

The annual net deforestation rate in Colombia peaked from 1996 to 1999 at approximately 40,400 ha, which increased from 18,600 ha during 1989–1996 (Etter et al., 2006). However, the rate declined more recently to 23,830 ha from 1999 to 2002 (Etter et al., 2006). Temporally, the decline in deforestation from 1999 to 2002 was largely attributed to peace talks with guerrillas that took place in the Caquetá Department where part of this area was demilitarized (Etter et al., 2006). The period of peak deforestation coincides with the period when the illegal economy of narcotics was booming in the region (UNODC, 2004). Although deforestation rates have slowed on average throughout Caquetá, the municipalities of Macareña and San Vicente del Caguán accounted for 80% of the regional clearing in 1999–2002 (Etter et al., 2006). During this time, government claims suggest that these municipalities were being used by rebel groups for illegal economic activities during the peace process (Etter et al., 2006). Although it has been debated as to what effects the Colombian armed conflict has on the deforestation processes (Dávalos, 2001), recent analyses showed that increased deforestation during the period from 1996–1999 was correlated with high guerrilla activity and low government presence (Etter et al., 2006). The magnitude of the forest resources threatened by the conflict between local authorities and paramilitary groups in Columbia is significant. About 33% of the remaining forests are in municipalities with medium to high activity by armed groups, and 20% of them are in municipalities where both guerrillas and paramilitaries are present (Álvarez, 2001, 2003). The environmental effects of these contests for land have been identified as a major factor in forest degradation (Cavelier & Etter, 1995; Henkel, 1995; Young, 1996; Álvarez, 2006). Etter et al. (2006) suggested that the presence of guerilla armies poses a major obstacle to managing deforestation in a planned manner, and prohibited any form of conservation planning and management.

Coca Production and Deforestation

The degradation of ecosystems associated with the production of coca and its processing into cocaine paste and then into cocaine hydrochloride constitutes one of Latin America's most important current environmental issues (Armstead, 1992; Viña et al., 2004). The entire production cycle of cocaine has been linked to ecosystem degradation, and particularly to tropical deforestation (Balslev, 1993; Viña et al., 2004). In Colombia the most obvious environmental effect of coca cultivation is the clearing of forests (UNODC, 2006). The tropical rain forests constitute the largest biome in Colombia, though over 11 of the original 44 million hectares have been lost. The Sub-Andean and Andean forests have lost 69 to 76% of their original cover, and though these areas are the most densely populated parts of the country, they are also favored areas for the production of coca (UNODC, 2006).

Although coca cultivation is only one factor in deforestation, the land area affected is significant. Estimates vary considerably regarding the total area of primary forest loss due to this activity, however. The most reliable data are provided from satellite imagery (UNODC, 2006). From 2000 to 2004, in total 413,000 ha of coca were planted in Colombia, a quarter (97,622 ha) of which was established on land cleared from primary forest. Although the annual conversion rate has decreased steadily by 60% during this time, 13,202 ha of primary forest were still converted in 2004 (UNODC, 2006). It is likely that several hundred thousand hectares of forest were cleared due to the direct and indirect effects of coca cultivation prior to 2000, before remotely sensed data were available, though exact numbers are not known (UNODC, 2006). However, the cumulative area of primary forest lost from conversion to coca production can be calculated for the period of 1990–2004. Assuming a 13% rate of annual deforestation directly attributable to coca cultivation (UNODC, 2006) and applying this proportion to an annual forest cover change estimated at 190,470 hectares/year (UNODC, 2006), coca cultivation accounted for approximately 345,233 deforested hectares over this period. This is a conservative estimate, however, since the actual area of primary forest cleared due to coca cultivation is greater than the area being directly cultivated for this purpose. Land used by the coca producers for subsistence farming, abandoned after soil becomes infertile, deforested by the farmers who leave areas dominated by drug traffickers and terrorists, deforested by the coca producers who are dispersed as a result of political violence, and cleared for landing strips (of which more than 100 exist at any one time), lab sites, and campsites also contributes to the total deforested area (UNODC, 2006). The actual area deforested is therefore likely to be greater than half a million hectares for this 14-yr period. Coca cultivation in Columbia is dynamic, and factors including favorable prices, pressure exerted by armed groups on farmers, the legal economy, and temporary crisis situations all lead to an increase in the cultivated area (UNODC, 2007). Conversely, factors such as forced eradication, aerial spraying, improved security conditions, and plant diseases contribute to reducing the cultivated area (UNODC, 2007).

EFFECT OF DISEASE ON AMPHIBIANS

Other human activities have been suggested as being partly responsible for the extinction of frogs. These range from increased exposure to ultraviolet radiation resulting from the release of substances that deplete stratospheric ozone, through the spread of diseases and the interaction of these with climate change. Of these, one fungal disease, chytridiomycosis, was identified as being responsible for the extinction of several frog species. This disease was first described from dead and dying frogs at sites of mass deaths in Australia and Panama from 1993 to 1998 (Berger et al., 1998). The chytrid that infected the Australian and Central American amphibians was identified as *Batrachochytrium dendrobatidis*, which has low host specificity and is likely to infect any species of amphibian (Longcore et al., 1999). Infections were detected in 15 amphibian families that include 94 species (Speare, 2001). Amphibian chytridiomycosis is an emerging infectious disease of amphibians that has been recognized as such on a global scale (Daszak et al., 1999;, 2003). This disease was identified as a key threatening process under the Environment Protection and Biodiversity Conservation Act 1999 of New Zealand (Speare 2001; Mendelson et al., 2006).

While chytridiomycosis has not yet been described from frogs in coca-growing areas of Colombia, humans are potential vectors of the disease though the carrying of spores on clothing and equipment (Krajick, 2006). Several studies indicated that the virulence of the fungal disease chytridiomycosis, one of the most commonly cited causes of enigmatic declines, is greater at higher elevations and among streamside species (Stuart et al., 2004). Thus, human activities in the growing of coca in remote areas may increase the spread of this disease to new areas of Colombia. The effects of this on rare or endangered species of amphibians in Colombia and elsewhere are potentially serious.

CONCLUSIONS

In summary, there are a number of human activities associated with the production of coca that present greater risks to amphibians than the glyphosate + Cosmo-Flux mixture used in the aerial eradication spraying. Under worst-case circumstances, several of the pesticides used to protect coca from pests (mancozeb, lambda cyhalothrin, endosulfan, diazinon, malathion, and chlorpyrifos) are as toxic, or more toxic, to amphibians than the Glyphos–Cosmo-Flux mixture. Furthermore, physical activities such as deforestation pose considerably greater hazards to amphibians in Colombia. Habitat destruction through the clearing and conversion of primary forests is of paramount concern, given the tendency of deforestation hotspots to overlap biodiversity hotspots in a country containing the second largest number of amphibians on earth and concomitantly the greatest production of cocaine. The potential for disease transmission (chytridiomycosis) is also enhanced as coca production further infiltrates remote areas of rain forest. Therefore, when considering the cumulative impacts and risks of coca production collectively in a multifactorial context to amphibian populations in coca growing regions, they are judged to be greater than those posed by the use of glyphosate and Cosmo-Flux employed for the spray control program.

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Annex 131-E

L.H. SANIN ET AL., "REGIONAL DIFFERENCES IN TIME TO PREGNANCY AMONG FERTILE WOMAN FROM FIVE COLOMBIAN REGIONS WITH DIFFERENT USE OF GLYPHOSATE"

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Regional Differences in Time to Pregnancy Among Fertile Women from Five Colombian Regions with Different use of Glyphosate

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The objective of this study was to test whether there was an association between the use of glyphosate when applied by aerial spray for the eradication of illicit crops (cocaine and poppy) and time to pregnancy (TTP) among fertile women. A retrospective cohort study (with an ecological exposure index) of first pregnancies was undertaken in 2592 fertile Colombian women from 5 regions with different uses of glyphosate. Women were interviewed regarding potential reproductive, lifestyle, and work history predictors of TTP, which was measured in months. Fecundability odds ratios (fOR) were estimated using a discrete time analogue of Cox's proportional hazard model. There were differences in TTP between regions. In the final multivariate model, the main predictor was the region adjusted by irregular relationship with partner, maternal age at first pregnancy, and, marginally, coffee consumption and self-perception of water pollution. Boyacá, a region with traditional crops and. recently, illicit crops without glyphosate eradication spraying (manual eradication), displayed minimal risk and was the reference region. Other regions, including Sierra Nevada (control area, organic agriculture), Putumayo and Nariño (illicit crops and intensive eradication spray program), and Valle del Cauca, demonstrated greater risk of longer TTP, with the highest risk for Valle del Cauca (fOR 0.15, 95% CI 0.12, 0.18), a sugar-cane region with a history of use of glyphosate and others chemicals for more than 30 yr. The reduced fecundability in some regions was not associated with the use of glyphosate for eradication spraying. The observed ecological differences remain unexplained and may be produced by varying exposures to environmental factors, history of contraceptive programs in the region, or psychological distress. Future studies examining these or other possible causes are needed.

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Glyphosate is one of the most widely used herbicides globally and has been registered for use in Colombia since 1972 for weed control in a wide range of crops and in the process of sugar cane maturation. Beginning in the early 1980s, it was used for eradicating the illegal crops of coca (*Erythroxylum coca*) and poppy (*Papaver sominferum*). Since 2000, it has been more widely used for the eradication of illicit crops. The area of coca sprayed with glyphosate has shown a steady increase over recent years, reaching 153,000 ha in 2007 (personal communication, National Police of Colombia, Bogotá, December 2007). According to Colombian use data, 10–13% of the total amount of glyphosate purchased in the country is used for aerial spraying of illicit crops; the remainder is used in both legal and illegal crop production (Solomon et al., 2007).

Colombia is organized into 32 administrative departments (*departmentos*). In 12 of them, illicit crops have been sprayed with glyphosate by aerial application since 2000. The location and amounts of glyphosate applied for this purpose are accurately known. Glyphosate is used for other purposes in all departments, but actual use statistics are not known as sales data are not collected.

In developed countries, investigators have increasingly used time to pregnancy (TTP) as a sensitive clinical marker of multiple early adverse reproductive effects (Baird et al., 1986; Joffe 1997, 2000; Joffe & Barnes 2000; Tingen et al., 2004; Joffe et al., 2005). Epidemiological studies examined the role of agriculture and pesticide exposure in reducing the probability of achieving conception in a menstrual cycle (also known as fecundability) with mixed results (De Cock et al., 1994; Larsen et al., 1998; Curtis et al., 1999; Thonneau et al., 1999; Abell et al., 2000; Petrelli & Figà-Talamanca, 2001; Sallmén et al., 2003; Idrovo et al., 2005; Bretveld et al., 2006; Lauria et al., 2006; Bretveld et al., 2008; Joffe et al., 2008).

There have been some reports in the literature of adverse reproductive outcomes associated with pesticide use, most of which are described in more detail in a recent review (Wigle et al., 2008). Arbuckle et al. (2001) observed a rise in the risk of early abortion when preconception self-reported exposures to phenoxyacetic acid herbicides were present (odds ratio [OR] = 1.5, $CI_{95\%}$ 1.1–2.1; positive effect if greater than 1) and for late abortions, self-reported preconception exposure to glyphosate (OR = 1.7, $CI_{95\%}$ 1–2.9) was associated with higher risks. In another study, Curtis et al. (1999) reported a positive association (decrease in fecundability of 20% or more) measured through the outcome, TTP, when both spouses reported exposure to pesticide activities, with 5 of 13 pesticides categories (dicamba, glyphosate, phenoxy herbicides, organophosphorus insecticides, and thiocarbamates). Garry et al. (2002), studying pesticide applicators in Minnesota through a cross-sectional study of 695 workers and 1532 children (offspring), observed that self-reported use of the herbicide glyphosate yielded an OR of 3.6 ($CI_{95\%}$ 1.3–9.6) in relation to attention deficit disorder/attention deficit-hyperactivity disorder (ADD/ADHD), and pointed out that herbicides applied in the spring might be a factor in the birth defects.

Our objective in the current study was to test for differences in TTP for first pregnancy among fertile women selected from five regions of Colombia with different use patterns of glyphosate. This study also took into account other known factors affecting fecundability. A priori, it was postulated that the use of glyphosate in aerial spraying programs for eradication of illicit crops might be associated with reduced fecundability, and, considering that there are no biomarkers for exposure to glyphosate, an ecological exposure index was chosen.

MATERIALS AND METHODS

Design and Population

Between August 2004 and February 2005, a cross-sectional study of first pregnancies was carried out among women based on residence in one of five different regions (departments) from Colombia (Figure 1). All participants were informed about the objectives of the study, and invited to participate if their first pregnancy occurred during the last 5 yr (since November 1999) and they did not use contraceptives during the year prior to becoming pregnant. The latter was to reduce reporting bias because there is no accurate method to adjust for the effect of the use of contraception on fecundity (Tingen et al., 2004). Only data on first pregnancies were used, to reduce recall bias and other potential biases that are associated with subsequent pregnancies. Only one pregnancy was used to maintain outcome independence and minimize the effect of previous reproductive history (Olsen & Skov, 1993).

Two days of training were carried out for interviewers and supervisors to explain the objectives of the project and the questionnaire to be applied. All interviewers lived in the study area and were supervised by local epidemiologists who knew the study area and who were well known to the population. In each area, studies started at the closest household where water and sediment samples were taken as part of the assessment of aerially applied glyphosate (Solomon et al., 2007). From the first household, the interview team moved away (centrifugally), visiting house by house to identify women who met the inclusion criteria until the sample size (600 women in each zone) was achieved. Because field workers were well known by the population, there were no refusals to enter the study, except in Valle del Cauca, where 3% of identified women declined to enter the study, mainly because their husbands did not allow them to participate. There were some differences among the five study sites that required us to visit more households in some areas than in others. For example, in Boyacá and Nariño, women start families at an early age; thus, when asked about first pregnancy in the last 5 yr there were many who were in the appropriate age group but had their first pregnancy more than 5 yr previously and therefore did not meet the inclusion criteria. In Valle del Cauca, most women had taken oral contraceptives in the last year, an exclusion criterion for the study. The population of Valle is different because it is a more developed department, was one of the first departments (if not the first) where extended family planning was initiated in the 1960s, and many villages (*veredas*) needed to be visited in order to obtain the sample size.

All women responding to the oral invitation were interviewed in their homes. Those who were confirmed as meeting the inclusion criteria were informed about the objectives of the study. Care was taken to ensure participants that there would be no reprisal for participation or nonparticipation, and that the investigators guaranteed the privacy of the information collected. Each participant provided written informed consent, in keeping with ethical approval by the Ethics Review Board of the Fundación Santa Fé de Bogotá, Colombia. Of a total of 3005 women interviewed, 233 women were excluded without TTP data and 21 with TTP values greater than 60 mo. Hence, 2751 (91.6%) were included in the analyses. However, for the

FIG. 1. Location of the study areas in Colombia (departments).

multiple regression and the alternative models, a restricted analysis was conducted without the 159 women who reported consultation with a physician because of fertility problems. This removed potential bias that may have been introduced by those who suspected themselves to be subfertile (Tingen et al., 2004; Idrovo et al., 2005; Joffe et al., 2005)

Exposure Assessment

As exposure could not be measured directly, an ecological design was used in which five different regions in the country, with different levels of exposure, were selected according to agricultural practices and presence or not of the aerial spray program for eradication of illicit crops with glyphosate. Table 1 shows the characteristics of the study areas.

Outcome Measurement

Valid data on TTP can be derived retrospectively, with a recall time of 14 yr or more (Joffe et al., 1995). A modified version of the key question from the questionnaire of Baird et al. (1986) was used to elicit TTP: "How many months were you having sexual intercourse before you became pregnant for the first time?" The questionnaire was field tested in the five different regions to ensure the question was clearly understood in all areas since the departments are far from each other and there are subtle differences in understanding some terms. TTP was defined as duration in months, not divided by menstrual cycle duration in days, because women are more able to recall time in months than in cycles (Joffe, 1997). In this case, months and cycles were treated as equivalents.

Potential Confounders

During the interview, participants also provided information on potential confounders, including age at which the woman started trying to become pregnant, age at first pregnancy, and current age; relationship with partner; work history and gynecologic and medical history prior to first pregnancy; x-ray exposure in the year prior to conception; body image perception prior to conception as a proxy for body mass index (Singh, 1994; Madrigal-Fritsch et al., 1999; Romieu et al., 2004); and lifestyle practices in the year prior to conception, such as

TABLE 1
Geographic, Population, Agriculture, and Pesticide Use Characteristics in the Study Regions

Department	Description of the study area	Most common crops	Usual level of pesticide use	Glyphosate aerial spray program
Boyacá	Boyacá is located 130 km northwest of Bogotá (Figure 1), and the west zone is at 850 m a.s.l. with an annual mean temperature of 24°C and rainfall of 2250 mm per year. Ten out of the 132 municipalities belong to this zone and 5 were selected for the study. Boyacá has 1,404,309 inhabitants, 36,136 of which reside in the municipalities selected. Thirty percent are women between 15 and 49 yr of age. The inhabitants of this department are mainly mestizos.	Vegetables, potato, maize, barley, sugar cane, wheat, plantain, and some fruits are the main crops in the area. Illicit crops have been grown since 1992	Herbicides, fungicides, insecticides, and rodenticides are used in the study area. Glyphosate is used as herbicide.	None (manual eradication of illicit crops)
Nariño	Tumaco (located in Nariño, Figure 1) is one of the largest municipalities in the country (3760 $km^{2)}$, located at 2 m a.s.l., has an annual mean temperature of 28ºC and rainfall of 2,531 mm. It is located at the southwest corner of the country and border Ecuador to the south. Forty-nine percent of the 162,606 inhabitants live in rural areas. The projected number of women in fertile age (15–49 yr) for 2004 was 36,386. The population of Tumaco is largely of African origin.	Agriculture makes up 80% of the economic activities of the population. Main crops are oil (African) palm, cacao, plantain, and coconut. Forestry is another important source of income, as well as fish and aquaculture. Illicit crops have been grown in the area during the last 10 yr and currently represent 10–12% of the production of drugs in Colombia.	Herbicides, fungicides, and insecticides are used in the study area but people report very low use of these compounds.	Aerial spraying of glyphosate has been conducted since 1999 and Tumaco accounts for 25–30% of the total spraying in the department of Nariño.
Putumayo	The project was carried out in the municipality of Puerto Asis located at 260 m a.s.l. with an annual mean temperature 27ºC. The area has 68,112 inhabitants, of whom 57.7% live in rural areas. Twenty percent of the total inhabitants are women of fertile age. The population of Putumayo and in the study area is mainly mestizo but people of Indian descent are found in this department.	Small crops of maize, plantain, and cassava are grown for local use.	Herbicides, fungicides, and insecticides are used in the study area. Low use of these compounds is reported by local inhabitants.	In 2003 and 2004, 15–24% of the aerial spraying of coca in Putumayo occurred in this municipality, indicating extensive spraying in the study area.
Sierra Nevada de Santa Marta	The National Park Sierra Nevada de Santa Marta is in the northern part of Colombia and has the highest peaks in the country, reaching more than 5000 m a.s.l. The selected area for the study is at the foothills of the Sierra at 700 m a.s.l. and rainfall of 3000 mm per year. The rural population of Santa Marta has 13,000 women 15–49 yr of age but only one village, where organic crops are cultured, was chosen for the study. The ethnicity of the population of the study area is mestizo but Indian heritage is less prevalent than in Putumayo or Boyacá.	Coffee plantations are the main crop in the study area of this region. Banana, peanuts, oranges, plantain, a type of sweet potato, and cacao, are also grown in the area.	No pesticide use for coffee plantation and other crops. Instead, native plants and biological control of pests are utilized.	None
Valle del Cauca	The study was carried out in the municipalities of Candelaria and Cerrito and the "*corregimiento*" (not large enough to be a municipality) of Rozo. Located at 1000 m .a.s.l. with an annual mean temperature of 24°C. Approximately 13% of the population lives in rural areas. The population in the area includes mestizos as well as people of African origin.	Main crop in Valle del Cauca and in the study area is sugar cane. Coffee, plantain, and banana are also grown to a lesser extent.	Substantial herbicide use in sugar cane including glyphosate.	Aerial spraying of glyphosate for cane maturation 2 wk before harvesting.

smoking, drug, coffee, and alcohol consumption. Data on life style practices and work status for the father were also collected. A variable for self-perception of pollution of water was included, as well as one related to the source of water consumption in the current domicile.

Statistical Analysis

For analysis purposes, if TTP was reported as zero months (or "unexpected"), the answer was interpreted as 1 mo. Cut points for categorization of continuous variables were set as follows: age at time of interview at ≤25 yr; age when attempting to get pregnant and age when first becoming pregnant was set at ≤20 yr. For each exposure and potential confounder variable, analysis of variance (ANOVA) of mean TTP was conducted.

Among the 2592 women, 2477 pregnancies and 12,393 months (11,033 for final model) were included in multivariate models. Each month was classified according to the relevant exposure and confounder variables and an indicator variable was generated for every month, giving information on whether the cycle under this exposure resulted in a pregnancy or not. Fecundability odd ratios (fOR) were calculated with 95% confidence intervals (95% CI) using a discrete time analogue of Cox's proportional hazard model (Baird et al., 1986; Curtis et al., 1999; Zhou & Weinberg, 1999). Because TTP was assessed for a period of 12 mo, a separate censor variable was introduced if a woman took >12 mo to conceive. A value of 0 (noncensored) was used if TTP was ≤12 mo and 1 if TTP was >12 mo. fOR below unity indicate subfertility. All analyses were performed using Stata 7.0 (Stata Corporation, College Station, TX) with macros developed by Dinno (2002).

The initial saturated multivariate model included all variables significant on bivariate analysis ($p < .10$) and variables of prime biological importance (age at time of trying to become pregnant). Several goodness-of-fit statistics for logistic regression were checked: Pearson chi-square, deviance, and Hosmer–Lemeshow statistics (Hosmer & Lemeshow, 1989). The final model consisted of only those variables that contributed to the explanatory value of the model at a .05 level of significance (coefficient of determination). Collinearity was tested with VIF (variance inflation factor). The assumption that the fecundability odds ratio was constant across time (Weinberg & Wilcox, 1998) was tested graphically and by including an interaction term between months to pregnancy and exposure or confounder variables in the final model. The latter were not significant, implying that the proportional assumption was not violated. Finally, to evaluate a possible selection bias based on wantedness, the analyses were repeated excluding the pregnancies occurring in the first month (Weinberg et al., 1994). No significant changes in the final model were observed.

An alternative model without perfect fitting is presented for the sake of research interest, even though it had some marginal variables (p values >.05).

RESULTS

TTP showed large differences in different regions (Table 2). The Department of Valle del Cauca displayed a low percentage for the first month and Boyacá and Nariño were exceptionally high for the twelfth month (Figure 2).

Participating women were generally young (mean and median age 21 yr, range 15–48 yr, but there was one of 54 yr of age) and had completed at least some secondary education (Table 3). The vast majority had regular menstrual cycles (96.7%); a substantial proportion had irregular partner relationships. Most became pregnant first at young ages (73.6% at 20 yr of age or less). During the year before first pregnancy (YBF), most were free of illness (84.3%), had not had x-rays (95.4%), and did not smoke tobacco (95.1%). Alcohol and coffee consumption were 51.8% and 80.3%, respectively.

In the crude analyses (Table 3), longer TTP was associated with region, older maternal age, ethnic group, irregular menstrual cycles, and irregular partner relationship. Previous visits to physician for problems related with fertility, x-rays taken in the year before pregnancy (YBP), and coffee consumption in the YBP were associated with longer TTP. A significant trend between coffee consumption and longer TTP was observed. Maternal overweight showed a borderline significant association with a longer TTP.

The majority of women were housekeepers at the time they become pregnant. A tendency to longer TTP was observed among those engaged in some waged work and with higher education. Paternal unemployment or self work, were associated with longer TTP. No other paternal data were related to the outcome.

Self-perception about bad quality of water was associated with longer TTP, and all sources of water presented risk when they were compared with pure water ("*nacimiento*"), except some few cases that used carried water ("*carro-tanque*").

TABLE 2
Time to Pregnancy and Percentage of Pregnancy by Month in the Study Regions

	Regions					
Months	Boyacá	Nariño	Sierra Nevada de Santa Marta	Putumayo	Valle del Cauca	Total
1	69.2	21.2	25.5	49.4	17.0	36.8
3	82.5	62.9	52.9	56.1	28.7	57
6	88	94.8	72.1	74.9	45.2	75.2
12	96.9	99.3	87.3	89	73.5	89.4
MTTP[a]	3	3.3	8.6	6.4	14	7
MTTP[b]	3	3.3	7.1	6	12.6	6.3

[a]MTTP, mean time to pregnancy in months.
[b]Censored to 60 mo (see text).

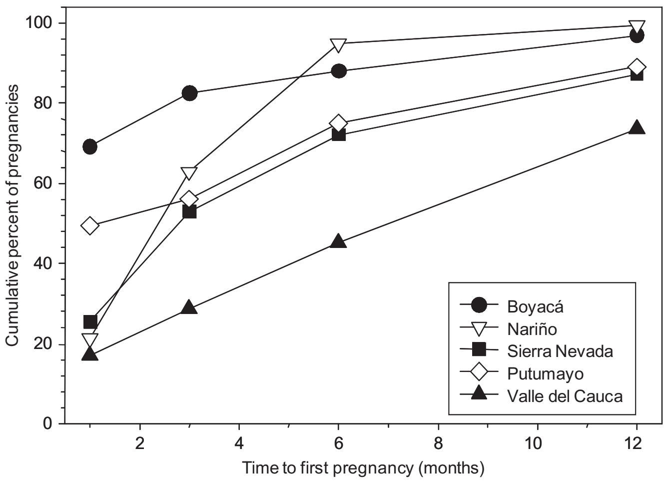

FIG. 2. Unadjusted cumulative percentage of pregnancies over time for the five study regions in Colombia.

In the final multivariate model (Table 4), the main predictor was region adjusted by irregular relationship with partner and maternal age at first pregnancy. Boyacá displayed minimal risk and was used as the reference. Nariño, Sierra Nevada de Santa Marta, and Putumayo showed higher risk, with the highest risk in Valle del Cauca. Goodness-of-fit statistics for the final model were optimal when adjustment for maternal age when the first pregnancy had occurred was carried out. Table 4 shows the analysis without including 159 women who reported visiting a physician because of fertility problems. In the crude analysis, irregular cycles and medication for this purpose were associated with longer TTP, but when potentially subfertile couples were excluded, these two variables were no longer included in the final model. Age at first pregnancy and irregular relationship remained in the model after excluding those with fertility problems. Table 5 shows that coffee consumption and perception of contamination of water, although no longer significant, were borderline. When categorized in number of cups, coffee consumption still showed a positive trend; the greater the number of cups, the longer was the TTP.

An alternative model is presented in Table 5 because that model includes variables such as coffee consumption and water pollution with marginal statistical significance but with strong biological and environmental significance.

DISCUSSION

This was the first study performed in Colombia with the objective of assessing whether an association existed between use of aerially applied glyphosate for eradication of illicit crops and subchronic effects on reproduction, such as TTP. A major problem in many epidemiological studies is the lack of appropriate exposure data based on actual measurements (Arbuckle et al., 2002; Harris et al., 2002; Coble et al., 2005; Ritter et al., 2006; Firth et al., 2007). In most cases, exposures are approximated through questionnaires, geographical regions, type of crop, season of application, chemical group, or classification according to mode of action (herbicides, insecticides, fungicides, etc). This is done because most pesticides lack a persistent biomarker, which prevents a measurement-based characterization of exposure for the majority of the pesticide products, including glyphosate (Acquavella et al., 2004).

For this reason, the acute effects of this herbicide are the most extensively documented (Acquavella et al., 1999) with predominant manifestations being eye irritation and other temporary dermal effects. Whether pneumonitis occurs is controversial (Pushnoy et al., 1998), and fatal cases have been recorded only with accidents or when glyphosate was ingested with the purpose of committing suicide (Williams et al., 2000). Some cases of Parkinson's disease have been associated with acute intoxication with glyphosate (Barbosa et al., 2001), but the small number of cases and lack of laboratory animal analogies do not allow assignment of causality.

Some authors have made efforts to identify the compounds used by study subjects. Several studies on different populations that specifically addressed the use of glyphosate were found and published since the last major reviews (Williams et al., 2000; Solomon et al., 2007). Studies related to cancer and to adverse reproductive and developmental effects reported equivocal and unclear relationships between glyphosate use and some reproductive outcomes (Curtis et al., 1999; Arbuckle et al., 2001; Garry et al., 2002; De Roos et al., 2005).

TABLE 3
Mean Time to Pregnancy (Without Censoring) and Crude Fecundability Odds Ratio (fORc) Analyzed by Different Sociodemographic Characteristics

Variable	*n*	Time to pregnancy (mo), X (SD)[a]	fORc ($CI_{95\%}$)[b]	*p*
Region				
Boyacá	582	3 (4.7)	1	–
Nariño	552	3.3 (3.3)	0.72 (0.62, 0.83)	<.01
Sierra Nevada de Santa Marta	551	7.1 (10.3)	0.41 (0.35, 0.48)	<.01
Putumayo	535	6 (8.3)	0.44 (0.38, 0.51)	<.01
Valle del Cauca	531	12.6 (13.5)	0.2 (0.17, 0.24)	<.01
Maternal age (yr)				
≤25	2356	5.7 (8.2)	1	–
>25	395	10 (14)	0.64 (0.56, 0.73)	<.01
Age to first pregnancy (yr)				
≤20	2026	5.5 (8)	1	–
>20	725	8.6 (12.3)	0.69 (0.62, 0.76)	<.01
Age at start TTP study period (yr)				
≤20	2094	6.2 (9)	1	–
>20	657	6.8 (10.5)	0.98 (0.88, 1.1)	.69
Ethnic group				
Mestizo	2121	6.5 (9.6)	1	–
Negro	508	6.3 (9.6)	1. (0.9, 1.14)	.83
Indígena	49	3.7 (4.1)	1.37 (0.9, 1.94)	.08
Zambo	41	3.6 (2.6)	1.38 (0.95, 2.01)	.09
Mulato	32	3.3 (2.6)	1.6 (1.05, 2.51)	.03
Grouped ethnic group				
Mestizo and Negro	2629	6.45 (9.6)	0.7 (0.56, 0.87)	<.01
Indígena, Zambo, and Mulato	122	3.54 (3.2)	1	–
Education				
None	42	4.9 (9.1)	1	–
Incomplete elementary school	582	4.6 (7.1)	0.93 (0.63, 1.39)	.74
Complete elementary school	526	5.6 (7.7)	0.76 (0.51, 1.13)	.17
Incomplete high school	459	7 (10.3)	0.66 (0.45, 0.98)	.04
Complete high school	130	9.7 (12.5)	0.47 (0.31, 0.73)	<.01
Zone				
Urban	5	15.2 (18.6)	–	–
Rural	2743	6.3 (9.4)	–	–
Marital status[c]				
Common law	1010	5.1 (8.3)	1	–
Not common law	1741	7 (9.9)	0.71 (0.64, 0.78)	<.01
Socioeconomic status[c,d]				
0	38	4.8 (5.8)	1.1 (0.75, 1.63)	.62
1	2013	6.4 (9.4)	1	–
≥2	493	6.6 (10.1)	1.03 (0.91, 1.17)	.60
Nutritional status[e]				
Low weight	111	7.1 (10.9)	0.91 (0.72, 1.15)	.42
Normal weight	2453	6.2 (9.3)	1	–
Overweight	184	7.2 (10.0)	0.83 (0.69, 1.00)	.04
Maternal work[c]				
Administrative, teacher, or student	678	6 (8.6)	0.99 (0.89, 1.11)	.92

(*Continued*)

TABLE 3
(*Continued*)

Variable	n	Time to pregnancy(mo), X (SD)[a]	fORc (CI $_{95\%}$)[b]	p
Home, no work, housekeeper	1631	6 (9.2)	1	–
Community mother, mining, various, other, occasional	229	8.7 (11.9)	0.7 (0.59, 0.83)	<.01
Health worker, independent worker, seller	126	8.7 (12.3)	0.74 (0.59, 0.93)	.01
Agriculture and floriculture	86	4.2 (4.6)	1.14 (0.87, 1.48)	.34
Maternal work in cocaine[c]				
No	2743	6.3 (9.4)	1	–
Yes	8	7.6 (7.4)	0.67 (0.29, 1.54)	.35
Menarche age (yr)				
<12	1031	6.6 (10)	1	–
13	802	5.8 (8.6)	1.06 (0.94, 1.19)	.32
14	523	6.4 (9.3)	1.02 (0.89, 1.16)	.81
15	392	6.6 (9.4)	0.94 (0.82, 1.09)	.43
Menstrual cycle				
Regular	2612	6.2 (9.3)	1	–
Irregular	88	9.5 (12.3)	0.64 (0.49, 0.84)	<.01
Previous consultation for pregnancy problems				
No	2592	5.8 (8.7)	1	–
Yes	159	15.2 (14.4)	0.33 (0.27, 0.41)	<.01
Smoking[c]				
No	2616	6.3 (9.5)	1	–
Yes	135	6.2 (7.9)	0.95 (0.77, 1.17)	.63
Alcohol consumption[c]				
No	1325	6.2 (9.4)	1	–
Yes	1425	6.3 (9.4)	0.97 (0.88, 1.06)	.52
Coffee consumption[c]				
No	543	5.3 (8.1)	1	–
Yes	2208	6.6 (9.7)	0.81 (0.72, 0.91)	<.01
Number of coffee cups/day[c] **				
0	543	5.3 (8.1)	1	–
1 to 3	1916	6.4 (9.5)	0.83 (0.73, 0.93)	<.01
≥4	292	7.4 (10.7)	0.73 (0.61, 0.87)	<.01
X-rays[c]				
No	2616	6.2 (9.2)	1	–
Yes	125	9.4 (12.5)	0.67 (0.54, 0.84)	<.01
Any kind of illness[c]				
No	2316	6.3 (9.3)	1	
Yes	432	6.4 (9.7)	0.97 (0.86, 1.10)	.68
STD[c,e]				
No	2717	6.3 (9.3)	1	–
Yes	27	7.3 (10.4)	0.84 (0.52, 1.38)	.50
Medication for regularizing menses[c]				
No	2721	6.3 (9.4)	1	–
Yes	30	11.2 (10)	0.45 (0.28, 0.71)	<.01
Medication for “sugar in blood”[c]				
No	2735	6.3 (9.4)	1	–

(*Continued*)

TABLE 3
(*Continued*)

Variable	*n*	Time to pregnancy(mo), $\bar{X}$ (SD)[a]	fORc (CI $_{95\%}$)[b]	*p*
Yes	16	7.6 (6.5)	0.7 (0.39, 1.24)	.22
Other medications[c]				
No	2027	6.8 (9.7)	1	–
Yes	703	5 (8.3)	1.36 (1.22, 1.51)	<.01
Paternal work[c]				
Administrative or student	160	6.3 (8.2)	0.86 (0.7, 1.05)	.14
No work, occasional	212	8.4 (12.5)	0.74 (0.61, 0.88)	<.01
Carpenter, driver, construction, mining, mechanic, industrial timbering	507	5.7 (9)	1.02 (0.89, 1.16)	.80
Other, health worker, independent worker, vendor	713	7.7 (10.8)	0.75 (0.67, 0.84)	<.01
Agriculture, floriculture, livestock	1157	5.4 (7.9)	1	–
Paternal work in cocaine[c]				
No	2457	6.4 (9.6)	1	–
Yes	292	5.5 (7.8)	1.07 (0.92, 1.24)	.40
Any disease of the father[c]				
No	2398	6.4 (9.5)	1	–
Yes	248	6.8 (9.4)	0.93 (0.80, 1.1)	.41
STD of the father[c,f]				
No	2608	6.4 (9.5)	1	–
Yes	37	6.1 (8.2)	0.99 (0.66, 1.47)	.94
Paternal alcohol consumption[c]				
No	1325	6.2 (9.4)	1	–
Yes	1425	6.4 (9.4)	0.97 (0.88, 1.06)	.52
Paternal smoking[c]				
No	2143	6.2 (9.3)	1	–
Yes	538	6.9 (10)	0.9 (0.80, 1.01)	.08
Paternal use of psychotropic drugs[c]				
Yes	2619	6.4 (9.5)	1	–
No	54	4.5 (5.7)	1.23 (0.88, 1.72)	.22
Perceived contamination of water				
No	1218	6 (9.2)	1	–
Yes	1533	6.6 (9.5)	0.9 (0.82, 0.98)	.02
Source of drinking water				
Municipal tap water	598	7.2 (11)	1.13 (1, 1.28)	.05
Rain water	65	5.3 (8)	1.38 (1.02, 1.88)	.04
Stream, ravine, or creek	257	6.1 (10.2)	1.36 (1.14, 1.61)	<.01
"Carried water"	10	14.8 (16.5)	0.44 (0.19, 1.05)	.07
"Pure water"	311	3.7 (5.7)	2.03 (1.73, 2.39)	<.01
Deep well	1040	7.4 (10)	1	–
River	470	4.6 (6.5)	1.52 (1.33, 1.74)	<.01

**There is a significant trend when $p < .05$.
[a]Mean and standard deviation.
[b]Crude fecundability odds ratio; 95% confidence interval.
[c]During the year prior to pregnancy.
[d]The population is classified in 6 socioeconomic strata, from 1 being the lowest to 6 the highest. A zero indicates extreme poverty.
[e]Based on self-reporting images scaled from 1 to 9. Low weight 1 to 4, normal 5 to 7, overweight 8 and 9 (BMI ≥25) (Madrigal-Fritsch et al., 1999).
[f]STD, sexually transmitted disease.

TABLE 4
Causes of Fecundability Adjusted[a] for the Relationship Between Time to Pregnancy (TTP) and Region[b]

Variable	fRMa[c]	EE[d]	IC $_{95\%}$[e]	*p*
Region[f]				
Nariño	0.53	0.044	0.45, 0.63	<.01
Sierra Nevada	0.36	0.030	0.30, 0.42	<.01
Putumayo	0.34	0.029	0.29, 0.41	<.01
Valle del Cauca	0.15	0.013	0.12, 0.18	<.01
Age at first pregnancy >20 yr[g]	0.81	0.048	0.72, 0.91	<.01
Irregular relationship with father[h]	0.76	0.041	0.68, 0.84	<.01

Note. n = 2592 mothers 11,270 cycles.
[a]Proportional risk model of Cox, modified after Dinno, (2002).
[b]Restricted to those mothers who did not consult a physician regarding problems in conceiving.
[c]fRMa Adjusted cause of fecundability.
[d]Standard error.
[e]95% Confidence interval.
[f]Compared to Boyacá as reference.
[g]Compared to ≤20 years as reference.
[h]Compared to regular relationship as reference.

TABLE 5
Causes of Fecundability Adjusted[a] for the Relationship Between Time to Pregnancy (TTP) and Region[b] Based on an Alternative Model

Variable	fRMa[c]	EE[d]	IC$_{95\%}$[e]	*p*
Region[f]				
Nariño	0.56	0.048	0.47, 0.66	<.01
Sierra Nevada	0.36	0.031	0.31, 0.43	<.01
Putumayo	0.35	0.029	0.29, 0.41	<.01
Valle del Cauca	0.15	0.014	0.13, 0.18	<.01
Age at first pregnancy >20 yr[g]	0.81	0.048	0.73, 0.91	<.01
Irregular relationship[h]	0.76	0.041	0.68, 0.84	<.01
Consumption of coffee[i]				
Medium (1–3 cups per day)	0.91	0.059	0.81, 1.04	.15
High (4 and more cups per day)	0.84	0.083	0.69, 1.02	.08
Perception of contamination of water[j]	0.91	0.51	0.81, 1.01	.08

Note. n = 2592 mothers, 11,270 cycles.
[a]Proportional risk model of Cox, modified after Dinno (2002).
[b]Restricted to those mothers who did not consult a physician regarding problems in conceiving.
[c]fRMa Adjusted cause of fecundability.
[d]Standard error.
[e]95% Confidence interval.
[f]Compared to Boyacá as reference.
[g]Compared to ≤20 years as reference.
[h]Compared to regular relationship as reference.
[i]Compared to no consumption as reference.
[j]Compared to no contamination as reference and based on self-perception and source of water normally consumed.

Other risk factors present in the rural and agricultural environment of the women studied and individual characteristics (genetic, for example) may be associated with TTP. Longer TTP were observed in some populations with higher physical activity (Florack et al., 1994) or psychological distress (Hjollund et al., 1999). Further, TTP may be influenced by knowledge and behavior, such as patterns of intercourse as well as biologic factors (Joffe et al., 2005), and these need to be considered as potential confounders (Tingen et al., 2004; Stanford & Dunson, 2007) The potential effect of these factors on TTP could not be isolated in this study, even though the fOR was adjusted for most known confounders and independent predictors.

As shown in Figure 2, there was no difference in cumulative TTP between Putumayo, where illicit crops were sprayed, and Sierra Nevada, where there was no herbicide use. In turn, the latter region showed lower cumulative percent pregnancies than Nariño, an eradication spray area, and Boyacá, where there is agricultural herbicide use but manual eradication of illicit crops. Although classification of exposure may be a source of bias in this type of study, no relationship between reduced fecundability in the studied regions and use of glyphosate specifically for spray eradication or use of pesticides in general can be established from our data. Prospective studies that prevent or reduce classification bias of exposures are recommended to further elucidate relationships between aerial spraying of glyphosate for eradication, agricultural pesticide use, and human health indicators.

Pesticides in general are likely not the cause either, as large differences in TTP were observed between two regions of high to moderate pesticide use, Valle del Cauca and Boyacá. The observed ecological differences remain unexplained, but may be produced by varying exposures to environmental factors, history of contraceptive programs in the region, or psychological distress. Future studies examining these causes are needed.

Table 3 shows crude association between coffee consumption and longer TTP with a significant trend. This association is not significant in the adjusted model but the level of significance was borderline. Published results regarding coffee or caffeine consumption and TTP are not conclusive. Some studies showed no association (Joesoef et al., 1990; Alderete et al., 1995), but other investigators found that coffee drinkers have a lower risk of pregnancy (Wilcox et al., 1988; Christianson et al., 1989; Williams et al., 1989; Hatch & Bracken, 1993; Curtis et al., 1997). This relationship needs to be further investigated.

Distribution of pregnancies in relation with months in different regions showed great differences (Table 2). In a previous study in Colombia (Idrovo et al., 2005), the percentage for first month was close to 30%, which is lower than more than 40% reported from a Danish study (Joffe et al., 2005). In our study, the region of Valle del Cauca showed a low percentage and Boyacá exceptionally high for first and twelfth months (Figure 2). The mean for 12 mo in developed countries is between 85 and 90%. These results are consistent with the National Survey of Demography and Health (Ojeda et al., 2005) that showed Boyacá as the Department with the lowest proportion of women who reported fertility problems (4.2%). Valle del Cauca (11.2%) and Magdalena (16.1%), where Sierra Nevada is located, were above the national average (10.6%).

A retrospective assessment of TTP as an outcome variable was conducted to evaluate ecological exposure to glyphosate. Although it is widely recognized that retrospective studies for TTP can be carried out, they are prone to some biases that need to be taken into account in the interpretation of our results. Difference in sexual behavior between exposed and nonexposed subjects, particularly in frequency of intercourse, has been pointed out as source of bias (Tingen et al., 2004; Stanford & Dunson, 2007). Women of reproductive age differed in reporting intercourse in the last 4 wk, from 48.8% in Boyacá and neighboring departments to 53.8% in the Pacific region where Tumaco (Nariño) is located (Ojeda et al., 2005). Couples who had not used contraception in the last year were included and, in the multivariate analysis, those who had had consultation because of fertility problems were excluded. These two criteria excluded those who may have become pregnant while using contraception (highly fecund couples) and subfertile couples (Bonde et al., 2006). Studies also evaluated whether there were other sources of bias such as pregnancy recognition (Joffe et al., 2005) by asking whether a miscarriage occurred, and thus it was possible to control for this variable. However, biological factors such as age at first pregnancy and use of contraception in the past were taken into account as these appear to be more important than lifestyle factors in assessing TTP (Axmon et al., 2006).

Classification of exposure was by location of residence. Nonexposed participants were those who lived in the region where organic crops were produced and who, in addition, did not report any use of pesticides in the interview. In the other four departments, there was exposure not only to glyphosate, but also to other herbicides and pesticides. Although place of residence is not an accurate surrogate for exposure to pesticides and may generate misclassification (Arbuckle et al., 2004), this ecological assessment is useful to explore, at the population level, whether an association exists between the putative exposure (aerial spraying of glyphosate) and outcome (Ritter et al., 2006). However, in this study, aerial spraying of glyphosate was not consistently associated with delayed time to pregnancy.

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Annex 131-F

M.H. BERNAL ET AL., "TOXICITY OF FORMULATED GLYPHOSATE (GLYPHOS) AND COSMO-FLUX TO LARVAL COLOMBIAN FROGS 1. LABORATORY ACUTE TOXICITY"

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Toxicity of Formulated Glyphosate (Glyphos) and Cosmo-Flux to Larval Colombian Frogs 1. Laboratory Acute Toxicity

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The spraying of coca (*Erythroxylum coca*) with glyphosate in Colombia has raised concerns about possible impacts on amphibians. There are few toxicity data for species other than those from temperate regions, and these have not been generated with the combination of formulated glyphosate (Glyphos) and the adjuvant, Cosmo-Flux (coca mix) as used in coca control in Colombia. In order to characterize toxicity of the spray mixture to frogs from Colombia, Gosner stage-25 tadpoles of *Scinax ruber, Dendropophus microcephalus, Hypsiboas crepitans, Rhinella granulosa, Rhinella marina, Rhinella typhonius, Centrolene prosoblepon,* and *Engystomops pustulosus* were exposed to the coca mix at concentrations of glyphosate ranging from 1 to 4.2 mg a.e./L diluted in dechlorinated tap water in glass containers. Cosmo-Flux was added to Glyphos in the proportion of 2.3% v/v, as used in aerial application for coca control. Exposures were for 96 h at 23 ± 1.5°C with 12:12-h light/dark cycle. Test solutions were renewed every 24 h. Concentrations, measured within the first hour and at 24 and 96 h using enzyme-linked immunosorbent assay (ELISA) (Abraxis, LLC), ranged from 70 to 130% of nominal values. LC50 values ranged from 1200 to 2780 µg glyphosate acid equivalents (a.e.)/L for the 8 species tested. Data suggest that sensitivity to Roundup-type formulations of glyphosate in these species is similar to that observed in other tropical and temperate species. In addition, sensitivity of larval amphibians to Roundup-type formulations spans a relatively narrow range. Finally, toxicity of the mixture as used to spray coca was likely driven by the surfactant in the glyphosate formulation, as the addition of Cosmo-Flux did not enhance toxicity above those reported for Vision = Roundup®.

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Extensive reviews of the effects of glyphosate and its formulated products on aquatic organisms concluded that glyphosate presents a negligible risk to aquatic organisms (World Health Organization International Program on Chemical Safety, 1994; Giesy et al., 2000; Solomon & Thompson, 2003). Although amphibians are physiologically unique and ecologically important, no regulatory agencies currently require amphibian toxicity data as part of their registration requirements. Determining direct and indirect effects of agrochemicals on amphibian species continues to be identified as a general research need (Linder et al., 2003).

Several recent publications reported that glyphosate (active ingredient) exerts low toxicity to larval amphibians. The 48-h LC50 values of technical-grade glyphosate isopropylamine (IPA) salt to larval Australian frogs (*Litoria moorei, Crinia insignifera, Lymnodynastes dorsalis*, and *Heleioporus eyrei*) were reported to range from >343,000 to >466,000 µg glyphosate acid equivalents (a.e.)/L (Mann & Bidwell, 1999). The 96-h LC50 of glyphosate IPA in *Rana clamitans* was reported to be >38,900 µg a.e/L from a static exposure study (Howe et al., 2001). From this limited data set, it appears that glyphosate IPA is essentially nontoxic to amphibians.

The toxicity of some formulated glyphosate products to amphibians is greater than that of the active ingredient. A study by Mann and Bidwell (1999) examined the acute toxicity of Roundup herbicide (MON 2139) for *C. insignifera, H. eyrei, L. dorsalis,* and *L. moorei* tadpoles and reported 48-h LC50 values ranging between 2900 and 11,600 µg a.e./L glyphosate. Using a formulation of glyphosate (Vision containing glyphosate and ethoxylated tallowamine surfactant [POEA] and equivalent to Roundup), 96-h LC50 values as low as 880 µg a.e./L were reported for tadpoles of *Xenopus laevis*, *Bufo* *americanus, Rana clamitans,* and *Rana pipiens* (Edginton et al., 2004). Embryo stages were less sensitive than Gosner stage 25 larvae, and toxicity was affected by the pH of the exposure medium, although not in a consistent manner. A study on *R. clamitans, R. pipiens, Rana sylvatica*, and *B. americanus* (Howe et al., 2004) reported 96-h LC50 values for Roundup Original of 2200, 2900, and 5100 µg a.e./L, respectively. A study on *Rana cascadae* reported a 48-h LC50 for Roundup of 2336 µg a.e./L using static exposures in glass tanks (Cauble & Wagner, 2005). In a study carried out with *R. catesbeiana, R. clamitans, Hyla versicolor, R. pipiens*, *B. americanus,* and *R. sylvatica*, 384-h LC50 for Roundup were reported to range from 977 to 1865 µg a.e /L (based on the assumption that the reported concentration of the AI was as the IPA; Relyea 2005). It is not clear why only the 16-d LC50 values were calculated when it appeared that mortality occurred early in the exposure period; however, the reported LC50s were not greatly different from those reported by other authors (discussed earlier).

The toxicity of some other formulations of glyphosate is less than that of Roundup. Roundup Biactive (MON 77920) was practically nontoxic to tadpoles, producing 48-h LC50 values of 328,000 µg a.e./L for *L. moorei* and >360,000 µg a.e./L for *C. insignifera*, *H. eyrei*, and *L. dorsalis* (Mann & Bidwell, 1999). It is clear that components of the formulation other than the active ingredient are drivers of acute toxicity.

Aerial applications of glyphosate to control illicit coca (*Erythroxylum coca*) and poppy (*Papaver sominferum*) crops have been made in Colombia since 1997. Since 2006, poppy has not been grown to a significant extent in Colombia and is no longer sprayed. It has been pointed out that the glyphosate–Cosmo-Flux mixture as used in the spray program in Colombia could present a risk to native frog species (Solomon et al., 2007). The 96-h LC50 for the spray mixture as used in Colombia to larvae of *X. laevis* was 1300 and 1100 µg a.e./L for the poppy and coca mixtures (Solomon et al., 2007), respectively (Wildlife International, 2006a, 2006b). This was not greatly different from the values reported in the literature for Roundup in the same species, suggesting that the addition of the adjuvant Cosmo-Flux did not alter the toxicity of the mixture. However, there are few data in the literature on the susceptibility of tropical frog species to formulations of glyphosate and there are no data for species native to Colombia. Because of this, acute laboratory tests on larvae of native Colombian species of frogs were conducted. This study describes the acute toxicity of the Glyphos and Cosmo-Flux mixture to tadpoles (Gosner stage 25) of the frog species, *Hypsiboas crepitans* (Wied-Neuwied, 1824), *Rhinella granulosa* (Spix, 1824), *Engystomops pustulosus* (Cope, 1864), *Rhinella marina* (Linnaeus, 1758)*, Scinax ruber* (Laurenti, 1768)*, Dendropsophus microcephalus* (Cope, 1886)*, Rhinella typhonius* (Linnaeus, 1758)*,* and *Centrolene prosoblepon* (Boettger, 1892), during a 96-h exposure period under static-renewal test conditions in the laboratory.

MATERIALS AND METHODS

Test Organisms

Species that occur in locations where coca is grown (≤ 1000 m a.s.l.) were the focus of the study. Embryos of the test species were collected in the locations shown in Table 1 and transported to the University of Tolima where they were raised to Gosner stage 25 at a temperature of 23–25ºC in tanks containing city water that was dechlorinated by continuous aeration for at least 48 h prior to use. Embryos were not fed while they developed to stage 25. Only the tadpoles of *R. typhonius* and *S. ruber* were caught directly in field in stage 25. Tadpoles were not fed for 24 h before or during the test.

Testing Procedures

Formulated glyphosate (Glyphos, a product sold in Colombia but similar to Roundup in terms of active ingredient and POEA surfactant) and Cosmo-Flux as used in the spray program were obtained and stored separately at room temperature in the dark. Glyphos contains 354 g glyphosate a.e./L (as the IPA) and between 10 and 15% ethoxylated tallowamine (POEA) surfactant. Cosmo-Flux contains a mixture of linear and aryl polyethoxylates

TABLE 1
Species of Larval Frogs Used in the Acute Toxicity Studies and Their Location of Collection

Species	Stage collected	Location	Altitude (m a.s.l.)
Hypsiboas crepitans	Gosner 10–11	Potrerillo (4º14'N; 74º58'W)	430
Rhinella granulosa	Gosner 10–11	Payandé (4º19'N; 75º06'W)	630
Engystomops pustulosus	Gosner 10–11	Ibagué (4°21'N; 75°06'W)	827
Rhinella marina	Gosner 10–11	Payandé (4º19'N; 75º06'W)	630
Scinax ruber	Gosner 25	Potrerillo (4º14'N; 74º58'W)	430
Dendrosophus microcephalus	Gosner 10–11	Potrerillo (4º14'N; 74º58'W)	430
Rhinella typhonius	Gosner 25	Ibagué (4º25'N; 75º12 W)	1200
Centrolene prosoblepon	Gosner 10–11	Falan (5°07'N; 74°58'W)	1100

(17% w/v) and isoparaffins (83% v/v) (Cosmoagro, 2004). The water used for testing was the same as that used for raising the tadpoles (described earlier). Specific conductance, hardness, alkalinity, and pH of the water were measured.

Test chambers were 2-L glass jars containing 1 L of test solution. The chambers were indiscriminately positioned by treatment group in an air-conditioned area of the laboratory designed to maintain the test temperature and day length throughout the test period. A primary stock solution was prepared by dissolving the Glyphos and Cosmo-Flux in dilution water to obtain a nominal concentration of 100,000 μg glyphosate a.e./L. All solutions were prepared using a positive displacement pipette. Cosmo-Flux was added in the proportion of 0.023 μl per 1 μl of Glyphos (2.3% v/v) to obtain the proportion of spray mix as used in the field. Nominal test concentrations were selected based upon the results of exploratory range-finding toxicity tests. Two replicates of each test solution were prepared by serial dilution of the stock solution with dilution water to yield a range of nominal concentrations in 1 L of solution of 4200 to 1000 μg glyphosate a.e./L. Each solution was mixed by inversion. Ten tadpoles were impartially placed in each of the two test chambers for a total of 20 tadpoles per concentration. The rate of biomass loading (defined as total wet weight of 10 tadpoles/L test water) was below 0.6 g/L as recommended in ASTM guidelines (ASTM, 1998), with the exception of *S. ruber*, which were about 0.7 g/L. Test solutions were renewed daily by transferring the test organisms to freshly prepared solutions. Mean measured test concentrations were determined from samples of test water collected from the pooled replicates for each treatment and control group at the beginning of the test (0 h) and from the test solutions for each treatment and control group at 24 h and at test termination (96 h). All samples were collected at mid-depth and were analyzed immediately without storage.

Fluorescent lights that emit wavelengths similar to natural sunlight (Phillips TLT 20W/54RS) were used for illumination of the test chambers. A photoperiod of 12:12-h light/dark cycle was controlled with an automatic timer. The temperature during the study was 23 ± 1.5°C. Temperature was measured in each test chamber at the beginning and end of the test and at approximately 24-h intervals during the test, including before and after renewals, using a liquid-in-glass thermometer. Temperature also was measured continuously during the test in one negative control test chamber using a maximum and minimum digital thermometer. Dissolved oxygen and pH were measured in each test chamber at the beginning and end of the test and at approximately 24-h intervals during the test, including before and after renewals. Dissolved oxygen was measured using a portable dissolved oxygen meter Hanna HI 8043, and measurements of pH were made using a Hanna HI 8314 membrane pH meter. Observations of mortality and other signs of toxicity, such as unusual swimming activity, were observed approximately 4, 24, 48, 72, and 96 h after test initiation. The cumulative percent mortality observed in the treatment groups was used to estimate LC50 values at 96 h.

Analytical Methods

The ELISA test kit manufactured by Abraxis, LLC (Warminster, PA), was used to measure the concentration of glyphosate in the test solutions. Calibration standards of glyphosate solutions, ranging in concentration from 0.15 to 5 μg/L, were prepared from the standard supplied with the test kit and used to construct the standard curve. A standard curve was prepared with each set of samples analyzed. The standard curve was constructed by plotting the %B/Bo (absorbance value for each standard/absorbance value for the zero standard) against the corresponding glyphosate concentration. Concentrations of glyphosate were determined by interpolation from the standard curve. Final concentration of glyphosate in the exposure solution was calculated by correcting for the mean quality control (QC) percent recovery based on analyses of two replicates of one concentration (0.5 μg/L) of the standard. The Abraxis glyphosate assay has an estimated minimum detectable concentration based on a 90% B/Bo of 0.1 μg/L. The method limit of quantitation (LOQ) for these analysis was defined as the lowest calibration standard, 0.15 μg/L. Two matrix blank samples were analyzed to determine possible interferences. No interferences were detected above the LOQ during the samples analysis.

It was not logistically possible to measure concentrations of Cosmo-Flux; however, the proportions of Glyphos and Cosmo-Flux were kept constant and were the same as those used in the aerial spraying of coca. The results are thus representative of realistic field exposures.

Statistical Analyses

For consistency with other studies, the mortality data were analyzed using the U.S. EPA Probit Program Version 1.5 (U.S. EPA, 1994). The LC1 was estimated as a regression-derived approximation of the no-observed-effect concentration, and the LC50 was calculated for comparison to other literature values. The LC1, which is derived from the response data, is preferred as an indicator of the low effect concentration as it is independent of the experimental design (Crane & Newman, 2000). Where insufficient data were available for the Probit program (no or one concentration with a response between 0 and 100%), LC50 values were estimated by interpolation from a graph of percent concentration versus response.

RESULTS AND DISCUSSION

Measurement of Test Concentrations and Water Quality

Samples collected at test initiation had measured concentrations of glyphosate that ranged from 75 to 125% of the nominal concentrations. Samples collected prior to the renewal of the test solutions at 24 h contained measured concentrations that ranged from 74 to 112% of the nominal concentrations. Samples collected at test termination contained measured concentrations that ranged from 71 to 130% of the nominal concentrations. When the measured concentrations of samples collected at 0, 24, and 96 h were averaged, the mean measured concentrations ranged from 85 to 105% of nominal concentrations. Because measured values were close to nominal, the nominal concentrations were used to determine the LC1 and LC50 values in order to compare responses of larval anurans reported under field conditions (Bernal et al., 2009) and those in other studies. Water temperatures were within the 23 ± 1.5°C range established for the test. Mean dissolved oxygen concentrations were about 6.85 mg/L. The 95% confidence interval of measurements of oxygen concentration, hardness, alkalinity, specific conductance, and pH in the dilution water at test initiation are summarized in Table 2.

Signs of toxicity, such as slow swimming and remaining on bottom with no movement, were generally noted at lower exposure concentrations, and uncontrolled fast swimming and remaining in a vertical position were more evident at concentrations close to and exceeding the LC50 concentration. In general, most of the toxic responses were expressed within 24 to 48 h of test initiation.

TABLE 2
Hardness, Alkalinity, Specific Conductance, and pH in the Dilution Water at Test Initiation

Parameter	Mean	95% Confidence interval
Oxygen concentration(mg/L)	6.85 (*n* = 96)	6.60–7.10
Hardness (mg/L as $CaCO_3$)	112 (*n* = 6)	97.1–126.8
Alkalinity (mg/L as $CaCO_3$)	89.3 (*n* = 6)	70.2–108.4
Specific conductance (mS/cm)	263.2 (*n* = 6)	197.4–328.9
pH	8.23 (*n* = 96)	8.20–8.25

Toxicity values for the eight species of frogs (Table 3) are presented in terms of glyphosate concentration (a.e.) to allow for comparison to data from the literature. The most sensitive species was *D. microcephalus* and the least sensitive was *E. pustulosus*. The slopes of the concentration-response relationships ranged from 7.18 to 13.47. These are large slopes and are consistent with literature data where such slopes have been reported for formulated glyphosate (Perkins et al., 2000) and surfactants (Dorn et al., 1993; Wong et al., 1997).

The LC50 values for these eight species of frogs were combined with those from the literature (Brain & Solomon, 2009) in a species sensitivity distribution (SSD). Plotting positions were calculated using standard procedures (Solomon & Takacs, 2002). The SSD data (Figure 1) illustrate that the larvae of frogs from Colombia are not more nor are they less sensitive than other frogs tested in other locations are to glyphosate formulations such as Roundup and Vision. This is consistent with the observed toxicity of the mixture to *X. laevis* (Wildlife International, 2006a, 2006b) where values were similar but slightly greater (less toxic) than those reported with the Vision formulation of glyphosate (Edginton et al., 2004). The 5th centile of the toxicity distribution was 692 µg a.e./L, suggesting that overall, 95% of larval frogs would have LC50s greater than this value.

CONCLUSIONS

The acute toxicity values determined in Colombian species of frogs suggest that sensitivity to Roundup-type formulations of glyphosate in these species is similar to that observed in other species tested in other locations (Brain & Solomon, 2009). There is no underlying assumption that would suggest that tropical species, such as those tested in Colombia, would have different sensitivity to pesticides such as those containing glyphosate and our observations are consistent with other observations on tropical and temperate species (Maltby et al., 2005). These data add to those currently in the literature and suggest that sensitivity of larval amphibians to Roundup-type formulations

TABLE 3
Toxicity Values for Colombian Frog Species Exposed to Formulated Glyphosate and Cosmo-Flux

Species	Slope[b]	Intercept[b]	LC1 (µg a.e./L)	95% Confidence interval (µg a.e./L)	LC50 (µg a.e./L)	95% Confidence interval (µg a.e./L)
D. microcephalus[a]	–	–	–	–	1200	–
R. typhonius[a]	–	–	–	–	1500	–
S. ruber	13.47	2.09	1103	716–1294	1642	1470–1783
H. crepitans	7.23	2.72	984	645–1225	2064	1835–2285
R. granulosa	9.09	1.62	1300	737–1632	2348	2036–2588
C. prosoblepon	7.18	2.24	1145		2414	
R. marina	9.75	0.74	1578	1122–1874	2733	2473–2982
E. pustulosus	8.78	1.09	1514	1040–1827	2787	2510–3057

[a]LC50 values estimated from a graph of concentration vs. percent response. Slope could not be calculated.
[b]Slope and intercept in log probit units.

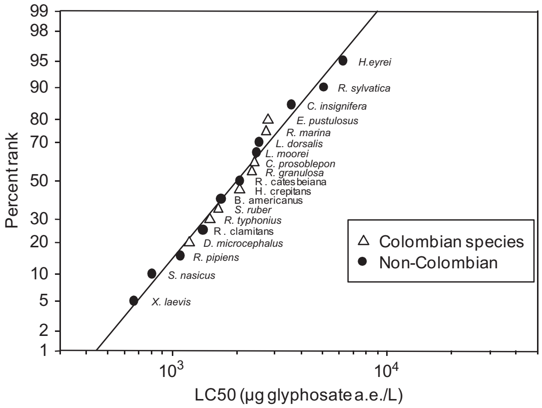

FIG. 1. Species sensitivity distribution of LC50 values for glyphosate plus Cosmo-Flux as used in the spraying of coca in Colombia in larval amphibians from Colombia and LC50 values for frogs from other locations to Roundup and Vision. Data for Roundup and Vision are from (Brain & Solomon, 2009).

spans a relatively narrow range. Toxicity of the mixture as used to spray coca was likely driven by the surfactant in the glyphosate formulation as the addition of Cosmo-Flux did not increase toxicity above those reported for Vision = Roundup (discussed earlier). The relatively low toxicity of Cosmo-Flux is consistent with the LC50 values reported in the fish, *Piaractus brachypomus*, which was 4,417 mg formulation/L in juveniles of 40 g mass (Rondon-Barragan et al., 2007).

Extrapolation of these toxicity values directly to the environment is inappropriate except for simple hazard ranking. In realistic environmental conditions where sediments and organic detritus are present in pools inhabited by amphibian larvae, concentrations of glyphosate and the POEA surfactant will decrease rapidly due to binding to sediments (Solomon et al., 2007) and this will likely reduce exposures and risks to amphibians. These hypotheses were tested and results are reported in a companion article (Bernal et al., 2009).

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Annex 131-G

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Toxicity of Formulated Glyphosate (Glyphos) and Cosmo-Flux to Larval and Juvenile Colombian Frogs 2. Field and Laboratory Microcosm Acute Toxicity

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The spraying of coca (*Erythroxylum coca*) with glyphosate (coca mixture, a combination of formulated glyphosate, Glyphos, and an adjuvant, Cosmo-Flux) in Colombia has raised concerns about possible impacts on amphibians. Although acute LC50 for 8 species of Colombian frogs ranged from 1.2 to 2.78 mg acid equivalents (a.e.)/L, these exposures were conducted in the laboratory in the absence of sediments and organic matter such as would occur under realistic field conditions. In order to assess the effects of overspray of frog habitat under field conditions, Gosner stage 25 tadpoles of *Rhinella granulosa, R. marina, Hypsiboas crepitans,* and *Scinax ruber* were placed in outdoor microcosms made from polyethylene plastic fish ponds (2.07 m in diameter, 37 cm high) in an experimental area in Tolima, Colombia. The bottoms of the microcosms were covered with a 3-cm layer of local soil and they were filled to a depth of 15 cm (above the sediment) with local spring water. After up to 100 tadpoles of each frog species were placed in the microcosms, they were sprayed with the coca mixture at concentrations greater and less than the normal application rate (3.69 kg glyphosate a.e./ha). Mortality at 96 h in the control microcosms was between 0 and 16% and LC50 values were between 8.9 and 10.9 kg glyphosate a.e./ha (equivalent to initial concentrations of 5963 to 7303 μg glyphosate a.e./L). Mortality >LC50 was only observed in the tested species when the application rate was >2-fold the normal application rate. In other experiments, juvenile and adult terrestrial stages of frogs were exposed by direct spraying to a range of concentrations of coca mixture. Juveniles and adults were exposed in plastic food containers (19 × 19 cm). The bottom of the container was filled with moistened soil and leaf litter to a depth of 1 cm and 0.5 cm, respectively. Mortality in the controls was low, from 0 to 10%, and from 0 to 35% at the normal application rate. LC50 values ranged between 4.5 kg a.e./ha and 22.8 kg a.e./ha, 1.5- to 6-fold greater than the normal application rate. Data indicate that, under realistic worst-case exposure conditions, the mixture of Glyphos and Cosmo-Flux as used for control of coca in Colombia exerts a low toxicity to aquatic and terrestrial stages of anurans and that risks to these organisms under field conditions are small.

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Although the toxicity of glyphosate formulations to larval amphibians has been relatively well characterized in the laboratory (Bernal et al., 2009), few studies have actually examined the effects of glyphosate-based herbicide formulations under realistic conditions or on terrestrial stages of amphibians. Field studies (Wojtaszek et al., 2004) conducted on larvae of *Rana clamitans* and *Rana pipiens* with the Vision formulation of glyphosate (equivalent to Roundup) showed that acute toxicity was strongly influenced by natural factors such as presence of sediment, aquatic macrophytes, and pH, generally resulting in lower toxicity relative to laboratory studies. Wojtaszek et al. (2004) reported 96-h LC50 values ranging from 2700 to 11,470 μg acid equivalents (a.e.)/L under conditions more relevant to the field. In addition, no significant differences in mean growth rates or maximum size at metamorphosis were observed for these two larval species even when exposed to concentrations as great as 14,300 μg a.e./L. These observations were consistent with an operational study (Thompson et al., 2004) where biomonitoring with caged amphibian larvae showed no significant responses of mortality (48 h) of either *R. pipiens* (p = .194) or *R. clamitans* larvae (p = .129). Mortality was also not significantly correlated with exposure concentrations for either amphibian species tested. Results suggested that exposures typically occurring in forest wetlands were insufficient to induce significant acute mortality in amphibian larvae.

In contrast, Relyea (2004) reported mortality and growth effects of Roundup Weed and Grass Killer on several amphibian species following exposures to four commercial formulations of pesticides (diazinon, carbaryl, malathion, and glyphosate) either alone or in combination. The glyphosate formulation used contained the ethoxylated tallowamine (POEA) surfactant and was tested at concentrations equivalent to either 740 or 1480 μg a.e./L, with Gosner stage 25 larvae exposed in 10-L plastic tubs housed outdoors for a period of 16 d. No significant effects on growth were observed for any species at ≥740 μg a.e./L. Significant levels of mortality were observed for *R. clamitans, R. catesbiana,* and *B. americanus* at 1480 μg a.e./L, while *Hyla versicolor* and *R. pipiens* showed no significant mortality at this exposure. In a subsequent paper (Relyea, 2005a), tadpoles of several amphibian species were exposed to the same glyphosate formulation already described (Relyea, 2004) in 1000-L cattle tanks serving as field microcosms. As Thompson et al. (2006) noted, this study utilized a single test concentration of 3800 μg a.e./L, equivalent to an application rate of 16 kg a.e./ha over water of 15 cm depth, both of which are in excess of typical environmental exposure concentrations or application rates. In a similar study, Relyea (2005b) examined the effects of the same formulation of glyphosate as reported in Relyea (2005c) at the same nominal concentration on tadpoles of three species when exposed in 1200-L cattle tanks with no soil, 19 L of sand, or 19 L of loam soil. The author reported no effect on the toxicity of glyphosate formulation by soil interaction. At this high test concentration, over a 20-d exposure period, the glyphosate formulation again resulted in a significant reduction in survival (<4%) in all 3 amphibian test species regardless of the soil treatment. Substantial mortality occurred within the first 24 h of exposure. This result contrasts sharply with other observations in the literature (Tsui & Chu, 2004; Wang et al., 2005) that demonstrated substantial reduction in acute toxicity of Roundup and the surfactant ethoxylated tallowamine (POEA) to test organisms in the presence of sediment. The discrepancy between these observations may have been the result of differences in the water–sediment ratios and the depth of the water above the sediment, which was greater in the study by Relyea (2005c).

Few studies reported toxicity of glyphosate formulations to terrestrial stages of amphibians. In a study in Australia, the 48-h LC50 values for Roundup herbicide tested against adult and newly metamorphosed *C. insignifera* ranged from 49,400 to 51,800 μg a.e./L and were greater than those reported for larvae (Gosner stage 25 for this species) (Mann & Bidwell, 1999). In a laboratory study (Relyea 2005b) in which juvenile terrestrial stages of 3 different species (*R. sylvatica, B. woodhousii fowleri, and H. versicolor*) were exposed to direct applications (1.2 mg a.e./m^2) in 10-L plastic tubs, 79% mortality was observed after only 24 h. The author stated that the formulated glyphosate was applied at a rate of 1.6 mg AI/m^2 (1.2 mg a.e./m^2), resulting from application of 6.5 ml of a formulation containing 1.9% glyphosate (IPA assumed) per tub (91 mg a.e./tub). Although the area of the tubs was not reported, to achieve the stated application rate with the volume of formulation used, a surface area somewhat greater than 75 m^2/tub would have been required. It was recently stated (Relyea, personal communication, September 2008) that there was a typographical error in the description of the experiment in the paper. This sentence has the typo: The "1.6 mg AI/m^2" should read "1.6 mL AI/m^2" and the rates of application were as recommended on the product label. However, active ingredient (AI) is normally expressed in terms of mass, not volume, and details of the methods are still incomplete. In addition, frogs were exposed on paper towels, a scenario not highly representative of field conditions.

A review of environmental effects of aerial applications of glyphosate to control illicit coca (*Erythroxylum coca*) pointed out that the Glyphos–Cosmo-Flux mixture as used in the spray program in Colombia could present a risk to native frog species exposed in shallow waters typically associated with wetland frog habitat (15 cm deep) (Solomon et al., 2007). However, this did not consider absorption and/or degradation of the glyphosate (AI) and the POEA surfactant in the presence of sediments, which was found to reduce exposures and, therefore, risk (Tsui & Chu, 2004; Wang et al., 2005). The study reported here was conducted to compare the toxicity of the mixture of Glyphos and Cosmo-Flux to larval amphibians as reported under laboratory conditions (Bernal et al., 2009) to responses under similar field conditions where sediments and suspended particles are present in shallow water systems. In addition, toxicity of the coca mixture was assessed in terrestrial stages of representative species under more realistic conditions in the presence of soil and leaf litter.

MATERIALS AND METHODS

Test Organisms

Four of the species previously tested in the laboratory (Bernal et al., 2009) were used for the field microcosm studies. They were collected from Potrerillo, Tolima, Colombia (4°14'N; 74°58'W) at 430 m altitude.

Testing Procedures—Microcosms

Six outdoor in-ground microcosms, constructed from food-grade high-density polyethylene plastic cattle tanks/fish ponds (2.07 m in diameter, 37 cm high), were placed in dug holes in the experimental area in Tolima. Microcosms were placed in a tree-shaded area where they were protected uniformly from full sunlight. Soil was backfilled around the pools (Figure 1) but the upper 22 cm of the wall was left uncovered to prevent water running into the pools. The bottoms of the microcosms were covered with a 3-cm layer of local soil and then filled to a depth of 15 cm (above the sediment) with local spring water

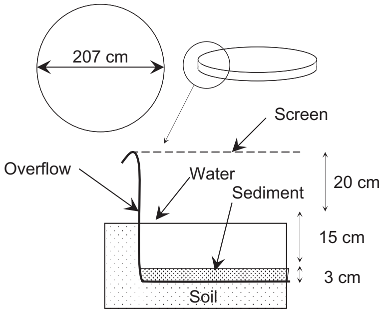

FIG. 1. Diagram of aquatic microcosm design.

with hardness equivalent to 41 mg $CaCO_{3/L}$ and an alkalinity equivalent to 51 mg $CaCO_{3/L}$. A screened overflow opening at 15 cm above the sediment allowed overflow in the case of rainfall. After filling with water, microcosms were covered with black plastic shade cloth (3 mm mesh) stapled to a wooden frame to exclude predators such as dragonflies and birds. The microcosms were allowed to stabilize for 4–5 d. Prior to adding the tadpoles, a fine screen nylon cloth (0.5 mm mesh) was placed in the microcosms and pressed into the sediment. This was done to facilitate collection of larvae after exposure.

In the first experiment, 100 Gosner stage 25 larvae of *Rhinella granulosa* and *R. marina* each were placed in each microcosm with a rate of biomass loading approximately of 0.0122 g/L, below the 0.6 g/L as recommended in ASTM guidelines (ASTM, 1998). Application rates of Glyphos–Cosmo-Flux mixture (coca mixture as is fully described in the companion article, Bernal et al., 2009) were selected on the basis of preliminary experiments. Immediately after adding the frog larvae, the microcosms were sprayed with the coca mixture at a range of concentrations equivalent to 0 (control) up to 29.52 kg glyphosate a.e./ha. The Glyphos and Cosmo-Flux formulations were those used previously (Bernal et al., 2009), and amounts were measured with a positive displacement pipette and then mixed with 500 ml water. The entire amount was sprayed over the pools, at a height of approximately 50 cm, with a small hand-held pump-up garden sprayer. Spray drift was minimized by (1) setting the sprayer to apply large droplets, (2) spraying in the absence of wind, and (3) spraying in circle from the center of the pool to the rim, but never over the edge. In addition, 20 cm of the wall of the pool was above the water level, which would have reduced loss of pesticide though spray drift. Based on spray drift tables for hand-held (pedestrian) sprayers using small droplet sizes for insecticides and fungicides (European Commission, 2000), loss to drift is estimated to be less than 5%. Water in the microcosms was sampled at 2, 24, 48, and 96 h after application and the concentration of dissolved oxygen, pH, and temperature were measured. After 96 h of exposure, the 0.5-mm nylon mesh was carefully removed from microcosms, and the tadpoles were transferred to a smaller container, identified, and counted. Missing animals were assumed to be lost in the recovery process or by decomposition after dying. Mortality was based on the number of dead and missing animals compared to the total animals added to the microcosm at the initiation of the exposure.

For the second experiment, the water and sediment were removed from the microcosms and replaced with fresh material. The preceding procedure was repeated but with larvae of *H. crepitans* (100 animals per each treatment) and *S. ruber* (65 animals per each treatment) with a rate of biomass loading approximately of 0.0153 g/L. Because of particulates present in the water, enzme-linked immunosorbent assay (ELISA) analysis was not possible and nominal initial concentrations were calculated from the application rates for comparison to the laboratory observations (Bernal et al., 2009).

Testing Procedures—Terrestrial Stages of Frogs

Juvenile terrestrial stages of frogs were obtained by raising frogs collected in the field under laboratory conditions as previously described (Bernal et al., 2009). In addition, small adults of two species of frogs were collected from the field for these experiments. Species used and sources are listed in Table 1. Polyethylene plastic food containers, 19 × 19 cm (internal surface area = 361 cm^2) and about 2.3 L capacity and with a tight-fitting lid in which a 7 × 7 cm mesh-screened ventilation opening was made, were used as terrestrial exposure microcosms. Soil and leaf litter, obtained from the botanical garden of the University of Tolima, a nonagricultural area, was added to a depth of 1 cm and 0.5 cm, respectively. The soil and leaf litter were moistened with distilled water to about 90% of holding capacity, giving a relative humidity from 80 to 95% in the containers. The chambers were indiscriminately positioned by treatment group in an air-conditioned laboratory where they were maintained at a temperature of 25 ± 2°C and 12:12 h light/dark cycle throughout the test period.

Based on preliminary tests, frogs were exposed to a geometric series of Glyphos–Cosmo-Flux concentrations higher and lower than the field application rate (3.69 kg a.e. glyphosate/ha). A primary stock solution was freshly prepared by mixing 30 ml Glyphos and 0.69 ml Cosmo-Flux (delivered by positive displacement pipette) with 500 ml water by inversion to give a concentration that would provide an application rate of 29.52 kg a.e. glyphosate/ha when 5 ml was sprayed over the area of the container (361 cm^2). The stock solution was serially diluted to provide application rates equivalent to 14.76, 7.38, 3.69, and 1.85 kg a.e. glyphosate/ha and one water control.

Two duplicate test chambers were used for each treatment rate and the control group. Groups of 10 frogs (*R. typhonius, R. granulosa*), 9 frogs (*R. marina* and *S. ruber*), and 5 frogs (*C. prosoblepon*, *E. pustulosus, P. taeniatus,* and *D. truncatus*) were impartially assigned to each test chamber for a total of 20, 18, and 10 frogs per concentration, respectively. Because

TABLE 1
Juvenile and Adult Frogs Used in the Terrestrial Microcosm Exposures

Species	Location of collection	Mean mass in mg (95% CI)
Rhinella typhonius (Linnaeus, 1758)	Ibagué (4°25'N; 75°12 W)	0.047 (0.042–0.051)
R. granulosa (Spix, 1824)	Potrerillo (4°14'N; 74°58'W)	0.063 (0.060–0.066)
R. marina (Linnaeus, 1758)	Potrerillo (4°14'N; 74°58'W)	0.114 (0.110–0.117)
Engystomops pustulosus (Cope, 1864)	Ibagué (4°21'N; 75°06'W)	0.175 (0.165–0.185)
Scinax ruber (Laurenti, 1768)	Potrerillo (4°14'N; 74°58'W)	0.182 (0.172–0.191)
Centrolene prosoblepon (Boettger, 1892)	Falan (5°07'N; 74°58'W)	0.251 (0.241–0.261)
Pristimantis taeniatus[a] (Boulenger, 1912)	Ibagué (4°25'N; 75°12 W)	0.853 (0.821–0.884)
Dendrobates truncatus[a] (Cope, 1861)	Potrerillo (4°14'N; 74°58'W)	1.583 (1.514–1.651)

[a]Adult frogs.

of lack of availability, not all species could be tested in larval as well as terrestrial stages. For quality control purposes, frogs were weighed as a group before being placed in the test chambers. At the end of the study, they were weighed individually to calculate the average body mass. Body mass was approximately similar between treatments. There are no guidelines for biomass loadings when testing terrestrial stages of frogs, but mortality was <10% in the controls in these studies, suggesting that the loadings were not excessive. Test solutions were freshly prepared and sprayed on the frogs using a modified domestic hand sprayer fitted to a test-tube reservoir to allow complete spraying of a total volume of 5 ml. This volume of spray solution was sprayed on the frogs, starting with the water control and then from the lowest to highest concentration. The sprayer was rinsed with clean water between tests. Observations of mortality and other signs of toxicity were made at 4, 24, 48, 72, and 96 h after test initiation. All frogs were fed ad libitum with small insects once per day during the experiments

Statistical Analyses

As in the laboratory studies (Bernal et al., 2009), LC1 and LC50 values were calculated using the U.S. EPA Probit Program Version 1.5 (U.S. EPA, 1994). Where insufficient data were available for the Probit program (no or only one concentration with a response between 0 and 100%), the LC50 was estimated by interpolation from a graph of percent concentration versus response.

RESULTS AND DISCUSSION

Water Quality

The concentration of dissolved oxygen in the microcosms (Figure 2) was different in the two experiments. Concentration at 0 h was generally lower in experiment 1 than in experiment 2. However, in both experiments, oxygen concentration declined over the exposure period in the microcosms treated at the greater rates of glyphosate, particularly at 14.7 and 29.5 kg glyphosate a.e./ha. The reason for this is uncertain but may be due to increased oxygen demand as a result of the death of larvae at these treatment rates or because the large amounts of glyphosate stimulated microbiological activity and produced an oxygen demand. This was only observed at rates of application that were greater than those used in the field (3.69 kg glyphosate a.e./ha). The pH in the microcosms was generally more consistent over the length of the exposures (Figure 2). Temperatures in the microcosms were consistent between microcosms (Figure 2). As expected, temperature showed no response to treatment concentration.

Responses in the Aquatic Microcosms

Mortality or loss of frog larvae in the control microcosm in all experiments was between 0 and 16%. In *R. granulosa,* there was a greater mortality (or loss), probably due to its smaller body size, which may have reduced efficiency of recovery of larvae. LC50 values in the treated microcosms were approximately similar between species (Table 2). *Rhinella marina* was the most sensitive species, but large mortalities were not observed until the application rate exceeded fourfold the normal rate of 3.69 kg glyphosate a.e./ha, when more than 80% mortality was observed. An LC50 could not be calculated for *S. ruber* but was estimated from graphical interpolation to be about 10.3 kg glyphosate a.e./ha (initial concentration of 6900 μg glyphosate a.e./L), almost threefold greater than the normal application rate. Larvae of *R. granulosa* and *H. crepitans* were less sensitive (Table 2,) and significantly higher mortalities were not observed until the application rate was about 14.8 kg glyphosate a.e./ha (initial concentration of 9916 μg glyphosate a.e./L).

In all cases, sensitivity of frog larvae in the field microcosms was less than in laboratory toxicity tests (Bernal et al., 2009). This is consistent with observations in the literature where both Roundup (Tsui & Chu, 2004) and surfactant POEA (Wang et al., 2005) were less toxic in the presence of sediment, likely as a result of rapid binding to sediment and/or breakdown by microbes, thus reducing exposures (and apparent toxicity) in the water column.

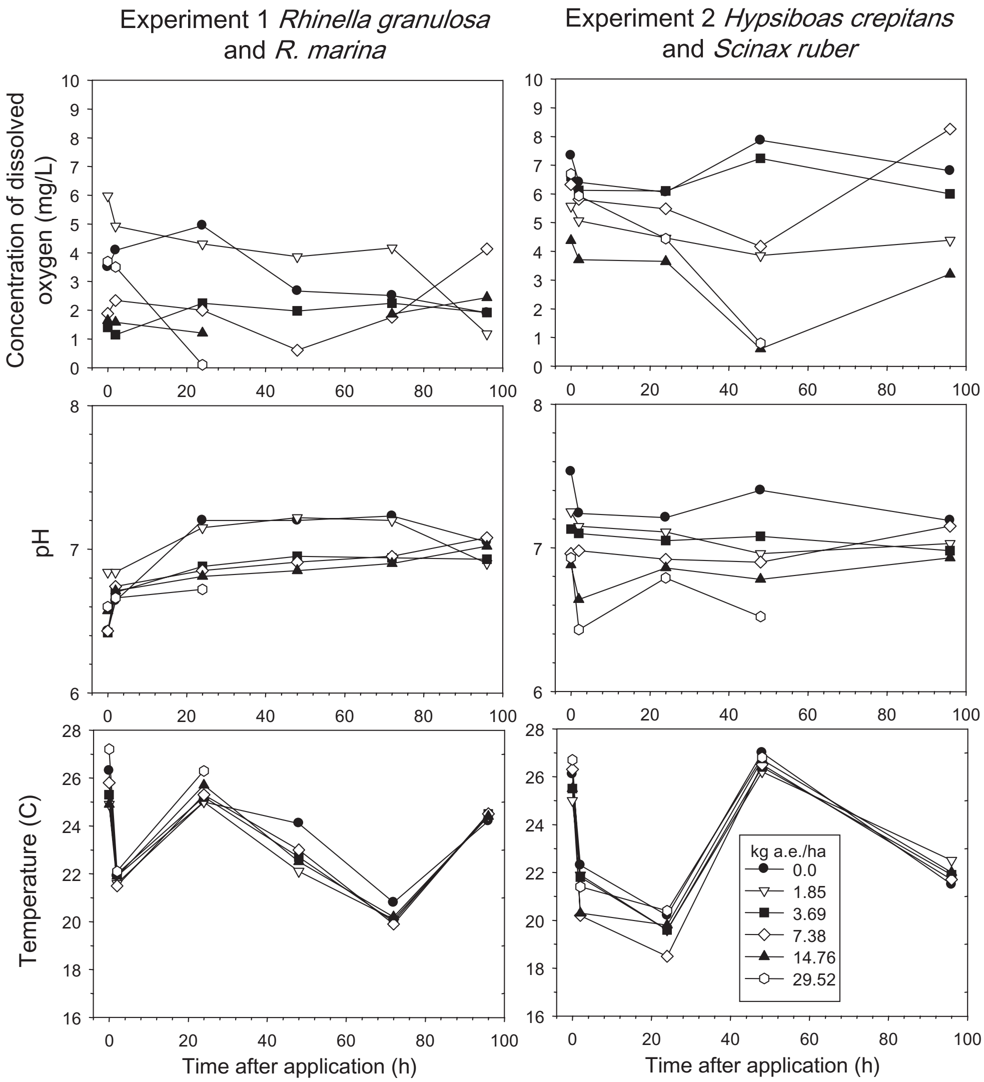

FIG. 2. Concentration of dissolved oxygen, pH, and temperature in the aquatic microcosms after treatment with various rates of the coca mixture of Glyphos and Cosmo-Flux. Application rates are of glyphosate (a.e.) in the mixture.

Responses in the Terrestrial Microcosms

Observations of frogs revealed signs of toxicity such as lack of normal movement or slow movement. In some frogs, the hind limbs were extended and thus were unable to walk. In *S. ruber* and *P. taeniatus,* a milky secretion from the skin was observed. In general, most of the adverse responses were expressed within 24 to 48 h of test initiation. Mortality data for the terrestrial stages of the eight species of frogs (Table 3) are presented in terms of nominal application rate (kg a.e. glyphosate/ ha) to allow for comparison to field application rates. Mortality in the controls was low, from 0 to 10%.

The range of LC50 values for adults (5-fold) was greater than that observed (Bernal et al., 2009) in larvae (2.3-fold), and a cumulative distribution of LC50 values (Figure 3) suggested

TABLE 2
Mortality for Colombian Tadpole Species Exposed to Mixtures of Glyphos and Cosmo-Flux in the Aquatic Field Microcosms

	Percent mortality at glyphosate application rates (kg a.e./ha)						LC values in kg a.e./ha (µg a.e./L)[a]	
Species	0	1.85	3.69	7.38	14.76	29.52	LC1	LC50
R. marina	10	13	25	41	82	100	2.4	8.9 (5963)
S. ruber	4.6	4.6	15.4	12.3	100	100	—	10.3 (6900)
R. granulosa	16	8	21	19	94	100	6.4	10.7 (7169)
H. crepitans	0	0	3	3	86	100	4.8	10.9 (7303)

[a]Nominal initial concentration estimated from application rate and depth (15 cm) of water with complete mixing but no adsorption to sediment or particulates.

TABLE 3
Mortality of Juvenile and Adult Stages of Colombian Frog Species Exposed to Mixtures of Glyphos and Cosmo-Flux in Terrestrial Microcosms

	Percent mortality at glyphosate application rates (kg a.e./ha)						LC values (kg a.e./ha)	
Species	0	1.85	3.69	7.38	14.76	29.52	LC1	LC50
C. prosoblepon	0	0	30	90	100	100	1.97	4.5
P. taeniatus[a]	0	0	20	70	—	—	1.93	5.6
R. granulosa	10	35	35	55	90	100	—	6.5
S. ruber	0	17	33	50	56	95	0.32	7.3
R. typhonius	10	10	15	35	50	80	1.56	14.8
E. pustulosus	0	0	0	0	30	80	7.02	19.6
R. marina	0	0	0	6	22	67	5.08	22.8
D. truncatus[a]	0	0	0	0	—	—	>7.38	>7.38

[a]Adult forms.

2 groupings of species in terms of sensitivity. Among the juveniles, the most sensitive was *C. prosoblepon* and the least sensitive was *R. marina*. Of the adults, *P. taeniatus* was sensitive and *D. truncatus* was very tolerant to the mix of Glyphos–Cosmo-Flux (Table 3).

There a number of possible reasons for these differences in sensitivity. It is possible that the higher sensitivity of *C. prosoblepon* and *P. taeniatus* is due to their thinner skin, which is smooth, translucent, and probably more permeable. In particular, this may also explain the greater sensitivity of *C. prosoblepon,* the internal organs of which are visible through the transparent underside, a feature that gives the common name of glass frogs to this species and others of the same family. However, *D. truncatus* also has thin skin and was insensitive. The higher sensitivity for *R. granulosa* may be attributable to small body mass (Table 1) and greater surface area to volume ratio. *Scinax ruber* had a larger body mass (Table 1) and smaller surface area to body mass ratio, but its sensitivity to glyphosate-Cosmo-Flux was similar to that of *R. granulosa*. In this case, it is also possible that the increased sensitivity is related to its thin skin. The lower sensitivity of *R. marina* may be attributable to the greater body mass of juveniles (Table 2) and to its thicker skin, and for *D. truncatus* to the greater body mass. There was also no obvious relationship between sensitivity and preferred habitat, which is related to ability to tolerate loss of water (Figure 1), but *D. truncatus* may be generally less sensitive to pesticides as it is routinely collected from agricultural areas where pesticides are used.

Overall, in 5 of 8 experimental species, mortality at the rate of 3.69 kg a.e/ha used in eradication spraying was between 15% and 35% and LC50 values were between 1.2- and 6-fold greater than the application rate for eradication spraying. Extrapolation of the species sensitivity distribution (Figure 3) gave a 5th centile intercept of 2.2 kg glyphosate a.e./ha (for the coca mixture), suggesting that >95% of the LC50 values for terrestrial frogs would not be exceeded at application rates less than this value.

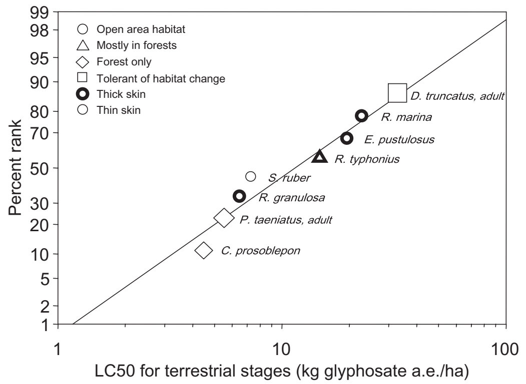

FIG. 3. Cumulative frequency distribution of acute LC50 values for terrestrial stages of frogs sprayed with the mixture of Glyphos and Cosmo-Flux used in eradication spraying. The relative mass of the frogs (Table 1) is indicated by the size of symbols. The value for *D. truncatus*, which was very insensitive (Table 3), is plotted for information but was not used in the regression.

CONCLUSIONS

The results of the aquatic and terrestrial microcosm studies show that responses of frogs under realistic field exposure conditions are less than would be predicted from laboratory toxicity studies and less than reported by some authors for other species. The reason for this is likely that glyphosate and the surfactant POEA adsorb rapidly to sediments and organic matter that is present in natural systems or are rapidly degraded. Although studies on the influence of the depth of the surficial water on the fate of glyphosate and POEA have not been conducted, this process is probably more rapid in shallow waters where diffusion and mixing would be expected to be more rapid. This may explain differences between the results observed in this study and observations of mortality in deeper water reported elsewhere (Relyea, 2005a, 2005c). Mixing in deeper water would be expected to be less rapid and adsorption to sediments and organic matter would be delayed for long enough that exposures in the surfice water might exceed thresholds of toxicity. Direct comparison of the two studies is not possible as the depths of water were different. The importance of the interactions between water depth, type of sediment, content of organic matter, and microbiological activity needs to be addressed in future environmental fate studies with pesticides and surfactants that adsorb strongly to sediments. Interactions between water-quality parameters such as concentrations of divalent cations, oxygen, and hydrogen ion (pH) may be an important area of general research as suggested in laboratory investigations on pH interactions with Vision in frog larvae (Edginton et al., 2004).

The differences in sensitivity between species of terrestrial stages of frogs were possibly due to a combination of differences in body mass (surface area to volume ratio) and skin permeability. However, these factors and others, such as habitat preference, did not fully explain the apparent bimodal distribution of sensitivity (Figure 3). A greater understanding of the toxicokinetics of uptake of the formulation may explain reasons for differences in susceptibility between species and would be an interesting subject for future work that may explain these differences.

For all species tested, the responses to the mixture of Glyphos–Cosmo-Flux were not large at the rate of 3.67 kg a.e./ha as used in Colombia for eradication spraying. The terrestrial microcosm experiments showed that juveniles of *S. ruber* and *R. granulosa* were relatively less tolerant to glyphosate–Cosmo-Flux mixture than their tadpoles. However, the results of *R. marina* (Tables 2 and 3) showed the opposite. In Australian frogs, Mann and Bidwell (1999) found that adults and new metamorphs of *C. insignifera* were less sensitive to Roundup than tadpoles, but this study was carried out under laboratory conditions; thus, these results are not directly comparable with ours. Data showed that mortalities ≥50% for tadpoles, juveniles, and adults were only observed at rates of application greater than the 3.69 kg glyphosate a.e./ha used in eradication spraying in Colombia.

Risk in the field will likely be lower because of less exposure. Sites >5 m outside the spray swath and with no vegetative cover would receive deposition rates (Hewitt et al., 2009) less than the LC1 observed in microcosms. For terrestrial species, assuming no vegetative cover, none of the observed LC50 values would be exceeded directly under the spray swath. A 10-m margin downwind of the spray swath would be protective of all measured LC1 values. Under actual conditions of use, interception by trees and other vegetation, such as observed in forestry spraying (Thompson et al., 2004) and also occurs under Colombian conditions (Hewitt et al., 2009), would further reduce exposures and subsequent risks. Multiple applications of eradication sprays are unlikely in the timeframe for complete dissipation of glyphosate and surfactants from water and/or soil. Sprays are very accurately applied and only one pass is made over the field (Solomon et al., 2007), minimizing the likelihood of a double application. While there may be small risks to frogs in unvegetated areas in coca fields that are directly oversprayed, the risks from exposures to other more toxic pesticides used by coca growers are much greater (Brain & Solomon, 2009). When considering the small area of Colombia that is actually sprayed each year (< 0.1% Solomon et al., 2007) and that frogs are not exclusively associated with coca growing (Lynch & Arroyo, 2009), it can be concluded that the Glyphos–Cosmo-Flux mixture as used in Colombia for eradication of coca presents a slight but not ecologically significant risk to larval and terrestrial stages of anurans.

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Annex 131-H

J. D. LYNCH ET AL., "RISKS TO COLOMBIAN AMPHIBIAN FAUNA FROM CULTIVATION OF COCA (*ERYTHROXYLUM COCA*): A GEOGRAPHICAL ANALYSIS"

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Risks to Colombian Amphibian Fauna from Cultivation of Coca (*Erythroxylum coca*): A Geographical Analysis

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The Colombian amphibian fauna is among the richest known in the world, with about 20 species of salamanders (order Caudata), 35 of the limbless caecilians (order Gymnophiona), and more than 700 species of frogs and toads (order Anura) recorded from localities within the country. The potential effects of exposure to glyphosate on amphibians arising from production of illegal crops (coca) were examined. The analysis was based on (1) behavior and ecology of species and (2) proximities of actual museum records to localities in which illegal crops are being grown and the subset of those that have been sprayed with glyphosate. Based on data on the location of amphibians collected in Colombia, records were obtained for 193 species (28% of the national diversity) of frogs and toads found in localities within 10 km of areas where coca is grown. Further analyses with ARC MAP software allowed for measurement of the direct distance separating collection locations for frogs, known coca fields, and areas where aerial spraying was being conducted. Records in or near coca fields included data for 11 of 13 families of frogs and toads known to be present in Colombia. Only Ceratophryidae and Pipidae were not reported from these locations and appear not to be at risk. For eight species (*Dendrobates truncatus*, *Craugastor raniformis*, *Pristimantis gaigeae, Smilisca phaeota, Elachistocleis ovale, Hypsiboas crepitans, Trachycephalus venulosus*, and *Pseudis paradoxa*) selected to represent several habitat preferences and life-cycle strategies, large areas of their distributions lie outside coca production regions and their populations as a whole are at low risk. For a limited number of species that barely enter Colombian territory, the consequences of coca production may be more serious and may have placed several species of frogs at risk. These include *Ameerega bilingua, Dendropsophus bifurcus, Pristimantis colomai, P. degener, P. diadematus, P. quaquaversus, P. variabilis,* and *Trachycephalus jordani.* Other species may also be at risk but exact numbers are unknown since few investigations were undertaken in these areas during the past 30 yr. The main ranges for these species were assumed to be in Ecuador.

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Currently the herbicide glyphosate (Glyphos) is used to control coca (*Erythroxylum coca*) production through an aerial spray eradication program (Solomon et al., 2007). Several concerns have been raised regarding the spray control program, ranging from peripheral crop damage to adverse environmental effects. As larval stages of amphibians are sensitive to formulated glyphosate (Bernal et al., 2009a), these organisms may be particularly at risk. In addition, the pesticides used by growers in the production of coca also present a risk to larval amphibians, should they be found in or close to the edge of coca fields (Brain & Solomon, 2009).

All amphibians have permeable skins and hence are especially susceptible to application of extraneous chemicals, such as pesticides, to their environment (Stebbins & Cohen, 1995). Pathways of exposure in terrestrial amphibians include direct contact of spray droplets on the exposed skin or through contact with sprayed surfaces, such as the animals moving over leaves that have been sprayed. In addition, contamination of water through direct overspray or spray drift may result in exposure to aquatic larval stages.

The behavior of most amphibians reduces the risk of direct exposure to spray. With few exceptions, Colombian amphibians are nocturnal organisms, emerging when the air temperatures have fallen and the relative humidity of the air exceeds the dew point. Aside from Dendrobatids, a frog family composed of nearly exclusively diurnal species, the nocturnal activity cycles of amphibians render them least likely to experience direct application of the sprays. Exceptions are some species that "sleep" in exposed positions—the *Rana platanera,* known to Colombians visiting the lowlands adjacent to the eastern cordillera, is a species (actually, a pair of species) with many casual observations of frogs "sleeping" on leaves in full sunlight—as well as juveniles of many species and tadpoles of some species. Since eradication spraying is only conducted in daylight and early in the day (Solomon et al., 2007), the most likely pathway of exposure is via contact with sprayed surfaces. Glyphosate and the polyethoxylated talowamine (POEA) surfactant with which it is formulated are strongly adsorbed to soils and organic matter (Tsui & Chu, 2004; Wang et al., 2005), reducing likelihood of exposure from these sources; however, contact with wet leaves may allow exposure. Other more toxic pesticides, such as are used by coca growers (Brain & Solomon, 2009), may not be strongly absorbed and may be more bioavailable by this route.

COCA PRODUCTION

In Colombia, coca plants grow in areas that were once wet lowland tropical forest. The plant is a shrub and grows to between 1.5 and 2 m. In most cases the coca plants are grown in clear-cut areas, but this illicit crop may be found in the middle of other crops such as banana plantations with the objective of avoiding detection. The most obvious characteristic of coca cultivation is the degradation of ecosystem. The farmers deforest from the canopy to the leaf litter in order to prepare the land for a coca plantation (see Anonymous, 2006, p. 49), leaving the habitat completely destroyed by physical activities.

Coca production results in the alteration of the natural habitat (Brain & Solomon, 2009), which may exert significant adverse effects on frogs. Illustrations in the book *Colombia/Monitoreo de Cultivos de Coca* (Anonymous, 2006, pp. 21, 23, 25, 27, 29, 31, 33–35) graphically show the degree of environmental alterations and/or destruction that accompanies coca plantations. Alteration in the habitat may exert significant adverse effects on frogs, and these are illustrated in a study conducted in the immediate vicinity of Leticia (the southeastern most city of Colombia (Lynch, 2005). A number of species of frogs and toads were detected from undisturbed habitats within a small area (approximately 5 km × 5 km) following an intensive inventory conducted during 3 mo early in 2003. The inventory revealed the presence of 96 species and additional efforts during the next 3 yr raised the number of captured species to 98. Beyond localities representing "natural" habitats, occasional samples were gathered along a transect defined by degree of intervention (or habitat modification): (1) Least intervened were the *chagras* (small holdings) of the indigenous communities of Huitotos and Ticunas, with more intervention (or habitat modification) evident at (2) abandoned farms of *colonos* (areas recovering to the native habitat), (3) active farms of *colonos*, (4) military installations, and (5) the green spaces within the urban center of Leticia. Thirty species were found in human communities as well as in areas undergoing recovery. About 20 species were found in active farms and in some areas of military installations. In military installations more removed from natural forests (for example, those immediately adjacent to Leticia), only 12 species of frogs and toads were found. In the parks of the city (and in undeveloped lots), only 6 species of frogs were detected.

These data provide a necessary background against which one can assess the effect of coca production (as an illegal crop) on the Colombian amphibian fauna. Cultivations of coca display alterations that are even more severe than *chagras* of the indigenous communities in the area of Leticia (Lynch, 2005). Using this as a basis for comparison, cultivation of coca is likely to reduce the resident frog fauna by approximately 90% (see earlier discussion), prior to consideration of any effects of glyphosate spraying upon the amphibian fauna.

Habitat alterations sometimes favor some amphibians. Based on a study of *Pristimantis*[*] (Lynch, 1998) in the Cordillera Occidental (an area that was originally covered with evergreen montane forests) and on the fauna in the immediate environs of Leticia (Lynch, 2005), an area that originally was wet lowland forests, there are some species in each fauna that appear to have benefitted from human intervention (or habitat modification). These species become common locally in areas that have experienced complete or partial removal of the natural vegetation, but that are rarely encountered during intensive searches within natural (forested) habitats. These species (including *Pristimantis brevifrons, P. erythropleura, P. palmeri,* and *Craugastor raniformis*) perhaps become more abundant because they have been relieved of the effect of competition with other species (most species in each community react adversely, in terms of numbers or visibility, to habitat alteration). However, additional clues are available from other species, such as *Trachycephalus venulosus,* a canopy-dwelling frog in lowland forests in Colombia. Although the adults live within the confines of the forest, the species appears to need "open" habitats in which to breed. Presumably, in times before human intervention (or habitat modification) became common, these frogs used clearings generated by the occasional tree-falls in natural forest ecosystems; now, of course, they have many more opportunities granted by the creation of pastures and croplands.

The objective of this study was to evaluate the likely risks to the Colombian amphibian fauna from cultivation of coca. Extensive occurrence records of the Colombian amphibian fauna are held at the Instituto de Ciencias Naturales, Bogotá.

*The classification of amphibians is subject to much debate and instability at this time and the authors acknowledge that nomenclature will change in the near future. The nomenclature used in this paper is current at this time except that Hedges et al. (2008a) is not followed in their partition of the family Brachycephalidae into four families because that study was a phenetic one masquerading as a phylogenetic study (furthermore, all new names proposed therein are not available because the paper did not meet Article 13.1.1; ICZN, 1999), and Wiens et al. (2005, 2007) rather than Frost et al. (2006) as concerns the Hemiphractidae were followed.

In order to evaluate the likely risks of coca production to this faunal group, the spatial records of occurrence for all species were compared with known areas of coca production and locations of eradication spraying. In addition, the known ecological and behavioral traits of species were reviewed, in relation to habitat loss and potential exposure to chemicals used for coca production.

MATERIALS AND METHODS

Identification of Groups of Amphibians at Risk

Based on habitat use and behavior, some amphibians are unlikely to be affected by coca production or eradication spraying. Caecilians are unlikely to be affected by application of glyphosate, because most are subterranean species, surfacing especially on rainy nights in search of earthworms. Three species of caecilians are aquatic and are distributed in larger rivers as well as streams and *ciénagas*, areas not used for coca production and hence unlikely to be exposed to pesticides.

The salamander fauna of Colombia is small and these species are distributed in the lowlands up to the *páramos*, about 3200 m above sea level (a.s.l.). Aside from a few species restricted (or nearly restricted) to the treeless *páramo* habitats, all of these animals require dense forest environments, rendering them relatively protected from pesticides used in coca production or eradication. Similarly, all salamanders are species with direct development, and embryos (or "eggs") are found in leaf litter or in epiphytes (again, with a minimal environmental exposure to extraneous chemicals).

The largest proportion of amphibians in Colombia is made up of frogs and toads, distributed across the full spectrum of the wet to dry habitats and from sea level to at least 4350 m a.s.l. Of the families of frogs and toads currently recognized (Wiens et al., 2005; Frost et al., 2006; Grant et al., 2006) for Colombia, the largest is the Brachycephalidae (38%), followed by the Hylidae (19%), and the Bufonidae (9%), Centrolenidae (10%), and Dendrobatidae (10%). The other 8 families are small (2 to 30 species) with a sharply reduced proportionality—each less than 1% to as much as 3% of the Colombian frog fauna (Aromobatidae, Ceratophryidae, Hemiphractidae, Leiuperidae, Leptodactylidae, Microhylidae, Pipidae, and Ranidae).

More than one-third of Colombian frog species belong to the family Brachycephalidae. Brachycephalid frogs are sensitive to available moisture and are absent (or nearly so) from the dry areas of Colombia (eastern Llanos, Caribbean lowlands, inter-Andean valleys, and the rain-shadows of the dry enclaves distributed along the Andean cordilleras). Aside from species restricted in distribution to above tree line (the *páramo* species), all native species of Brachycephalids are denizens of forests. With these exceptions, Brachycephalids in Colombia are usually found in forested habitats, substantial modification of which results in the species becoming rare (or disappearing). In Colombia, there are species of Brachycephalids in the lowlands, but, aside from the Pacific lowlands of Colombia, the species are rarely encountered (e.g., are not captured and/or seen every night). At least 90% of the Brachycephalids of Colombia are restricted in distribution to the Andean cordilleras (and Sierra Nevada de Santa Marta) and have small distributional areas, arranged in altitudinal bands on the flanks of the mountains (Lynch, 1998, 1999b). Brachycephalids are also atypical of the North Temperate vision of proper frogs and toads in that these frogs are direct developers (no tadpole stages). The remaining species of Colombian frogs and toads are divided among 12 families, most of which include substantial fractions of the local diversity with "typical" life histories (e.g., aquatic tadpoles) and may be exposed to pesticides in both the terrestrial and aquatic stages. The following sections review the distribution of Colombian frogs and toads in relation to general distribution.

About 60% of the Colombian frog fauna is confined to the Andes and Sierra Nevada de Santa Marta (Lynch et al., 1997) and nearly all of the species endemic to the country occur in the Andean zone or in the Chocó biome. Those high levels of endemicity result mostly from the fact that Andean species tend to have small distributional areas, whereas lowland species tend to be more widely distributed. Coca cultivation (as an illegal crop) is not randomly distributed in the country (Figures 1–4 in this article; and see Anonymous, 2006, figures on pp. 9 and 12 and see p. 80 for the geographical pattern of distribution for aerial spraying) and is more prevalent in the lowlands. Those cases in which a high proportion of known localities for some frogs species (in Colombia) are at, near, or surrounded by coca production are restricted to species having only a small part of their distributions within Colombia. For these species, the high density of coca production in the lowlands of western Caquetá and Putumayo plus eastern Cauca poses a high risk of exposure to pesticides used for production and eradication of coca. The same is true for the lowlands of western Nariño.

For the other 12 families of frogs and toads, Lynch (1999a) noted that most groups of frogs and toads were sorted into Andean (including the lowlands of the Pacific) or lowland groups and that this sorting extended virtually to the level of genus. Three other families (Aromobatidae, Bufonidae, and Dendrobatidae) have significant representation in both elevated zones and in lowlands, whereas the remaining families may be considered as either Andean or of lowlands. The dominant mode of reproduction for these 12 families (excepting Hemiphractidae) includes an aquatic tadpole stage.

The predominant species family (Hylidae) for the lowlands has a minor Andean component; this family also has a significant representation (19% of species recorded for Colombia) in the country. All species of Hylidae also are "typical" frogs for having aquatic tadpoles. Within this family, many species exhibit a low fidelity to forests, especially during their reproductive seasons. This lack of fidelity to conditions that might reduce exposure to pesticides used in the production and eradication

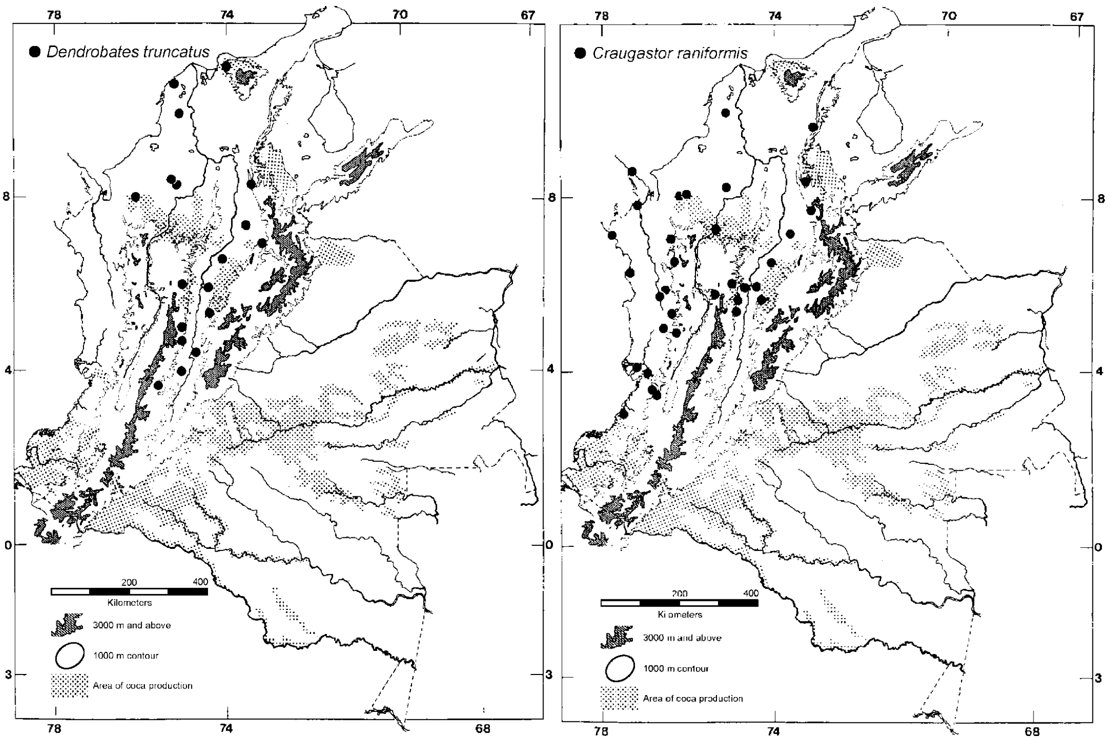

FIG. 1. Distribution of *Dendrobates truncatus* (a Colombian endemic) and *Craugastor raniformis* based on records documented in the Collection of Amphibians of the Instituto de Ciencias Naturales.

of coca raises their likelihood of experiencing negative effects from coca production. In addition, there are many species "typical" of open (naturally or produced by intervention (or habitat modification)) situations, that is, not covered by forests.

The true toads (family Bufonidae) are better represented in the Andes (and Sierra Nevada de Santa Marta) than in lowlands. The Andean species either have tadpoles adapted to currents (*Atelopus*) or exhibit direct development (*Osornophryne, Rhamphophryne*). *Atelopus* deposit their egg masses in the water, usually attached to the undersurfaces of rocks. The habitat (above the altitude where coca is grown) and reproductive biology reduce exposure to pesticides used in production and eradication of coca. In the lowlands (and the lower parts of the mountain slopes), one finds the more "typical" toads (*Chaunus, Dendrophryniscus, Incilius, Rhaebo,* and *Rhinella*) with tadpoles either in ponds or in slow-moving streams. Except for the *Chaunus,* these are organisms of heavy native forests and, by virtue of living beneath an undisturbed canopy, are unlikely to be exposed to pesticides used in production and eradication of coca.

The Glass frogs (family Centrolenidae) are typical of streams in the Andes and the Sierra Nevada de Santa Marta. In addition, these are organisms that require some measure of the original vegetation (but are tolerant of gallery forests within pasturelands). The majority of species deposit their embryos on vegetation (above a stream) where the initial week or so of development occurs. Subsequently, the tadpoles fall into a stream and resist the current by hiding in vegetation within the stream or by burrowing into the substrate. These tadpoles are active at night. Centrolenid frogs are also are present in most wet lowland forests of Colombia but are rarely collected there, presumably because the adults occupy the canopy. Once again, the requirement of forest cover reduces the likelihood of exposures to pesticides used in production and eradication of coca. However, the fact that they survive (apparently well) in mere remnants (gallery forests) might result in exposure of egg masses.

The Dendrobatidae family is widely distributed in Colombia (sea level to just above 4000 m.a.s.l.) and nearly always associated with areas with abundant moisture. Virtually all of the species of this family are exclusively diurnal (in contrast to nearly all

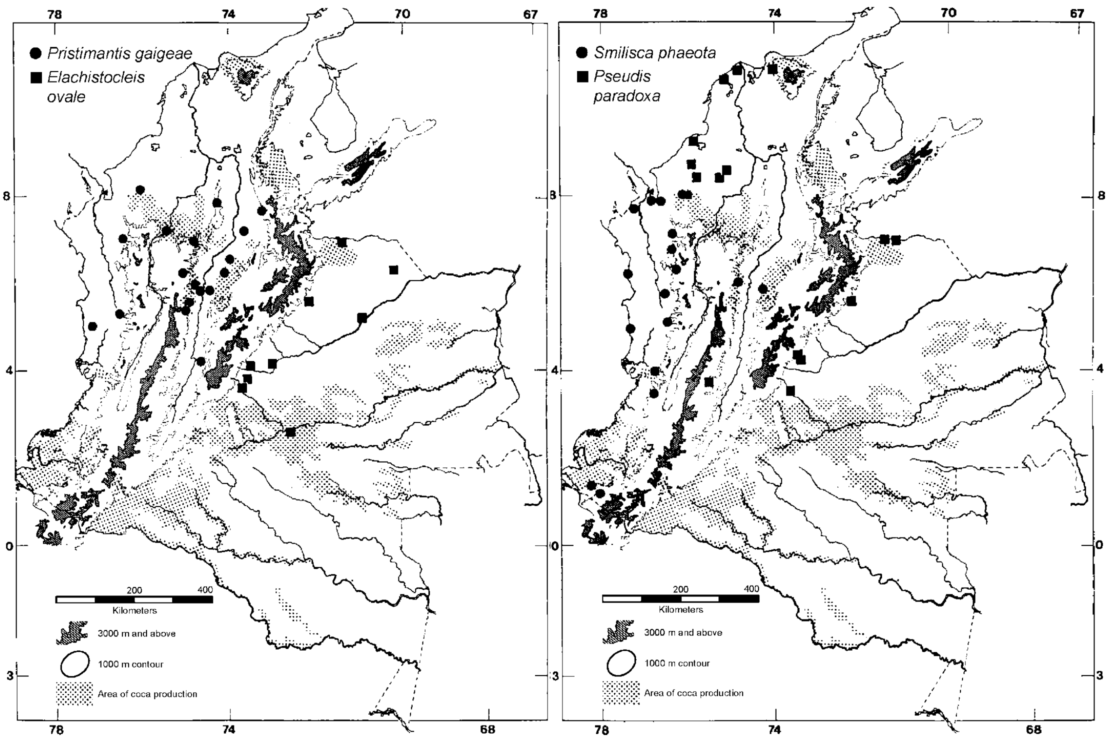

FIG. 2. Distribution of *Elachistocleis ovale*, *Pristimantis gaigeae*, *Pseudis paradoxa*, and *Smilisca phaeota* based on records documented in the Collection of Amphibians of the Instituto de Ciencias Naturales. Additional records of *P. gaigeae* are available in Lynch (1999b) and for *S. phaeota* in (Duellman & Trueb, 1986).

other frog species in Colombia), which indicates that they may be exposed to pesticides used in production and eradication of coca that are applied during daylight hours. The exceptional species (exceptional for living in relatively dry environments) *Dendrobates truncatus* is widely distributed across the Caribbean lowlands and up the Madgalena valley in areas that were once dry tropical forest. The reproductive biology of frogs of this family is unusual in that the terrestrial eggs are large and few in number (deposited in leaf litter and guarded by a parent). Large eggs are usually associated with direct development, but in the case of Dendrobatidae they develop into tadpoles. The attending parent permits the hatched tadpoles to climb onto its back and the tadpoles are transported to bodies of water and released. The bodies of water vary from arboreal and terrestrial bromeliads to cavities in fallen logs or small ponds and sluggish streams. Given that species of the family have terrestrial eggs, they are obliged to live in wetter areas and their distributions are markedly associated with evergreen forests, offering some protection from pesticides used in production and eradication of coca.

The smaller families of frogs and toads (Aromobatidae, Ceratophryidae, Hemiphractidae, Leiuperidae, Leptodactylidae, Microhylidae, Pipidae, and Ranidae) include one (Hemiphractidae) confined to forested regions with little or no intervention (or habitat modification). Hemiphractid frogs are mostly (or exclusively) species without larval stage. The family Aromobatidae was separated recently (Grant et al., 2006) from the Dendrobatidae and shares the same ecological and reproductive characteristics.

The Ceratophryidae, Leiuperidae, Leptodactylidae, Microhylidae, Pipidae, and Ranidae are families that in Colombia are exclusive to the lowlands (or nearly so), and some species are present in open habitats, indicating that some of these frogs cope well with a degree of human intervention (or habitat modification) of the habitat. Pipids are aquatic and rarely venture onto the land. Eggs of Ceratophryids, Microhylids, and Ranids are deposited in water (or on water in the case of Microhylids), whereas the eggs of Leiuperids and Leptodactylids are deposited in foam nests floating on the surface of ponds or concealed within burrows constructed by the frogs themselves. All of

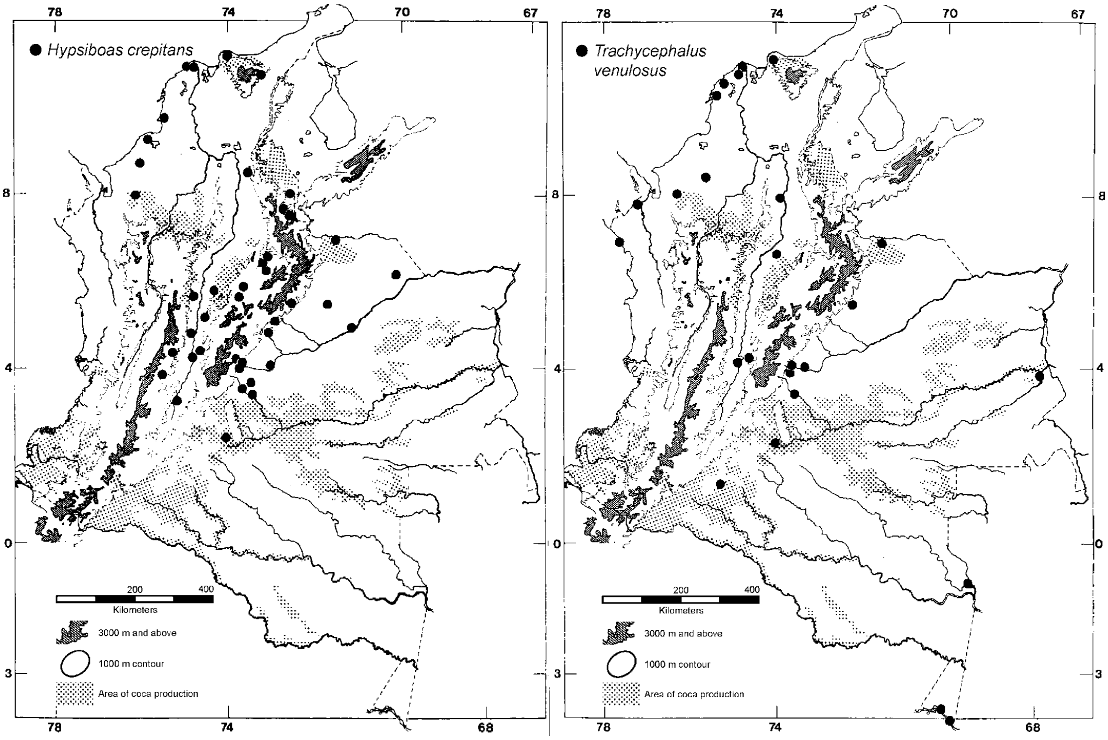

FIG. 3. Distribution of *Hypsiboas crepitans* and *Trachycephalus venulosus* based on records documented in the Collection of Amphibians of the Instituto de Ciencias Naturales. Additional records for *H. crepitans* are available in (Lynch & Suarez-Mayorga, 2001).

these have aquatic tadpoles. The foam nests presumably represent an adaptation to seasonally dry conditions and provide a moist environment in which the embryo develops. In some species the foam nests are found within the cover of forests, but in most of these species (Leiuperids and Leptodactylids), foam nests may be observed in areas of intense intervention (or habitat modification) (e.g., agricultural lands and pasturelands). There are no data in the literature on the penetration of pesticides into the foam nest. One of the two species of Ceratophryids is confined to natural forests in Amazonia; the other occurs in nonforested habitats along the Caribbean coast.

Some species of Leiuperids and Leptodactylids are denizens of deep, undisturbed forests, but in each group one finds species commonly seen in areas subject to human intervention (or habitat modification). At least three species of Microhylids are animals associated with nonforest environments, and although the adults are burrowers, the fact that all produce a floating surface film of eggs means that this sensitive stage of the life cycle may be at risk from pesticides used in production and eradication of coca. The four aquatic Pipids include two with direct development and two with tadpoles. Perhaps because these are aquatic frogs, they appear to exhibit relatively little fidelity to forested habitats where they are less likely to be exposed to pesticides used in production and eradication of coca.

Specific Locations of Frogs in Relation to the Production of Coca

The largest and most complete repository of amphibians from Colombia is the Instituto de Ciencias Naturales (ICN), with more than 55,000 records including specimens of at least 98% of the species known for Colombia. This study permitted us to systematize this large collection (i.e., generate an electronic database) and, for most locality records, to determine the geographic coordinates of the collection locality. This activity allowed us to characterize the expected (and documented) geographic distribution for 750 species with a high level of precision. Further, working with the Antinarcotics Police, it was possible to localize all known cultivations of coca (also georeferenced), so as to measure with precision the geographic separations of populations of amphibians from areas where pesticides are used in production and eradication of coca.

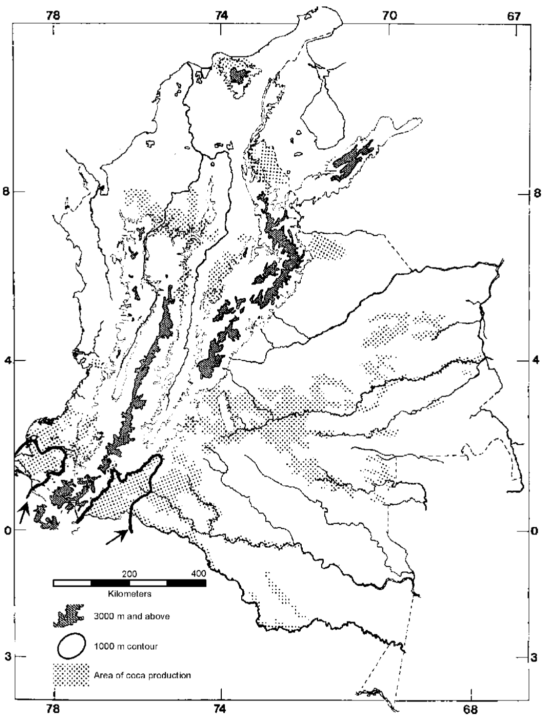

FIG. 4. Locations in Colombia where amphibians are at risk from the production of coca. Heavy lines (marked with arrows) enclose two areas harboring all known Colombian records for a variety of Brachycephalid, Dendrobatid, and Hylid frogs adversely affected by habitat destruction and possibly augmented by pesticides used in the production and eradication of coca (however, intensive inventory work has not been done in these areas).

Frogs and toads were recorded from localities that are within 10 km of those areas where coca is grown. For many of these records, the original collections were made before significant plantations of coca (as an illegal crop) appeared. For reasons of personal security, none of these sites was revisited by herpetologists from the ICN. Analyses were conducted with Arc Map software version 9.2 (ESRI, 2006) so that direct distance separating collection locations for frogs, known coca fields, and areas where aerial spraying was being conducted could be measured.

RESULTS

Based on data from the ICN amphibian database, records exist for 193 species (28% of the national diversity) of anurans that are within 10 km of those areas where coca is cultivated. Records in or near crops of illegal plants include those for 11 of the 13 families of frogs and toads known to be present in Colombia. Only Ceratophryidae and Pipidae were not reported from these locations and would not be at risk.

To illustrate the issue of co-location of frogs and coca production and aerial eradication spraying, eight species of frogs well known in Colombia were selected to represent several habitat preferences and lifecycle strategies. *Dendrobates truncatus* (Figure 1) was selected because it is diurnal and not closely tied to deep forests. *Craugastor raniformis* (Figure 1), *Pristimantis gaigeae* (Figure 2)*,* and *Smilisca phaeota,* Figure 2) were selected because each tolerates habitat modification well. *Elachistocleis ovale* (Figure 2)*, Hypsiboas crepitans* (Figure 3)*,* and *Trachycephalus venulosus* (Figure 3) were selected because (1) these species either prefer open habitats or (2) also reproduce there, and (3) each deposits the eggs as films on water surfaces, and *Pseudis paradoxa* (Figure 2) because this species inhabits open areas and is aquatic. The effect of local extinctions upon the integrity of the entire species is beyond the scope of this study; however, one might view with alarm how much (approximately 25%, Figure 1) of the known distribution of an endemic Dendrobatid (*D. truncatus*) is overlapped by coca production and/or aerial eradication spraying, given that this is a diurnal frog and may be more exposed to pesticides used in production of coca, though it is relatively insensitive to the glyphosate formulation used in the eradication of coca (Bernal et al., 2009a). Among the other species, there is some co-occurrence with coca production, but most species are also recorded from coca-free areas. Location of other frogs in relation to coca production and eradication spraying are summarized in the following subsections.

Family Aromobatidae

Rheobates palmatus has 6 records within 10 km of coca crops (0.2 to 9 km from zones of aerial aerial eradication spraying). Four other species (*Allobates "brunneus,"* probably = *A. trilineatus*], *A. femoralis, A. picachos,* and *A. talamancae*) have one or two records within 9 km of coca production 1.7 to 6 km away. Aromobatids may be relatively tolerant of human intervention (or habitat modification) but their sensitivity to pesticides is unknown. The eggs are terrestrial and are hidden in leaf litter. Some species require heavy forest to sustain populations, but others seem able to cope with modest intervention (or habitat modification).

Family Brachycephalidae

Forty-seven species (all formerly of the genus *Eleutherodactylus*; see earlier footnote) have between 1 (23 species) and 8 records within 10 km of coca production [or in three cases (*E. boulengeri, E. scopaeus*, and *E. w-nigrum*) close to poppy production]. Data are given in Table 1. The proximity records for *E. mantipus* and *E. permixtus* involve altitudinal differences as well (coca fields lie at elevations ≤1000 m a.s.l. whereas these frog species occur above 1500 m a.s.l.); hence, it is inappropriate to consider these two records as pertinent to the investigation.

TABLE 1
Records of the Family Brachycephalidae Found Within 10 km of Coca and Their Proximity to Production Areas or Eradication Spraying

Species	Number of records	Distances to coca production or spraying
Pristimantis achatinus	4	1 to 8 km
Strabomantis anatipes	2	at 9 km and in a coca field
Pristimantis anomalus	4	1 to 9 km
Diasporus anthrax	1	7.5 km
Hypsodactylus babax	2	2.6 to 7 km
Pristimantis boulengeri	3	0.25 to 7.6 km
Pristimantis brevifrons	1	7.6 km
Strabomantis bufoniformis	5	1 to 9 km
Pristimantis caprifer	1	9 km
Strabomantis cerastes	1	9 km
Pristimantis chalceus	2	2.6 and 3 km
Pristimantis colomai	1	4.3 km
Pristimantis conspicillatus	2	1 km and eradication spray at 2 km
Pristimantis cruentus	1	1 km
Pristimantis degener	1	2.2 km
Pristimantis diogenes	1	9 km (spray)
Hypsodactylus dolops	2	3.5 and 6.5 km
Pristimantis epacrus	2	3.5 and 6.5 km
Pristimantis erythropleura	2	2.6 and 9 km (spray)
Pristimantis fallax	1	4.5 km
Craugastor fitzingeri	2	1.6 and 7.5 km
Pristimantis gaigeae	7	0.5 to 7.5 km
Diasporus gularis	5	0.5 to 9 km (9 km spray)
Pristimantis hectus	1	7.6 km
Pristimantis jaimei	2	2.6 and 9 km (spray)
Pristimantis labiosus	1	4.3 km
Pristimantis lanthanites	2	1 km, 2 km (spray)
Pristimantis latidiscus	3	1.6 to 9 km
Craugastor longirostris	6	0.5 to 8.7 km
Hypsodactylus mantipus	1	4.5 km
Pristimantis ockendeni	3	0.6, 1 and 2 km (spray)
Strabomantis opimus	1	9 km
Pristimantis palmeri	1	9 km (spray)
Pristimantis parvillus	3	2.2 to 4.3 km
Pristimantis penelopus	1	2.2 km
Pristimantis permixtus	1	4.5 km
Pristimantis pugnax	2	3.5 and 6.5 km
Craugastor raniformis	8	0.2 to 7.5 km (spray at 6 km)
Pristimantis ridens	2	1 and 9 km
Pristimantis scopaeus	1	0.25 km
Strabomantis sulcatus	3	1, 2 (spray) and 3 km
Pristimantis taeniatus	8	1 to 7.5 km
Pristimantis tamsitti	2	3.5 and 6.5 km
Diasporus tinker	2	1 and 2 km
Pristimantis thectopternus	1	1 km
Pristimantis viejas	3	1–10 km
Pristimantis vilarsi	3	1 (spray), 1.7 and 3.0 km
Pristimantis w-nigrum	6	0 to 9 km (spray at 9 km)
Strabomantis zygodactylus	1	9 km

(*Continued*)

TABLE 1
(*Continued*)

Note. Formerly in the genus *Eleutherodactylus* but now partitioned into four families and seven genera by Hedges et al. (2008a, 2008b).

Family Bufonidae

Fourteen species (*Andinophryne atelopoides, A. olallai, Atelopus famelicus, A. sanjosei, Chaunus granulosus, C. marinus, Dendrophryniscus minutus, Rhaebo blombergi, R. guttatus, R. haematiticus, R. hypomelas,* and *Rhinella dapsilis,* and two species termed to date *Rhinella* sp.) have records (1 to 14) within 10 km of coca crops. Coca production and aerial eradication sprays 2 km away are known for *Rhinella dapsilis,* 9 km for *Rhaebo blombergi* and *R. haematiticus,* 0.6 and 9 km for *Atelopus sanjosei* and *A. famelicus,* 2 and 6 km for *Dendrophryniscus minutus,* and 2 to 11 km for *Chaunus granulosus* and *C. marinus.* Most of the species discussed earlier require dense forest and do not react well to intervention or habitat modification. However, the two *Chaunus* appear to prefer open (= nonforested) habitats. In the case of *C. marinus,* the "preference" is so marked that a collector is well advised to search for specimens in villages or on farms, where they are very common. Given that coca production involves a marked alteration of the environment, these toads are likely to be among the few native Colombian frogs to be found (and to breed) within such enclaves and are likely to be exposed to pesticides used for coca production and eradication spraying.

Family Centrolenidae

Twenty-one species of this family have 1–4 records within 10 km of coca cultivation and 3 of these records are within 0.1 km of areas where eradication spraying occurred. The species involved are *Centrolene grandisonae* (record within a cultivation plot), *C. hybrida, C. ilex, C. litorale, C. medemi, C. peristictum, C. prosoblepon* (four records), *Cochranella chami, C. griffithsi, C. orejuela, C. oreonympha, C. punctulata, C. ramirezi, C.*

rosada, C. savagei, C. susatamai, C. xanthocherida, Hyalinobatrachium aureoguttatum, H. colymbiphyllum, H. fleischmanni, and *H. valerioi*. Centrolenid frogs are probably protected from adverse effects of glyphosate by the fact that they are extremely rare (or absent) when no trace of the forest cover remains. However, apparently healthy populations with obvious evidence of reproduction—egg masses applied to the surfaces of leaves—have been encountered in the narrow gallery forests that border streams passing through pasturelands on the Andean slopes.

Family Dendrobatidae

Nineteen species of these small diurnal frogs have 1–6 records within 10 km of coca production: *Ameerega hahneli* (cultivation within 1 km, aerial eradication spraying within 2 km), *A. ingeri* (cultivation within = 0.6 km, eradication spraying at 6 km), *A. trivittata* (2 records at 1–3 km from coca crops and coca production and aerial eradication spraying at 6 km), *Colostethus fraterdanieli* (2 records, cultivations at 1.6 and 5.6 km), *C. inguinalis* (2 records at 0.2 and 2 km, eradication spraying at 6 km), *C. pratti* (cultivation at 1 km), *C. ruthveni* (cultivation at 2 km), *D. truncatus* (6 records at 0.2 to 4 km from cultivation, eradication spraying at 6 km), *Epipedobates boulengeri* (cultivation at 3.5 km), *Hyloxalus fascianigrus* (cultivation and eradication spraying at 9 km), *H. fuliginosus* (2 records at 3.5 and 6.5 km), *H. lehmanni* (2 records at 2.2 and 9 km, eradication spraying at 9 km), *H. saltuarius* (cultivation at 6.5 km), *Hyloxalus* sp. (cultivation at 6.5 km), *Oophaga histrionica* (5 records at 0.5 to 9 km from crops, eradication spraying at 0.1 to 3 km), *Phyllobates bicolor* (2 records at 3.5 km from cultivation with eradication spraying at 4.5 km), *Ranitomeya opisthomelas* (1 km from cultivation), *R. virolinensis* (2.5 km from cultivation), and *Silverstoneia nubicola* (at 1 km). Dendrobatids may be relatively tolerant of human intervention (or habitat modification) and *D. truncatus* adults were found to be the most tolerant of 8 species to glyphosate (Bernal et al., 2009b). However, if habitat destruction is extensive, the peculiarities of the reproductive mode (terrestrial eggs in leaf litter—that are moisture-sensitive) may result in local extinctions. Some species require heavy forest for their persistence but others seem able to cope with modest intervention (or habitat modification). The fact that these are diurnal frogs increases the risk of direct exposure to eradication spraying.

Family Hemiphractidae

Two species (*Cryptobatrachus boulengeri* and *C. fuhrmanni*) have 1 or 3 records within 10 km of coca crops. Frogs of this genus are strict denizens of forested streams. As such, they probably behave in much the same way as do Centrolenids (a relatively high tolerance of intervention (or habitat modification)) as long as the intervention (or habitat modification) does not remove all the trees.

Six species of *Gastrotheca* (*G. angustifrons, G. argenteovirens, G. bufona, G. dendronastes, G. espeletia,* and *G. guentheri*) each have 1 known locality within 10 km of a coca field with coca production and aerial eradication sprays between 3 and 9 km away. *Gastrotheca* either are common animals or are extraordinarily rare in collections. The genus *Flectonotus* barely enters Colombia along the mountain border with Venezuela, where it is locally abundant but rare in collections. The Colombian species either occur in treeless areas (*páramos*) above the altitudes at which coca are grown or occupy dense forest areas where the forest offers protection from pesticides used in coca production and eradication spraying. The physical alteration of the habitat by *cocaleros* likely results in local extinction of populations of these frogs near coca crops.

A single species (*Hemiphractus fasciatus*) has two records (1 to 9 km distant) near coca production. *Hemiphractus* appear to be among the most sensitive of frog species to habitat alteration because all accumulated records of the five species known for Colombia come from pristine forest habitats—and subsequent visits to those sites (by experienced collectors) after habitat alterations failed to detect the animals.

Family Hylidae

At least 49 species of this predominantly lowland family have 1 to 8 records within 10 km of coca production, as listed in Table 2. Aerial eradication spraying occurred between 0.1 and 11 km from the locality records, potentially influencing *Dendropsophus ebraccatus, D. leucophyllatus, D. mathiassoni, D. microcephalus, D minutus, D. parviceps, D. triangulum, Hyloscirtus alytolylax, H. palmeri, H. simmonsi, Hypsiboas boans, H. cinerascens, H. crepitans, H. geographicus, H. lanciformis, H. pugnax, H. punctatus, Osteocephalus taurinus, P. paradoxa, Scarthyla vigilans, Scinax blairi, S. cruentommus, S. garbei, S. ruber, Smilisca phaeota, S. sila, Sphaenorhynchus carneus,* and *T. venulosus*. Although the common name given to the family (treefrogs) suggests that these animals absolutely require forests, the reality is somewhat different. Many species are obligate denizens of intact forests and a small portion of these appear to not come to the ground surface even for reproduction (Lynch, 2005), while others require that some part of the forest persist for the continued existence of the local population (e.g., *Dendropsophus ebraccatus, D. triangulum, Hypsiboas boans, Osteocephalus taurinus, T. venulosus*). Yet other species appear to do even better (in terms of population size) in open habitats than in dense forests (e.g., *Dendropsophus minutus, D. triangulum, Hypsiboas lanciformis, H. punctatus, Scinax ruber*). Lastly, there are lowland species that appear to not use the forests at all (e.g., *Dendropsophus mathiassoni, D. microcephalus, H. crepitans, H. pugnax, Phyllomedusa hypocondrialis, P. paradoxa, Scarthyla vigilans, Scinax blairi, S. rostratus,* and *S. wandae*). In a study of the frogs found in the vicinity of Villavicencio (Lynch, 2006), these species were characterized best able to tolerate human intervention (or habitat

TABLE 2
Records of the Family Hylidae Found Within 10 km of Coca and Their Proximity to Production Areas or Eradication Spraying

Species	Number of records	Distances to coca production or spraying
Agalychnis spurrelli	1	9 km
Cruziohyla calcarifer	1	9 km
Dendropsophus columbianus	1	2.6 km
Dendropsophus ebraccatus	1	0.2 km
Dendropsophus leucophyllatus	1	1 km
Dendropsophus marmoratus	1	3 km
Dendropsophus mathiassoni	5	1 to 10 km
Dendropsophus microcephalus	5	1 to 6.4 km
Dendropsophus minutus	1	1 km
Dendropsophus parviceps	1	1 km
Dendropsophus triangulum	1	1 km
Hylomantis buckleyi	1	6.5 km
Hyloscirtus alytolylax	1	9 km
Hyloscirtus lindae	2	3.5 to 6.5 km
Hyloscirtus palmeri	9	0.5 to 9 km
Hyloscirtus platydactylus	1	1 km
Hyloscirtus simmonsi	1	9 km
Hyloscirtus torrenticolus	2	3.5 to 6.5 km
Hypsiboas boans	4	0.2 to 7.5 k
Hypsiboas calcaratus	1	5 km
Hypsiboas cinerascens	3	0.6 to 2.7 km
Hypsiboas crepitans	4	1 to 7.5 km
Hypsiboas geographicus	1	1 km
Hypsiboas lanciformis	4	1 to 10 km
Hypsiboas picturatus	1	9 km
Hypsiboas pugnax	3	within 1 km
Hypsiboas punctatus	8	1 to 10 km
Hypsiboas rosenbergi	1	1 km
Osteocephalus carri	1	6.5 km
Osteocephalus oophagus	1	4 km
Osteocephalus taurinus	4	1 to 6.5 km and spraying at 2.5 km
Osteocephalus verruciger	2	3.5 and 6.5 km
Phyllomedusa hypocondrialis	2	5 to 10 km
Phyllomedus perinesos	2	3.5 and 6.5 km
Phyllomedusa venustus	1	2 km
Pseudis paradoxa	1	10 km
Scarthyla vigilans	4	1 to 10 km
Scinax blairi	4	1 to 9.3 km
Scinax cruentommus	2	1 and 3 km
Scinax garbei	2	1 and 2.5 km (spray)
Scinax ictericus	2	3.5 and 6.5 km
Scinax rostratus	6	1 to 10 km
Scinax x-signatus	1	10 km
Scinax ruber	3	2.7 and 3 km, spraying at 11 km
Smilisca phaeota	7	0.2 to 9 km
Smilisca sila	2	0.2 and 1 km
Sphaenorhynchus carneus	2	1 km and 2.5 km (spray)
Sphaenorhynchus lacteus	1	5 km
Trachycephalus venulosus	3	1, 2, and 2.5 km (spray)

modification). However, their tolerance also renders them most likely to be adversely affected by coca production and aerial eradication spraying. Among these tolerant species one finds species that deposit their eggs as films on the surface of water (e.g., *H. crepitans, H. pugnax, T. venulosus*) and others depositing their eggs on the surfaces of leaves (e.g., *Dendropsophus mathiassoni, D. microcephalus, Phyllomedusa hypocondrialis*)—habits that may expose the spawn to adverse effects of coca production and aerial eradication spraying.

Family Leiuperidae

Five species of this family have records within 10 km of coca production: *Engystomops petersi* (at 1 km of production, within 2 km of aerial eradication spraying), *E. pustulosus* (7 records at 0.2–5 km from coca production and aerial eradication spraying at 6 km), *Pleurodema brachyops* (at 2 km of production), *Pseudopaludicola pusilla* (3 records 1–2 km from production with coca production and aerial eradication spraying at 6 km), and *Physalaemus fischeri* (at 5 km of production). Some Leiuperids are restricted to undisturbed forests (e.g., *Edalorhina, Pseudopaludicola ceratophyes*), but most are either tolerant of some intervention (or habitat modification) (*Engystomops petersi*) or virtually restricted to open habitats. Most species of this family employ foam nests in which the embryos are protected from desiccation and it remains to be determined whether glyphosate penetrates the foam surface.

Family Leptodactylidae

These abundant lowland animals include 14 species with records within 10 km of coca production: *Leptodactylus andreae* (at 1 km from coca production and 2 km from aerial eradication spraying), *L. colombiensis* (at 5 km), *L. fragilis* (2 records at 0.5 and 2 km from cultivations), *L. fuscus* (6 records at 0.8 to 9.3 km from production with aerial eradication spraying at 6 to 8 km), *L. hylaedactylus* (at 0.6 km from production with aerial eradication spraying at 6 km), *L. insularum* (5 records at

2 to 10 km from production and aerial eradication spraying at 6 to 11 km), *L. knudseni* (2 records at 0.8 to 3 km), *L. mystaceus* (at 1.7 km with aerial eradication spraying at 1 km), *L. poecilochilus* (at 1 km), *L. rhodomerus* (at 8.7 km), *L. riveroi* (3 records at 0.8 to 4 km from production), *L. savagei* (3 records at 1 km from production and aerial eradication spray at 9 km), *L. ventrimaculatus* (at 2.2 km), and *L. wagneri* (2 records at 3.5 and 6.5 km). The habitat preferences and the reproductive biology of this family parallel closely those of the preceding family with only some notable differences. Several species of *Leptodactylus* deposit their eggs in foam nests within burrows, possibly a physical protection from pesticides used for coca production and eradication spraying.

Family Microhylidae

Eight species of this small family (small for Colombia, but a large family for the Old World) have records within 10 km of coca production: *Chiasmocleis bassleri* (at 1.7 km with aerial eradication spraying at 1 km), *C. panamensis* (at 7.5 km), *Elachistocleis ovale* (1 record within 6 km of coca production and aerial eradication spray), *Otophryne pyburni* (at 3 km), *Nelsonophryne aterrima* (at 7.5 km), *Relictivomer pearsei* (3 records at 2 to 9.3 km, aerial eradication spraying at 8 km), *Synapturanus mirandaribeiroi* (at 3 km), and *S. rabus* (at 1 km with aerial eradication spraying at 2 km). Most of the species (15) of this family in Colombia are denizens of forests and appear to be confined to undisturbed forests. Nonetheless, four species occupy open and/or heavily intervened habitats (*Chiasmocleis panamensis, E. ovale, Nelsonophryne aterrima,* and *Relictivomer pearsei*) and thus may be at risk from pesticides used for coca production and eradication spraying because all deposit their embryos as films on the surface of ponds. In contrast, the adults are burrowers, are active on the ground surface only at night, and do not climb vegetation (except for one species of deep forests in Amazonia—*Syncope antenori*).

Family Ranidae

Two species (*Lithobates palmipes* and *L. vaillanti*) have 4 and 8 records within 10 km of coca production. Two of these records are within 2.5 km of aerial eradication spraying. Although these two species occupy forested areas, they also are common in open areas, including those with significant human intervention (or habitat modification). Reproduction is confined largely to water courses with a current and eggs are submerged in the water.

CONCLUSIONS

Anyone concerned about the persistence of natural habitats must be concerned by the effects of (1) ecological damage done in order to facilitate the illegal production of coca and (2) the potentially negative effects on biodiversity of efforts at eradication. These concerns are greater for amphibians because (a) amphibians are especially diverse in Colombia and (b) amphibians do not necessarily have the integument protection available to other terrestrial vertebrates.

However, those concerns need to be related to the magnitude of the problem. Coca production and aerial eradication sprays are restricted geographically to areas where this activity can be accomplished without government intervention and do not cover the country's latitudinal extent or the altitudinal dimension—coca is usually "commercially" grown at ≤1000 m a.s.l. The 153,134 ha of land that was subject to aerial eradication spraying in 2007 (personal communication, National Police of Colombia, Bogotá, December, 2007) represents only about 0.15% of the total land area of Colombia (Solomon et al., 2007). Reviewing the anuran faunas of lowland Colombia, one notes three areas that might be identified as diversity "hotspots"—one in the extreme southeast, a second in the northern half of the Pacific lowlands, and the third a lens lying along the eastern base of the Andes in southwestern Colombia. Coca production is modest within the first two of these "hotspots" and apparent in the third (Figure 4).

Vast areas of the distributions of most species lie outside of the efforts of Colombian authorities to control coca production (Figures 1–3). Further, the consequences of coca production may be more serious for only a limited number of species that barely enter Colombian territory. Especially in Nariño, in western Putumayo and adjacent areas of Cauca and Caquetá, the effects of coca production and aerial eradication sprays have placed several species of frogs at risk (Figure 4), at least in terms of their distribution in Colombia. These include *Ameerega bilingua, Dendropsophus bifurcus, Pristimantis colomai, P. degener, P. diadematus, P. quaquaversus, P. variablis,* and *Trachycephalus jordani.* Other species may also be at risk, but exact numbers are unknown because few investigations were undertaken in these areas during the past 30 yr. As these species are mostly found in Ecuador, it is assumed that healthy populations persist there.

Overall, the risks from pesticides used for coca production and eradication spraying must be placed in the context of the greater toxicity of products used by growers (Brain & Solomon, 2009) and the sensitivity of frogs from Colombia to the mixture of glyphosate and Cosmo-Flux as used in the aerial eradication spraying. Laboratory-based toxicity studies showed that aquatic larval stages of Colombian species are not differentially sensitive as compared with frogs from other locations (Bernal et al., 2009a). When tested under realistic conditions—in shallow water (15 cm deep) in the presence of sediment and particulates that absorb glyphosate and the more toxic surfactant—toxicity was reduced (Bernal et al., 2009a). Terrestrial stages were less susceptible than aquatic stages (Bernal et al., 2009b). In contrast, some of the products used by growers may be more bioavailable in the environment and risks to these may not be mitigated. Of greater significance is the effect on amphibians and other fauna and flora of habitat change associated with forest clearance for coca production. Some insight into this was provided by Lynch (2005) in the region of Leticia, where species richness declined from 98 species in rural areas to 6 species in the city parks, reflecting the effects of increasing disturbance and habitat fragmentation.

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Annex 131-I

C. Bolognesi et al., "Biomonitoring of Genotoxic Risk in Agricultural Workers from Five Colombian Regions: Association to Occupational Exposure to Glyphosate"

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Biomonitoring of Genotoxic Risk in Agricultural Workers from Five Colombian Regions: Association to Occupational Exposure to Glyphosate

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In order to assess possible human effects associated with glyphosate formulations used in the Colombian aerial spray program for control of illicit crops, a cytogenetic biomonitoring study was carried out in subjects from five Colombian regions, characterized by different exposure to glyphosate and other pesticides. Women of reproductive age (137 persons 15–49 yr old) and their spouses (137 persons) were interviewed to obtain data on current health status, history, lifestyle, including past and current occupational exposure to pesticides, and factors including those known to be associated with increased frequency of micronuclei (MN). In regions where glyphosate was being sprayed, blood samples were taken prior to spraying (indicative of baseline exposure), 5 d after spraying, and 4 mo after spraying. Lymphocytes were cultured and a cytokinesis-block micronucleus cytome assay was applied to evaluate chromosomal damage and cytotoxicity. Compared with Santa Marta, where organic coffee is grown without pesticides, the baseline frequency of binucleated cells with micronuclei (BNMN) was significantly greater in subjects from the other four regions. The highest frequency of BNMN was in Boyacá, where no aerial eradication spraying of glyphosate was conducted, and in Valle del Cauca, where glyphosate was used for maturation of sugar cane. Region, gender, and older age (≥35 yr) were the only variables associated with the frequency of BNMN measured before spraying. A significant increase in frequency of BNMN between first and second sampling was observed in Nariño, Putumayo, and Valle immediately (<5 d) after spraying. In the post-spray sample, those who reported direct contact with the eradication spray showed a higher quantitative frequency of BNMN compared to those without glyphosate exposure. The increase in frequency of BNMN observed immediately after the glyphosate spraying was not consistent with the rates of application used in the regions and there was no association between self-reported direct contact with eradication sprays and frequency of BNMN. Four months after spraying, a statistically significant decrease in the mean frequency of BNMN compared with the second sampling was observed in Nariño, but not in Putumayo and Valle del Cauca. Overall, data suggest that genotoxic damage associated with glyphosate spraying for control of illicit crops as evidenced by MN test is small and appears to be transient. Evidence indicates that the genotoxic risk potentially associated with exposure to glyphosate in the areas where the herbicide is applied for coca and poppy eradication is low.

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Glyphosate (*N*-phosphonomethyl glycine), a nonselective herbicide, is the active ingredient of a number of herbicide formulations and one of the most widely used pesticides on a global basis (Baylis, 2000; Woodburn, 2000; Duke & Powles, 2008). It is a postemergence herbicide, effective for the control of annual, biennial, and perennial species of grasses, sedges, and broadleaf weeds. The relatively high water solubility and the ionic nature of glyphosate retard penetration through plant hydrophobic cuticular waxes. For this reason, glyphosate is commonly formulated with surfactants that decrease the surface tension of the solution and increase penetration into the tissues of plants (World Health Organization International Program on Chemical Safety, 1994; Giesy et al., 2000).

A large number of glyphosate-based formulations are registered in more than 100 countries and are available under different brand names. One of the most commonly applied glyphosate-based products is Roundup, containing glyphosate as the active ingredient (AI) and polyethoxylated tallowamine

(POEA) as a surfactant. Glyphosate and its formulations have been extensively investigated for potential adverse effects in humans (Williams et al., 2000). This pesticide was reported to exert a low acute toxicity to different animal species. Experimental evidence showed that glyphosate did not bioaccumulate in any animal tissues (Williams et al., 2000). Chronic feeding studies in rodents did not find evidence of carcinogenic activity or any other relevant chronic effects (U.S. EPA, 1993; World Health Organization International Program on Chemical Safety, 1994).

With in vitro studies with tissue cultures or aquatic organisms, several of the formulated products are more toxic than glyphosate AI (Giesy et al., 2000; Williams et al., 2000). Differences in the response of test organisms to the AI and the commercial formulation, e.g., Roundup, are likely due to the toxicity of different formulants and surfactants contained in commercial products. There is a general agreement that adjuvants may be more toxic for animals than glyphosate itself (Giesy et al., 2000; Williams et al., 2000; Richard et al., 2005). Cytotoxicity of the commercial formulation Roundup to human peripheral mononuclear cells was 30-fold higher (LC_{50} = 56 mg/L) than for the AI (LC_{50} = 1640 mg/L) (Martinez et al., 2007). Several in vitro and in vivo studies with parallel testing of glyphosate AI and Roundup showed that only the commercial formulation was genotoxic (Rank et al., 1993; Bolognesi et al., 1997b; Gebel et al., 1997; Grisolia 2002). Cytotoxic and genotoxic effects were observed with Roundup and other formulations of glyphosate, but not with glyphosate AI alone in comparative studies involving different experimental systems (Peluso et al., 1998; Richard et al., 2005; Dimitrov et al., 2006). The observed differences were attributed to some ingredients of Roundup, mainly surfactants, and/or to a synergic effect of glyphosate and components of the formulation (Sirisattha et al., 2004; Peixoto 2005).

Epidemiological studies generally showed no consistent or strong relationships between human exposure to glyphosate or glyphosate-containing products and health outcomes in human populations. No statistically significant association in humans was found with spontaneous abortion, fetal deaths, preterm birth, neural tube defects (Rull et al., 2006), and cancer incidence overall, although a suggested association between cumulative exposure to glyphosate and the risk of multiple myeloma was reported (De Roos et al., 2005).The epidemiologic evidence is insufficient to verify a cause–effect relationship for childhood cancer (Wigle et al., 2008). Four case-control studies suggested an association between reported glyphosate use and the risk of non-Hodgkin's lymphoma (NHL) in age groups from 20 to 70 yr (Hardell & Eriksson, 1999; McDuffie et al., 2001; Hardell et al., 2002; De Roos et al., 2003; Eriksson et al., 2008).

Glyphosate AI and Roundup were extensively tested for genotoxicity in a wide range of in vitro and in vivo systems evaluating different genetic endpoints (gene mutation, chromosome mutation, DNA damage and repair) using bacteria and mammalian somatic cells (Williams et al., 2000). The active ingredient did not induce any relevant genotoxic effects such as gene mutations in a variety of in vitro bacterial assays including the *Salmonella typhimurium* reversion assay, with and without metabolic activation (Wildeman & Nazar 1982; Moriya et al., 1983; Li & Long, 1988) and *Escherichia coli* WP-2 (Moriya et al., 1983; Li & Long, 1988). The active ingredient was also negative in the Chinese hamster ovary cell HGPRT gene mutation assay and in primary hepatocyte DNA repair assay (Li & Long, 1988). The genotoxic potential of the formulation Roundup was investigated in a number of studies evaluating various genetic endpoints in different biological systems and was (1) negative in the *S. typhimurium* reversion assay (Kier et al., 1997), (2) negative in the sex-linked recessive lethal assay with *Drosophila melanogaster* (Gopalan & Njagi, 1981), and (3) negative for in vivo micronucleus (MN) induction in mouse bone marrow (Rank et al., 1993; Kier et al., 1997; Dimitrov et al., 2006). The Roundup formulation was reported in a number of studies to exert weak genotoxic effects in short-term assays.

Differences in the response of test organisms to the active ingredient glyphosate and the commercial formulation Roundup might be due to the toxicity of different co-formulants and surfactants contained in commercial products. Several studies with parallel testing of glyphosate and Roundup showed that only the commercial formulation was genotoxic (Rank et al., 1993; Bolognesi et al., 1997b; Gebel et al., 1997; Grisolia 2002). A recent study on the genotoxic potential of glyphosate formulations found that in some cases the genotoxic effects were obtained under exposure conditions that are not relevant for humans (Heydens et al., 2008).

An in vitro study described a concentration-dependent increase of DNA single-strand breaks (SSB), evaluated by comet assay, in two different human cell lines treated with glyphosate at sublethal concentrations (Monroy et al., 2005). Roundup formulations were shown to affect the cell cycle by inhibiting the G2/M transition and DNA synthesis leading to a genomic instability (Marc et al., 2004a, 2004b). Evidence of DNA damage in peripheral lymphocytes from a small group of subjects potentially exposed to glyphosate was reported in a recent paper (Paz-y-Miño et al., 2007). The number of subjects (21 control and 24 exposed) was small and there were 23 females and only 1 male in the exposed group, making interpretation of the results difficult.

Frequency of MN in human lymphocytes has been widely used for biomonitoring exposure to pesticides (Bolognesi, 2003; Costa et al., 2006; Montero et al., 2006). The MN test, an index of chromosomal damage, is one of the most appropriate biomarkers for monitoring a cumulative exposure to genotoxic agents. Chromosomal damage, as a result of inefficient or incorrect DNA repair, is expressed during the cell division and represents an index of accumulated genotoxic effects. The cytokinesis-block micronucleus (CBMN) methodology (Fenech & Morley, 1985) allows a distinction to be made between a mononucleated cell that did not divide and a binucleated cell that has divided once, expressing any genomic damage associated to recent exposure. The test in its comprehensive application, as was proposed by Fenech (2007) including a set of markers of gene amplification, cellular necrosis, and apoptosis, allows evaluation of genotoxic and cytotoxic effects induced by exposure to a genotoxic agent.

Colombia's anti-drugs strategy includes a number of measures ranging from aerial spraying of a mixture of a commercial formulation of glyphosate (Glyphos) and an adjuvant, Cosmo-Flux (Solomon et al., 2007b), to manual eradication, including alternative development and crop substitution programs (UNODC, 2007). In order to assess the potential genotoxic risk associated with the aerial spraying program with the glyphosate mixture, a cytogenetic biomonitoring study was carried out in subjects from five Colombian regions, characterized by different exposure to glyphosate formulations and other pesticides.

MATERIALS AND METHODS

The study was carried out in five regions of Colombia, with different potential exposure to glyphosate as reported by Sanin et al. (2009). Briefly, the characteristics of the study areas are described here:

Sierra Nevada de Santa Marta—where organic coffee is grown without use of pesticides.

Boyacá—an area of illicit crops, where manual eradication is performed and the use of pesticides and other chemical agents is common.

Putumayo and Nariño—where aerial spraying of glyphosate is performed for coca and poppy eradication. The aerial application rate for eradication of coca is 3.69 kg glyphosate a.e. (acid equivalents)/ha (Solomon et al., 2007b). In order to maximize penetration and effectiveness of the spray formulation, Glyphos is tank-mixed with an adjuvant (Cosmo-Flux® 411F; Cosmoagro, Bogotá).

Valle del Cauca—where glyphosate is applied through aerial spraying for sugar cane maturation. Roundup 747 is the most commonly used product and is applied at a rate of 1 kg a.e./ha, and has no additional adjuvant (personal communication, ASOCAÑA, the Colombian Association for Sugar Growers, December 2008).

Study Population

Two hundred and seventy-four individuals were included in the study. The objective was to sample 30 couples of reproductive age in each area and, where possible, the same couples in the study conducted by Sanin et al. (2009) were sampled. In Putumayo, Nariño, and Valle del Cauca, the population was selected based on the scheduled aerial spraying of glyphosate. This schedule was confidential and provided exclusively for the purpose of the study by the Antinarcotics Police (Putumayo and Nariño) or ASOCAÑA (Valle del Cauca). In Valle del Cauca, a sample size of 30 couples could not be achieved because spraying was not carried out in populated areas of the study region. Most spraying during the study period was carried out on sugar cane crops where no inhabitants were found. All reported areas to be sprayed in Valle del Cauca were visited to search for couples; however, only 14 could be included.

In Sierra Nevada de Santa Marta and Boyacá, the same areas investigated in a previous study (Sanin et al., 2009) were identified, although, due to the instability of the population and high migration, most couples from the previous study were not located. In all regions, the same strategy as described before (Sanin et al., 2009) was followed, visiting household by household until completing 30 couples who fulfilled the inclusion criteria, women of reproductive age (15–49 yr of age) and their spouses, who voluntarily accepted to participate in the study.

Field Data Collection

Field data collection was carried out between October 2006 and December 2007. Epidemiologists and interviewers in the five regions who participated in the Sanin et al. (2009) study were informed about the objectives of the study and trained for data collection. The Ethical Committee of Fundacion Santa Fe de Bogotá approved the study protocol and the informed consent forms used for the study. All the subjects were informed about the aims of the study. All of them gave their informed consent and volunteered to donate blood for sampling. They did not self-report illness at the time of blood sampling and interviews. Every volunteer was interviewed with a standardized questionnaire, designed to obtain relevant details about the current health status, history, and lifestyle. This included information about possible confounding factors for chromosomal damage: smoking, use of medicinal products, severe infections or viral diseases during the last 6 mo, recent vaccinations, presence of known indoor/outdoor pollutants, exposure to diagnostic x-rays, and previous radio- or chemotherapy. A simplified food frequency questionnaire that had already been used in other regions of Colombia was also applied, in order to evaluate dietary folic acid intake. Folic acid intake was characterized because of the role of folic acid deficiency in baseline genetic damage in human lymphocytes (Fenech & Rinaldi, 1994). Specific information about exposure at the time of aerial spraying in Putumayo, Nariño, and Valle del Cauca was addressed in the questionnaire.

Blood Sampling and Cell Culture

Blood samples were collected twice in Boyacá, at the beginning of the study and 1 mo after the first survey, and at 3 different times in Nariño, Putumayo, and Valle del Cauca: immediately before spraying, within 5 d after spraying, and 4 mo later. A sample of 10 ml whole blood was collected from each subject, by venipuncture, using heparinized Vacutainer tubes kept at room temperature and sent within 24 h for the establishment of the lymphocyte cultures. The samples were coded before culturing. The modified cytokinesis-blocked method of Fenech and Morley (1985) was used to determine frequency of MN in lymphocytes. Whole blood cultures were set up for cytogenetic analysis in Bogotá (Colombia) by personnel specifically trained by cytogeneticists from Environmental Carcinogenesis Unit of the National Cancer Research Institute (Genoa, Italy).

Three sterile cultures of lymphocytes were prepared. A 0.4-ml aliquot of whole blood was incubated at 37ºC in duplicate in 4.6 ml RPMI 1640 (Life Technologies, Milano, Italy) supplemented with 10% fetal bovine serum (Gibco BRL, Life Technologies SrL, Milano, Italy), 1.5% phytohemoagglutinin (Murex Biotech, Dartford, UK), 100 units/ml penicillin, and 100 µg/ml streptomycin. After 44 h, cytochalasin B (Sigma, Milano, Italy) was added at a concentration of 6 µg/ml. At the end of incubation at 37°C for 72 h, cells were centrifuged (800 × g, 10 min), then treated with 5 ml of 0.075 m*M* KCl for 3 min at room temperature to lyse erythrocytes. The samples were then treated with pre-fixative (methanol:acetic acid 3:1) and centrifuged . The cellular pellets were resuspended in 1 ml methanol. At this step the samples were sent to the Environmental Carcinogenesis Unit (National Cancer Research Institute, Genoa, Italy). All the samples were centrifuged in methanol. Treatment with fixative (methanol:acetic acid, 5:1) followed by centrifugation was repeated twice for 20 min. Lymphocytes in fresh fixative were dropped onto clean iced slides, air-dried, and stained in 2% Giemsa (Sigma, Milano, Italy). MN analysis was performed blind only on lymphocytes with preserved cytoplasm. On average, 2000 cells were analyzed for each subject. Cells were scored cytologically using the cytome approach to evaluate viability status (necrosis, apoptosis), mitotic status (mononucleated, binucleated, multinucleated) and chromosomal damage or instability status (presence of micronuclei, nucleoplasmic bridges, nucleoplasmic buds) (Fenech 2007). The proliferation index (PI) was calculated as follows:

PI = (number of mononucleated cells + 2
× number of binucleated cells + 3
× number of polynucleated cells)/ total number of cells.

Statistical Analysis

Continuous variables were characterized using mean and standard deviation, while categorical variables were expressed as proportions. Dependent variables, micronuclei per binucleated cell (BNMN), and differences in MN between sampling were square-root transformed where required to comply with the required assumptions of normal distribution and equal variances. Comparison of MN between areas was made by one-way analysis of variance (ANOVA). A significance level at 5% was used to assess differences among areas. For multiple comparisons, the Bonferroni test was applied ($\alpha = .05$). Significance of differences in frequency of BNMN between first and second, and second and third sampling were tested by the unpaired *t*-test with equal variances. Difference and 95% confidence interval were used to compare between samplings.

Bivariate analysis between dependent variables and putative risk factors was performed by one-way ANOVA, comparing exposed and nonexposed subjects. In cases where risk factor was continuous, such as age, folic acid intake, alcohol consumption, and coffee consumption, the correlation coefficient was used.

A multiple linear regression was conducted to assess association with BNMN at the first sampling with different variables: region, age (as continuous variable as well as categorical age), ethnicity as a dichotomous variable, exposure to genotoxic products as defined earlier, gender (female vs. male), and intake of folic acid (categorized in quartiles). Regression analysis was conducted with transformed variables, with square root transformation of BNMN and natural logarithm of age, to obtain a normal distribution.

RESULTS

Demographic characteristics and habits of the study groups are described in Table 1. The study population comprised 274 subjects (137 female and 137 male; average age 30.4 ± 7.8 yr). The mean age of the subjects was similar in the different regions. A large part of the studied population was mestizo, with the exception of the Nariño area consisting of individuals of African origin. In the total population, 38% of interviewees had not completed primary education. Putumayo had the largest proportion with education and Valle del Cauca the lowest as shown in Table 1. Only 10% of all subjects were smokers, (20% in Putumayo); a large majority of subjects were drinkers of beer or liquor with a consistent consumption of guarapo (traditional alcoholic beverage prepared by fermentation of maize) in Santa Marta and Boyacá. No statistically significant differences of folic acid intake were observed between different regions (the mean values ranged from 750 and 1189 μg/wk).

One hundred and nine (39.8%) of 274 participants reported current use of pesticides in their occupation or other activities. Nariño (76.6%) and Putumayo (61.7%) were the two regions where prevalence of use of genotoxic pesticides was higher; Boyacá (24.2%) and Valle del Cauca (28.6%) reported lower use. None of the study subjects in Santa Marta reported use of pesticides. No data regarding quantity of pesticide used were available. Fifty (18.3%) out of 273 who gave information

TABLE 1
Demographic Characteristics and Possible Confounding Exposures in the Study Populations

Area	Santa Marta	Boyacá	Putumayo	Nariño	Valle del Cauca
Number of subjects	60	62	60	64	28
Age (mean (SD))	27.0 (5.6)	29.1 (8.8)	31.4 (7.2)	32.5 (7.4)	33.4 (8.7)
Ethnicity (%)					
Mestizo	100	100	88.3	3.1	60.7
African			6.7	96.9	39.3
Indian			5.0		
Education (%)					
None		4.8	1.7		
Primary incomplete	26.7	38.7	53.3	42.2	21.4
Primary complete	21.7	29.0	20.0	23.4	32.1
High school incomplete	25.0	8.1	20.0	25.0	28.6
High school complete	26.7	19.4	3.3	9.4	17.9
Technical			1.7		
Occupation (%)					
Agriculture	10.0	41.9	60.0	62.5	7.1
Housewife	40.0	50.0	38.3	34.4	50.0
Other	50.0	8.1	1.7	3.1	42.9
Health insurance (%)					
Uninsured	50.0	9.7	36.7	71.9	7.1
Subsidized	38.3	83.9	60.0	18.7	50.0
Insured	11.7	6.4	3.3	9.4	42.9
Coffee consumption (cups/day)					
Mean (SD)	1.8 (2.3)	1.7 (0.8)	2.3 (4.1)	1.3 (0.4)	1.7 (1.2)
Percent of population	80.0	67.7	88.3	76.6	82.1
Smoking (%)					
Nonsmokers	91.7	95.2	80.0	87.5	92.9
Alcohol (%)					
Liquor	28.3	25.8	53.3	78.1	78.6
Beer	51.6	67.7	63.1	82.8	64.3
Guarapo	6.7	59.7	1.7	3.2	10.7
Users of illicit drugs (%)	6.7	0	5.0	7.8	0
Diet					
Folic acid intake (μg/wk)	1189	873	750	1160	812

about x-ray examination reported to having been exposed at some time; however, only 21 out of 46 who gave information on dates of x-ray reported exposure in the last 6 mo before the interview and first blood sample. Sixty-one percent of population reported viral infections, the highest prevalence in Nariño (89.5%) and the lowest in Putumayo (49.2%). However, 89.3% of viral infections were the common cold and 6.1% dengue fever. Hepatitis was reported by six interviewees without any specification of the type of the infection.

The means and standard deviations of frequency of MN and related parameters according to regions are shown in Table 2 and presented graphically in Figure 1. Compared with Santa Marta, where people grow organic coffee without the use of pesticides and which is considered as a reference area, the baseline frequency of BNMN was significantly greater in subjects from the other four regions. The highest frequency of BNMN was in Boyacá, where no aerial eradication spraying of glyphosate was carried out, and Valle del Cauca, where aerial spraying was for maturation of sugar cane. There was no significant difference between mean frequency of BNMN in Boyacá and Valle del Cauca. There was no significant difference in frequency of BNMN between Putumayo and Nariño,

TABLE 2
Mean (SD) Frequency of Binucleated Cells with Micronuclei (BNMN), Total Micronuclei (MNL) per 1000 Binucleated Peripheral Lymphocytes, Frequency of Mononucleated Cells per 1000 Lymphocytes (MNMO), and Proliferation Index (PI) by Region before the Exposure (Phase 1), 5 d after Spraying (Phase 2) and 4 mo Later (Phase 3)

Region	Santa Marta	Boyacá	Putumayo	Nariño	Valle del Cauca
Phase 1					
Number of subjects	60	62	58	63	28
BNMN	1.83 (0.97)	5.64 (1.72)	3.61 (1.51)	4.12 (1.65)	5.75 (2.48)
MNL	1.97 (1.05)	6.16 (1.91)	3.90 (1.66)	4.36 (1.85)	6.02 (2.50)
MNMO	0.41 (0.44)	0.99 (0.64)	0.47 (0.51)	0.51 (0.39)	1.12 (0.88)
PI	1.54 (0.14)	1.45 (0.14)	1.68 (0.15)	1.47 (0.12)	1.51 (0.15)
Phase 2					
Number of subjects	ND	55	53	55	27
BNMN		4.96 (2.00)	4.64 (2.45)	5.98 (2.03)	8.64 (2.81)
MNL		5.41 (2.25)	5.02 (2.95)	6.35 (2.18)	8.98 (2.93)
MNMO		0.87 (0.65)	0.44 (0.46)	0.70 (0.45)	1.65 (0.62)
PI		1.72 (0.14)	1.66 (0.20)	1.40 (0.18)	1.51 (0.14)
Phase 3					
Number of subjects	ND	ND	50	56	26
BNMN			5.61(3.08)	3.91 (1.99)	7.38 (2.41)
MNL			5.96 (3.23)	4.13 (2.20)	8.17 (2.72)
MNMO			0.82 (0.54)	0.55 (0.42)	0.98 (0.60)
PI			1.43 (0.17)	1.41 (0.14)	1.45 (0.20)

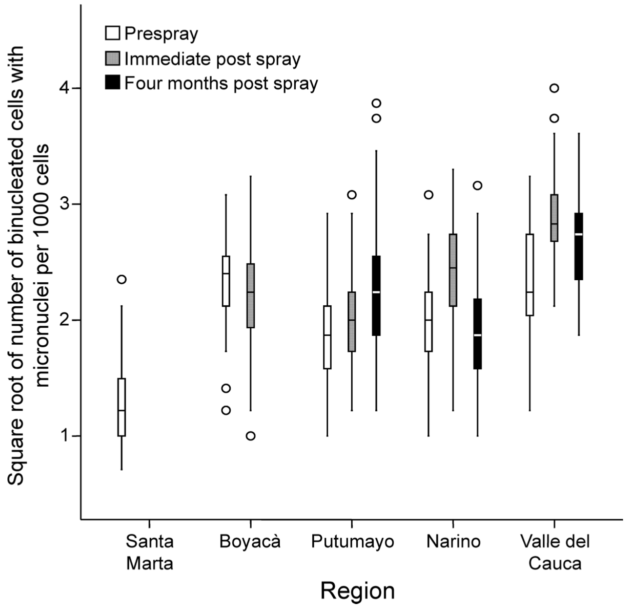

FIG. 1. Box plot of frequency of BNMN in the five study regions with samples taken prespray, 4–5 d post-spray, and 4 mo post-spray. Box plots: The center horizontal line marks the median of the sample. The length of each box shows the range within which the central 50% of the values fall, with the top and bottom of the box at the first and third quartiles. The vertical T-lines represent intervals in which 90% of the values fall. The ❍ symbols show outliers. See text for description of statistically significant differences.

although Boyacá and Valle del Cauca showed a significantly higher frequency than Nariño and Putumayo. A higher frequency of BNMN in Boyacá was also observed in a second sampling 1 mo later.

There were differences in frequency of BNMN between sampling periods. A statistically significant difference in frequency of BNMN between first and second sampling was observed in Valle, Putumayo, and Nariño immediately (<5 d) after spraying. Four months after spraying in Nariño, there was a statistically significant decrease in the mean frequency of BNMN compared with the second sampling, but in Valle del Cauca the decrease was not significant nor was the increase observed in Putumayo significant (Figure 1 and Table 2).

The frequency of mononucleated cells with micronuclei (MOMN) was used as an index of background level of chromosomal damage accumulated in vivo (Table 2). The lowest frequency of MOMN for the first sampling was observed in Santa Marta; however, there was no marked difference in frequency of MOMN in Santa Marta, Putumayo, and Nariño and no statistically significant difference between Valle and Boyacá. However, Valle and Boyacá had a significantly higher frequency of MOMN than Putumayo, Nariño, and Santa Marta at first sampling. Immediately after spraying, Valle showed a significantly higher frequency of MOMN compared to Putumayo and Nariño, and Nariño was also higher than Putumayo. Between first and second sampling, the increase in frequency of MOMN in Nariño and Valle was statistically significant, but there was no difference in Putumayo nor in Boyacá 4 mo after the first sampling. Data suggest greater exposure to genotoxic agents in these populations is independent of the exposure to glyphosate products.

The proliferation index (PI) in all the studied groups was in the range of normal values described in the literature. No significant reduction of PI was observed in association with environmental exposures in groups of subjects from the different regions. A statistically significant correlation coefficient (0.288) between PI values from the first and the second samplings was observed, confirming the association with individual characteristics and not with any toxicity related to the exposure or to the culture techniques. Due to the low frequency observed, data with respect to other nuclear alterations, including in cytome analysis (Fenech, 2007), are not described in Table 2: the mean frequency of nucleoplasmic bridges (NPB) for all subjects was 0.010 per 1000 cells, that of nuclear buds was 0.022 per 1000 cells, and only rare necrotic and apoptotic cells were found in some samples.

Gender was the most important demographic variable affecting the BNMN index. Frequencies of BNMN in females were greater than those in males (mean 4.43 ± 2.36 vs. 3.61 ± 1.82, respectively, in total population) (Table 3). The groups of subjects were evenly matched for gender by including only couples in the study. No association was found between frequency of MN and age as a categorical variable, nor was there an association with smoking, but prevalence of smoking was low (~10% in the total population). A higher baseline frequency of MN was observed in subjects of African origin, suggesting greater susceptibility. Other lifestyle factors such as alcohol, coffee consumption, or illicit drug intake were not associated with initial measures of BNMN and MOMN.

One hundred and thirty-four of the 152 subjects in Nariño, Putumayo, and Valle reported information on contact with Glyphos and Cosmo-Flux after eradication spraying. The other 18 did not provide information in the second survey or blood samples were inadequate for testing micronuclei. Sixty-six (49.2.0%) reported no contact with the spray and 68 (50.8%) reported coming into contact with the spray because they entered sprayed fields or reported contact with the spray droplets. The mean BNMN in Nariño and Putumayo was greater in respondents who self-reported exposure, but differences were not statistically significant (Table 4). In Valle, only one respondent reported contact with glyphosate.

Region, gender, and older age (≥35 yr) were the only variables associated with the frequency of BNMN before spraying (Table 5). In fact, using Santa Martha, where no use of pesticides was reported, as reference, Boyacá, Valle del Cauca, Putumayo, and Nariño showed a statistically significant higher mean frequency of BNMN. There were also significant differences between Boyacá and Valle and Putumayo and Nariño. Females had a statistically higher mean frequency of BNMN than males after adjusting for all other variables. Greater age was also associated with greater frequency of BNMN. Neither exposure to genotoxic products, nor ethnicity, nor intake of folic acid was associated with frequency of BMMN at the first sampling. The multiple linear regression analysis of difference between second and first sampling only demonstrated statistically significant association with region after adjusting for all other variables, indicating that Putumayo, Nariño, and Valle had significantly greater differences between second and first sampling than Boyacá.

DISCUSSION

The main objective of this study was to test whether there was an association between aerial spraying of glyphosate and cytogenetic alterations, evaluated as frequency of MN in peripheral leukocytes. Biomonitoring was carried out in three regions of Colombia in populations exposed to aerial spraying of glyphosate: Putumayo and Nariño, where the application was performed for eradication of coca and poppy, and Valle del Cauca where the herbicide was used for maturation of sugar cane. Two control populations not exposed to aerial spraying of glyphosate were also selected: the first one from Sierra Nevada de Santa Marta, where organic coffee is grown without the use of any pesticides, and the other from Boyacá, with a region of illicit crops, where manual eradication is performed and subjects were potentially exposed to several pesticides but not glyphosate for aerial eradication. The ex vivo analysis of leukocytes in the presence of cytochalasin B, added 44 h after the

TABLE 3
Association of Mean (SD) Frequency of Binucleated Cells (First Sampling) with Micronuclei (BNMN/1000 Binucleated Lymphocytes) and Demographic Variables

Variable	Santa Marta	Boyacá	Putumayo	Nariño	Valle del Cauca	Total
Sex						
Females	1.98 (1.03)	6.22 (1.79)	3.91 (1.71)	4.57(1.77)	6.45 (2.82)	4.43 (2.36)
Males	1.68 (0.90)	5.06 (1.46)	3.31 (1.25)	3.66 (1.39)	5.05 (1.94)	3.61 (1.82)
p	.236	.007	.131	.028	.138	.002
Age						
18–24 yr	2.00 (1.14)	5.50 (1.96)	3.32 (1.25)	3.64 (1.72)	6.19 (2.15)	3.67 (2.16)
25–34 yr	1.66 (0.87)	5.70 (1.66)	3.53 (1.17)	4.20 (1.77)	4.20 (0.76)	3.97 (2.08)
35 yr and older	1.93 (0.67)	5.62 (1.73)	3.84 (1.86)	4.25 (1.52)	6.04 (2.84)	4.41 (2.19)
p	.438	.929	.574	.564	.313	.093
Ethnicity						
Mestizo	1.83 (0.97)	5.64 (1.72)	3.72 (1.52)	4.75 (1.06)	5.82 (2.44)	3.94(2.24)
Africa and Indian	0	0	2.86 (1.31)	4.10 (1.66)	5.64 (2.65)	4.20(1.90)
p			.162	.588	.850	.368
Smoking						
Yes	2.00 (1.06)	5.33 (0.76)	3.31 (1.00)	4.77 (1.51)	4.50 (1.41)	3.83 (1.60)
No	1.82 (0.97)	5.65 (1.76)	3.80 (1.56)	4.03 (1.66)	5.90 (2.57)	4.07 (2.20)
p	.693	.756	.395	.233	.459	.592
Folic acid intake (quartiles)						
1	1.92 (0.99)	6.11 (1.95)	3.23 (1.12)	4.50 (1.75)	5.86 (2.34)	3.89 (2.23)
2	1.64 (0.66)	5.70 (1.75)	3.47 (1.49)	3.80 (1.47)	5.86 (2.74)	3.97 (2.21)
3	1.69 (0.92)	5.69 (1.82)	4.00 (1.37)	3.85 (2.04)	6.58 (2.84)	4.47 (2.22)
4	1.94 (1.20)	4.94 (1.13)	3.69 (2.429)	4.28 (1.51)	4.63 (2.05)	3.75 (1.89)
p	.779	.399	.515	.645	.612	.220

TABLE 4
Mean Frequency of Binucleated Cells with Micronuclei (BNMN) at the Second Sampling per 1000 Binucleated Lymphocytes and Self-Reported Exposures to the Glyphosate Spray in Three Areas Where Aerial Application Had Occurred

	Nariño (n = 55)		Putumayo (n = 53)		Valle del Cauca (n = 26)	
Route of exposure	*n*	Mean BNMN (SD)	*n*	Mean BNMN (SD)	*n*	Mean BNMN (SD)
No exposure	28	5.81 (1.85)	13	3.84 (1.30)	25	8.56 (2.90)
Spray in air	5	7.30 (0.57)	1	5.50 (0)		
Spray on skin	8	5.62 (1.60)	15	4.90 (1.87)	1	9.50 (0)
Entered sprayed field	14	6.06 (2.77)	24	4.87 (3.18)		
p Value (ANOVA)		0.472		0.612		0.760
Any exposure	27	6.16 (2.22)	40	4.90 (2.69)	1	9.50 (0)
p Value (no exposure vs. any exposure)		0.525		0.181		0.760

Note. The data comprise respondents in the second survey from which blood samples were obtained.

TABLE 5
Multiple Linear Regression Analysis Adjusted for Region, Age, Gender, Ethnicity, and Folic Acid Intake

Variable	Coefficient	p	95% CI
Region			
Boyacá	3.75	≤.0001	3.19, 4.31
Putumayo	1.58	≤.0001	1.00, 2.16
Nariño	2.06	≤.0001	1.49, 2.64
Valle del Cauca	3.65	≤.0001	2.92, 4.39
Age (yr)			
25–34	0.28	.250	–0.20, 0.76
35 and older	0.75	.008	0.20, 1.31
Gender			
Females	1.00	≤.0001	0.60, 1.40

start of cultivation, made it possible to distinguish between nondividing mononucleated cells—as an index of accumulated chromosomal damage—and binucleated cells, which had completed one nuclear division during in vitro culture and expressed MN associated with recent exposure to genotoxic agents.

The baseline level of chromosomal damage, evaluated as frequency of BNMN, was associated with the different regions considered in our study. The frequency of BNMN before spraying was also associated with region, gender, and age. Gender difference in the background incidence of MN in peripheral leukocytes, with the frequency being consistently higher in females, and a strong correlation between MN frequency and increasing age are well documented (Bonassi et al., 1995, 2001; Bolognesi et al., 1997a).

Data demonstrated no significant effect of smoking, confirming findings from the literature (Bonassi et al., 2003) although prevalence of smoking in our study population was small (7–20%, Table 1). No association with alcohol consumption was observed. A higher susceptibility of people of African origin compared to the mestizo group was suggested by a greater baseline frequency of BNMN and increased frequency at the second sampling period.

There was some indication of an association between BNMN and exposure to pesticides in general. The lowest frequency of BNMN was observed in Sierra Nevada de Santa Marta, where people self-reported that they did not use pesticides. The mean frequency of BNMN in this group of subjects (1.83 ± 0.97) was similar to that observed in healthy unexposed subjects for the same range of age (Bolognesi et al., personal communication). The higher mean frequency of BNMN observed in Boyacá and Valle del Cauca (5.64 ± 1.72 and 5.75 ± 2.48, respectively) and that in Nariño and Putumayo (4.12 ± 1.65 and 3.65 ± 1.51, respectively), compared to Santa Marta, are in agreement with similar biomonitoring studies carried out in subjects exposed to pesticides using the MN test or other genetic endpoints (Bolognesi, 2003; Bull et al., 2006).

There was no clear relationship between BNMN and the reported use of pesticides classified as genotoxic. Participants in Boyacá and Valle del Cauca showed higher frequency of BNMN than those in Putumayo and Nariño. However, a greater proportion of participants in the latter regions self-reported the use genotoxic pesticides (76.6% in Nariño and 61.7% in Putumayo). There is no information available on other relevant factors such as frequency of use, rate applied, time of exposure, and protective measures used, and we could therefore not characterize exposures to explain the differences. There were further inconsistencies; for example, in Boyacá, where more frequent use of pesticides was expected, only 24.2% of participants self-reported use, compared with the greater values in Nariño and Putumayo. However, it is possible that in areas such as Boyacá, individuals might be potentially exposed to persistent pesticides applied in the past and still present in the environment.

There was no evidence of an association between BNMN and folic acid deficiency. An assessment of folic acid intake from the semiquantitative food frequency questionnaire showed that, according to accepted recommendations (Herbert, 1987), the diet of the study populations was not deficient in folic acid and there were only small differences between regions. Consistent with these data, no association was found between MN and folic acid intake, either as a continuous variable or by quartiles.

The frequency of BNMN increased after spraying with glyphosate but not consistently. The results obtained with a second sampling, carried out immediately after the glyphosate spraying, showed a statistically significant increase in frequency of BNMN in the three regions where glyphosate was sprayed. However, this was not consistent with the rates of application use in the regions. The increase in frequency of BNMN in Valle (application rate = 1 kg a.e. glyphosate/ha) was greater than that in Nariño and Putumayo (3.69 kg a.e. glyphosate/ha).

There was no significant association between self-reported direct contact with eradication sprays and frequency of BNMN. The frequency of BNMN in participants who self-reported that they were exposed to glyphosate because they entered the field immediately after spraying (to pick the coca leaves), felt spray drops in their skin, or they thought they were exposed because they had contact with the chemical in the air, was not significantly greater than in subjects living in the same areas but who were not present during spraying. Decreases in frequency of BNMN in the recovery period after glyphosate spraying were not consistent. The third sampling, 4 mo after spraying, demonstrated a statistically significant decrease in frequency of BNMN only in Nariño.

Overall, these results suggest that genotoxic damage associated with glyphosate spraying, as evidenced by the MN test, is small and appears to be transient. The frequencies of BNMN in Nariño and Putumayo during the second and the third sampling fell within the range of values observed in Boyacá, an area where people were exposed to a complex mixture of different pesticides (including glyphosate). A greater increase in frequency of BNMN was observed in Valle del Cauca, but it cannot be attributed only to the glyphosate exposure, because the application rate of the herbicide in this area was one-third compared with that in Nariño and Putumayo. This conclusion is further supported by the frequency of MN in mononucleated cells (MOMN), which provides an indication of the background level of chromosome/genome mutations accumulated in vivo (Manteuca et al., 2006). A statistically significant increase of MOMN was observed in Boyacá and Valle del Cauca before and after the aerial spraying, suggesting exposure to other genotoxic compounds in these populations was independent of the exposure to glyphosate. Evidence indicates that the genotoxic risk potentially associated with exposure to glyphosate in the areas where the herbicide is applied for eradication of coca and poppy is of low biological relevance. One of the strengths of our study was the detection of a transient chromosomal damage, evaluated as MN frequency in peripheral blood of the exposed subjects, since it was possible to compare the baseline before spraying with the effects detected immediately after spraying. Glyphosate persists in the environment for only a short time (half-life for biological availability in soil and sediments is hours, and 1-3 d in water; Giesy et al., 2000), is rapidly excreted by mammals and other vertebrates (Williams et al., 2000; Acquavella et al., 2004) and chronic effects, if any, would not be expected.

One of the major drawbacks of environmental epidemiology studies is the characterization of exposures to the agents being investigated. In this study two approaches were used to characterize exposures to glyphosate: ecological and self-reported. In the ecological study design, frequency of BNMN in participants was compared from regions with different patterns of pesticide use. As previously discussed (Sanin et al., 2009), this ecological design may result in misclassification of exposures (Arbuckle et al., 2004), but as an exploratory assessment of exposure it is useful (Ritter et al., 2006).

Others have attempted to improve assessment of exposure to pesticides in epidemiological studies. One study used a self-administered questionnaire for the assessment of exposure to glyphosate, which was defined as (a) ever personally mixed or applied products containing glyphosate; (b) cumulative lifetime days of use, or "cumulative exposure days" (years of use times days/year); and (c) intensity-weighted cumulative exposure days (years of use times days/year times estimated intensity level) (De Roos et al., 2005). A pesticide exposure score based on self-reported work practices was recently developed to estimate annual exposure level (Firth et al., 2007). Based on an algorithm to estimate lifetime exposure to glyphosate from questionnaire information, a moderate correlation was found with concentrations of glyphosate in urine and no significant correlation with self-reported exposure (Acquavella et al., 2004).

In our study, questions related to whether there was direct contact with the spray were used but this did not consider area of skin exposed, region of skin exposed, differences in rates of penetration, or personal hygiene.

Given the situation, the best approach possible, a prospective cohort, was used but the need to use better procedures to estimate the exposure is acknowledged. Based on the applicable Bradford–Hill guidelines (Hill, 1965), it is not possible to assign causality to the increases in frequency of BNMN observed in our study. There was a smaller frequency of BNMN and MOMN in the region of no pesticide use compared with the regions where pesticides (including glyphosate) were used, which is consistent with other reports in the literature. Although temporality was satisfied in the increase in frequency of BNMN after spraying, this response did not show strength as it was not consistently correlated with the rate of application. Recovery was also inconsistent with decreases in frequency of BNMN in the areas of eradication spraying but not in the area where lower rates were applied on sugar cane.

Further studies are needed to better characterize the potential genotoxic risk associated with the application of glyphosate for sugar cane maturation. The smaller number of subjects recruited in this study and small amount of information about the exposure precluded any conclusions. Many pesticides are used in conventional agriculture in Colombia and many pesticides are used in the production of coca (Solomon et al., 2007a, 2007b); however, there is not sufficient information to correlate the frequency of MN to the pesticide exposure.

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Annex 132

CENTRE FOR TOXICOLOGY AND ENVIRONMENTAL HEALTH, L.L.C., UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES, *GLYPHOSATE FREQUENTLY ASKED QUESTIONS*, 2009

(Available at: http://www.akrr.com/pdf/PR_2335%20Glyphosate_Toxocologist%20FAQ.pdf (last visited 7 March 2010))

Center for Toxicology and Environmental Health, L.L.C.

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GLYPHOSATE
Frequently Asked Questions

What is glyphosate?
Glyphosate is N-phosphonomethyl glycine. Glyphosate agricultural products are broad-spectrum, non-selective herbicides used on most species of green plants. You may know the product name, or have purchased the product for your own home use by one of its common names i.e., Roundup, WeatherMax or Roundup Ultramax. Glyphosate has been used for more than 35 years and is probably the world's most widely used herbicide. It is registered in more than 130 countries and is approved for weed control in more than 100 crops. The glyphosate formulation that will be used by the Alaska Railroad Corporation (hereafter referred to as "ARRC") is called Aquamaster Herbicide and contains 53.8% glyphosate (isopropylamine salt). In addition to glyphosate, the formulation typically includes water and a surfactant system. The surfactant system enables the product to adhere to the plant surfaces. A few days after treatment, the plant wilts and yellows. In addition to being approved for use on land, Aquamaster is approved for weed control in aquatic environments, including ponds and reservoirs, waterfowl sanctuaries, and recreational waterways. Only a few herbicides have the favorable toxicological and environmental characteristics that allow them to be directly applied to aquatic vegetation. Most recently, AquaMaster was selected by the State of Florida to rid the Everglades of invasive weeds. The University of Florida in their publication on glyphosate, discuss why land managers should continue to use glyphosate containing products to protect managed habitats from weeds without concern for unreasonable adverse environmental impacts.

Glyphosate is water soluble and binds tightly to soil. The product works by disrupting a plant enzyme essential for plant growth. The enzyme is called EPSP synthetase and is not present in humans or animals. Therefore, the biochemical pathway affected is specific to plant species (not humans, mammals, or fish) contributing to the low risk to human and animal health from use of glyphosate according to the label directions used by ARRC.

In addition to agricultural use, glyphosate is used to control weeds in utility right-of-ways, on roadsides, along railways or in places around the home such as sidewalks and gardens. Glyphosate is also used by Wildlife organizations to protect and restore wildlife habitats threatened by invasive, non-native vegetation. Conservation groups have chosen glyphosate formulations because of their effectiveness against most weeds and because they have very low toxicity to wildlife.

How does glyphosate compare in toxicity to other commonly used chemicals?
Glyphosate has been the subject of hundreds of health, safety, and environmental studies. To get a clear picture of the environmental and toxicological characteristics of glyphosate it is important to consider the total weight of evidence from scientific studies provided by regulatory agencies,

industry, universities, governmental agencies, and scientists from around the World. The U.S Environmental Protection Agency (EPA), Health Canada, European Commission, U.S. Department of Agriculture Forest Service, World Health Organization and other scientists have reviewed this data. Those reviews applied internationally accepted methods, principles and procedures in toxicology and have determined that there are no grounds to suggest concern for human health. Their overwhelming consensus is that glyphosate when used according to label directions, poses no unreasonable risk to people, wildlife, or the environment. Researchers from New York Medical College similarly conclude that glyphosate does not have the potential to produce adverse effects in humans. Short-term exposure to glyphosate and its breakdown products is estimated to be 7,350 to 1,730,000 times lower than their corresponding median lethal dose (LD50) values, thus demonstrating that potential short-term exposure is not a health concern. Several toxicology text books have developed a relative ranking system for chemicals by their LD50 values to help people answer the question "how toxic is this stuff"? The ranking system listed below puts glyphosate in the category of slightly toxic and is less toxic than table salt.

Table 1.
General Toxicity Ranking Categories

Toxicity ranking	Dose (mg/kg)	For Average Adult
Practically nontoxic	>15,000	> 1 quart
Slightly Toxic	5,000-15,000	1 pint to 1 quart
Moderately toxic	50 – 5,000	1 ounce to 1 pint
Very toxic	50 – 500	1 teaspoon to 1 ounce
Extremely toxic	5 – 50	7 drops to 1 teaspoon
Supertoxic	< 5	< 7 drops

Table 2
Relative Toxicity Ranking of Glyphosate Compared to Other Compounds

Actual Ranking #	LD_{50} (mg/kg)	Chemical
14	10,000	Alcohol (ethanol)
13	**>5,000**	**Glyphosate**
12	4,000	Sodium Chloride (table salt)
11	2,400-3,480	biphenyl
10	1,500	Ferrous Sulfate (iron supplement)
9	1,375	Malathion (pesticide)
8	900	Morphine (opiate analgesic)
7	150	Phenobarbital (sedative)
6	142	Tylenol (acetaminophen)
5	2	Strychnine (rat poison)
4	1	Nicotine (stimulant found in cigarettes)
3	0.5	Curare (arrow poison)
2	0.001	2,3,7,8-TCDD (dioxin)
1	0.00001	Botulinum toxin (food poison)

Can glyphosate cause genetic damage?
Genetic toxicity tests are performed to provide information on the production of heritable changes (mutations) that could lead to further adverse biological consequences. In other words, will the chemical cause DNA damage? Glyphosate has been studied extensively in a wide battery of genetic toxicity tests. Such extensive data sets are sometime difficult to interpret but for glyphosate this is not the case. The overwhelming evidence indicates that glyphosate does not damage DNA. No genotoxic activity is observed in standard assays conducted according to international guidelines. A number of regulatory agencies, scientists, and researchers conclude that glyphosate is neither mutagenic nor clastogenic (causing chromosome breaks). Thus, glyphosate does not pose a risk of heritable (passed from parent to child) or somatic (body cell) mutations in humans.

Can glyphosate cause cancer?

The long-term toxicity and cancer potential of glyphosate has been evaluated in studies with mice and rats. Glyphosate was not carcinogenic to either species. These studies and results have been evaluated by a number of regulatory agencies and scientific organizations. Each group has concluded that glyphosate is not carcinogenic. The EPA uses a summary ranking system for human and animal cancer studies. These rankings place the overall evidence in classification Groups A through D. Group A rankings are chemicals that are known human carcinogens, whereas Group D chemicals are not classifiable as to human carcinogenicity. Accordingly, EPA has classified glyphosate as Group D, "Not classifiable as to human carcinogenicity" because there is inadequate evidence that glyphosate causes cancer in animals and no evidence that it causes cancer in humans.

Have other studies indicated health issues with Glyphosate?

A basic principle of toxicology was first stated by the 16th century physician Paracelsus, who said *"all substances are poisons; there is none which is not a poison. The right dose differentiates a poison and a remedy."* In other words, all chemicals are toxic at some dose, and conversely, there is some dose at which no toxicity is apparent. For all chemicals, the toxicity resulting from exposure is determined by the dose of chemical absorbed by the organism. As the dose of a chemical increases, its effects increase in magnitude and severity; conversely, as the dose of a chemical decreases, so does the magnitude and severity of its effects. This concept is termed "dose-response," and forms one of the basic foundations of toxicology. For all chemicals there is a dose (termed the "threshold dose") below which no effect is elicited. This is true for both the beneficial (pharmacological) and harmful (toxicological) effect of chemicals. Some studies show toxicity of glyphosate at very high concentrations. Given the fact that there are literally hundreds of toxicology studies on glyphosate, the question should not be "have other studies indicated health issues with glyphosate?", but rather "would health effects be expected from AKRR's use of glyphosate along railroad right-of-ways?"

The answer to this question is that glyphosate poses no substantial concern for systemic toxic effects in workers or the general public at the recommended application rate. Adult applicators and children have been identified as the most sensitive subpopulations because they have the highest potential exposures to glyphosate. Estimates of exposure to these two subpopulations are typically evaluated using a "Margin of Exposure" or MOE analysis where toxicologists compare the lowest No Observable Adverse Effect Levels (NOAELs) determined from animal and human studies to worst-case levels of human exposure. MOEs of greater than 100 are considered by authoritative bodies to indicate confidence that no adverse health effects would occur. The MOEs for worst-case chronic exposure to glyphosate ranged from 3,370 to 5,420. Based on these values, it can be concluded that glyphosate does not have the potential to produce adverse effects in humans. The only real risk from glyphosate exposure is possible skin or eye irritation from direct contact with the liquid by those individuals preparing the spray for weed control. Irritant effects are considered to be transient and reversible.

What is the environmental fate of glyphosate?
As with the human health risks described above, there is very little indication that glyphosate will cause adverse effects in the environment at the anticipated levels of exposure from use of this product on railroad right-of-ways. Glyphosate binds readily with soil particles, which limits its movement in the environment; therefore it does not have herbicidal activity once it contacts soil. Glyphosate is also not absorbed from the soil by plant roots. Glyphosate has a low Koc (measure of soil adsorption) which is an indication that glyphosate will not move readily through soil and is unlikely to leach into non-target areas. When applied to foliage, glyphosate is readily absorbed and translocated to various parts of plants via the phloem. Glyphosate is readily degraded by soil microbes with an average half-life of two months in soil and two to 10 weeks in water. The major degradation product is aminomethylphosphonic acid (AMPA). AMPA is further degraded in the environment to carbon dioxide and phosphate. In plants, glyphosate is slowly metabolized. The potential for glyphosate to leach into groundwater has been evaluated in a number of studies which reveal that glyphosate is unlikely to cause groundwater contamination. Most studies show no adverse effect on soil microorganisms.

How rapidly does glyphosate break down in the Alaska environment?
The University of Alaska with assistance from the Alaska Railroad and the US Department of Agriculture is conducting a study on the environmental fate and soil dissipation of glyphosate in the Alaskan environment. The first phase of the study near Seward included two separate rail bed sites; one site in the Seward Yard and the other near the Upper Trail Lake area. Monitoring wells were installed and samples of glyphosate were taken over time from surface soils, root zone soils, below root zone soils, and groundwater. Results agree with the discussion above in that glyphosate is degraded relatively rapidly in Alaskan soil and does not migrate to a significant degree in the soil environment. In addition, the results indicate that the levels of glyphosate detected in soil and groundwater after treatment would not be toxic to humans or animals including fish. The second phase of the study is being concluded near Fairbanks.

What effect does Glyphosate have on birds, insects, and mammals?
Glyphosate has been tested on a variety of wildlife birds and mammals in both laboratory and wild land environments. Furthermore, there are several available field studies that examine the effects of glyphosate application comparable to those that will be used by AKRR. The toxicity studies on terrestrial animals are generally consistent with those on experimental mammals. The available field studies clearly show that at plausible levels of ambient exposure, direct toxic effects are unlikely. In fact, if any effects are seen in terrestrial mammals after the application of glyphosate, they are most likely to be associated with changes in habitat rather than direct toxic effects. The changes would be no different than from mechanical clearing of vegetation. Data for single

exposures classify glyphosate as practically non-toxic to tested insects and birds. Glyphosate is no more than slightly toxic to mammals. EPA does not expect that most endangered terrestrial organisms will be affected by the registered uses of glyphosate. The small mammal is a conservative target species for characterizing risks because small organisms, compared with large organisms generally receive higher doses at fixed levels of exposure in environmental media (e.g., contaminated food, water). Also, available toxicity data does not suggest systematic differences in sensitivity to glyphosate among species. The primary route of exposure for a terrestrial animal is from contaminated vegetation. For this source, levels of exposure remain below those of concern even at the highest allowed application rates of glyphosate. At application rates that ARRC would use, levels of exposure are substantially below those of concern. This analysis is consistent with field studies on glyphosate that indicate that it would be unlikely for glyphosate to have direct toxic effects on wildlife. Based on current data, EPA has determined that the effects of glyphosate on birds and mammals are minimal. The available data indicate that glyphosate does not bioaccumulate in terrestrial species including carnivores, herbivores, and omnivores.

What effect does Glyphosate have on aquatic species including fish?

There is not much evidence that aquatic animals or plants will be adversely affected by normal applications of glyphosate. Although glyphosate is registered for use as an aquatic herbicide, it is only effective on plants with vegetation growing above the water level. Most species of algae and macrophytes do not appear to be more sensitive than fish or aquatic invertebrates to glyphosate. For most aquatic species, glyphosate levels of 1 mg/L are not likely to cause adverse effects. Field studies indicate that maximum initial concentrations of glyphosate in water after aerial or ground applications is considerably less than 1 mg/L.

A review of the published toxicity studies on fish indicate that glyphosate is relatively non-toxic to fish with 24-96 hours LC50 values ranging from approximately 10 mg/L to >200 mg/L. EPA and USDA examined the toxicity of glyphosate to a variety of fish species including rainbow trout, various salmonid species including chinook, coho, sockeye, as well as fingerlings, fry, and early life stages. EPA and USDA determined that glyphosate effects on fish would not be expected based on registered application rates. Glyphosate does not bioaccumulate in fish.

What happens if I eat berries from along the tracks?

Glyphosate application along right-of-ways creates the potential for accidental overspray of wild foods such as berries that could be later collected for consumption. Consideration of actual glyphosate use patterns, the percentage of forests or roadsides that actually receive treatment, and the resulting phytotoxic effects on the sprayed plants, suggests that inadvertent exposure will be extremely unlikely. Residual levels of glyphosate arising from mock overspray of berries have been measured and the potential dietary exposure quantified. Peak glyphosate residue levels were 19.5 ug/g and it was estimated that maximal berry consumption for an individual might be 150 g for an adult and 30 g for a 1-6 year old child. These parameters predict an exposure of 45 ug/kg body wt for both subgroups and rely on the assumption that the surface residues were not reduced by washing before consumption. This dose is considerably below the NOAEL for chronic toxicity and more than two times below the EPA reference dose for glyphosate, indicating that occasional eating of berries containing a glyphosate residue would not result in adverse human health effects.

What can you tell me about the toxicity of the "inert ingredients" i.e., the surfactant Agri-Dex?
Agrid-Dex is a trade name of a product and is approved for use in aquatic applications. Agri-Dex is a surfactant used with glyphosate. The surfactant system enables the products to adhere to the surface of leaves so the active ingredient (glyphosate) can penetrate. AGRI-DEX is designed to be compatible with a wide range of pesticides and form stable emulsions in their tanks mixes. Agri-Dex is classified as practically non-toxic to both fish and vertebrates.

What is the overall Risk of Herbicide Program Proposed by ARRC?
To address the overall risk and potential toxicity impact of glyphosate uses specific to the state of Alaska ARRC contracted a study with the University of Alaska Fairbanks to address the transport and degradation of glyphosate under real-world conditions that mimic use by the ARRC. As previously mentioned the preliminary results of this study indicate that glyphosate has low mobility on the environment and is being degraded in the soil. Concentrations of glyphosate measured in soil and water were well below those that would harm humans or animals, including fish. The results of this study build on the large knowledge base of the environmental impacts of glyphosate which indicate that the herbicide program proposed by ARRC would not have an adverse impact on the health of humans or the environment.

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Annex 133

TECHNICAL DATA SHEET FOR ROUNDUP SL

(Agriculture and Livestock National Exchange Market (Bolsa Nacional Agropecuaria S.A.*)*

<table>
<tr><td rowspan="3">Agriculture and Livestock National Exchange Market</td><td rowspan="3">FORMAT PRODUCT TECHNICAL DATA SHEET</td><td>CODE</td></tr>
<tr><td>VALIDITY SINCE</td></tr>
<tr><td>VERSION</td></tr>
</table>

<table>
<tr><td colspan="3">PRODUCT TECHNICAL DATA SHEET</td></tr>
<tr><td>PRODUCT NAME</td><td colspan="2">ROUNDUP SL</td></tr>
<tr><td>SUPPLIER REQUIREMENTS</td><td colspan="2">1. to have valid ICA registration number as producer and/or seeds distributor
2. Comply with Resolution 148 issued by ICA
3. to have adequate places for seeds storage

Valid ICA registration, for offered species that have it. Seeds must be treated to prevent insects and pathogens.
To have more than 5 years' operation in the market
To have made transactions for at least 950 minimum monthly wage in force the previous year</td></tr>
<tr><td>TYPE</td><td colspan="2">Agricultural Herbicide, Soluble Liquid (certificate).</td></tr>
<tr><td rowspan="8">TECHNICAL CHARACTERISTICS OF THE PRODUCT</td><td>Active ingredient</td><td>Glyphosate, Isopropyl amine Salt</td></tr>
<tr><td>State</td><td>Liquid</td></tr>
<tr><td>Appearance and smell</td><td>Amber viscous liquid with a slight amine smell</td></tr>
<tr><td>Solubility</td><td>Very soluble in water</td></tr>
<tr><td>pH</td><td>4,4 to 4,9 (Solution at 1%)</td></tr>
<tr><td>Crystallization point</td><td>< 0 °C</td></tr>
<tr><td>ICA Registration Number</td><td>756-R</td></tr>
<tr><td colspan="2">Roundup SL is not flammable, nor explosive. It is considered harmful if ingested; it might be irritant in contact with eyes</td></tr>
<tr><td></td><td>Additional information
Risks Identification</td><td>Acute toxicity: It is very unlikely that exposure to Roundup SL poses risk of</td></tr>
</table>

		acute toxicity. It may cause slight irritation on skin and moderate to severe in eyes.
		Chronic Toxicity: Chronic effects on humans have not been documented attributable to chronic exposure; studies on mutagenicity and carcinogenicity have resulted negative.
		Ecotoxicity: It is not harmful to aquatic organisms (middle toxicity to rainbow trout, not toxic to birds). It must not be poured near channels, drains, nor running water or water reservoirs. It is not toxic to bees under recommended use directions.
PRESENTATION	Plastic container of 1, 4 or 10 liters; metal container of 10 and 20 liters	
QUANTITY	50 liters	
LIFE SPAN	1 year (validity)	
ADDITIONAL INFORMATION	Refusal conditions: Not compliance with any of the conditions of this technical data sheet.	
	Submit in person the product in 22 Mayors' Office or UMATAS [Municipal Agricultural Technical Assistance Units] in the municipalities (except Puerto Colombia Municipality) in which productive projects of medicine plants, or in the rural producers associations determined by the Economic Development Office, according to the list of beneficiaries, term, and Schedule set by the mentioned audit and/supervising office.	
	The supplier pays on the cost of transport, downloading and delivery of the product.	

Prepared by: Ivette Salas Rodriguez
Reviewed by: Martin Atencio Garcia

Notice: This format was established by the Agriculture and Livestock National Exchange Market [BNA] as a guide for the preparation technical data sheets for products to be traded in the BNA. Items describe herein must be filled out according to the applicability of the product to be traded. Other items may be added if required according to the applicability of the product to be traded.

Annex 134

LABEL AND SAFETY DATA SHEET FOR GLY-41

(Colombian Agriculture & Livestock Institute (ICA), *Compañía Agrícola Colombiana, Ltda. y Cia. S.C.A.*)

SECTION 1

READ THE LABEL BEFORE USING THIS PRODUCT
KEEP OUT OF CHILDRENS REACH

CAUTION AND USE WARNINGS

Spray solutions of this product should be mixed, stored, and applied using only stainless steel, alumina, fiberglass or plastic-lined steel containers.

DO NOT MIX, STORE OR APPLY THIS PRODUCT OR SPRAY SOLUTIONS IN GALVANIZED STEEL OR UNLINED (EXCEPT STAINLESS STEEL) STEEL CONTAINERS OR SPRAY TANKS. This products or spray solutions of this product react with such containers and tanks to produce hydrogen gas which may form a highly combustible gas mixture. This gas mixture could flash or explode causing serious personal, if ignited by open flame, spark or a welder's torch, a lighted cigarette or other ignition source.

AVOID CONTACT OF HERBICIDE WITH FOLIAGE, GREEN STEMS, EXPOSED ROOTS OR FRUIT OF CROPS, DESIRABLE PLANTS AND TREES, BECAUSE SEVERE INJURY OR DESTRUCTION MAY RESULT

CAUTION:
THIS PRODUCT CAUSES EYE IRRITATION. Avoid contact with eyes and clothes.

FIRST AID

Call a medical center or doctor for treatment advice
IF IN EYES: - Hold eye open and rinse slowly and gently with water for 15 - 20 minutes. - Remove contact lenses if present after the first 5 minutes then continue rinsing eye.
TOXICOLOGICAL EMERGENCIES PHONE NUMBER
Have the product container or label with you when calling a poison control center or

doctor, or going for treatment EMERGENCY NUMBERS 24 HOURS In Bogotá: Outside Bogotá CISPROQUIM 288 6012 01 8000 916012

DOMESTIC ANIMALS: This product is considered to be relatively nontoxic to dogs and other domestic animals; however, ingestion of this product or large amounts of freshly sprayed vegetation may result in temporary gastrointestinal irritation (vomiting, diarrhea, colic, etc.). If such symptoms are observed, provide the animal with plenty of fluids to prevent dehydration. Call a veterinarian if symptoms persist for more than 24 hours

STORAGE AND DISPOSALWASTE
When storing or disposing the product, do not contaminate water, foodstuffs, animal foodstuff or seeds. Do not store at home. DO not transport or store in vehicles or places where seeds or foodstuffs for human consumption are transported or stored. Keep container closed to prevent spills and contamination. DESTROY THIS CONTAINER AFTER USING THIS PRODUCT. No container that has contained herbicides should be used to store water or food for human or animal consumption.

Approval date by ICA: 25/11/2008

[Caution symbols]

[ICA’s Approval seal]

<u>SECTION 2</u>

GLY-41 SL

Herbicide for land and aerial applications to remove unwanted vegetation in non-agricultural sites

ICA SALES REGISTERED No. 4294

GUARANTEED COMPOSITION

ACTIVE INGREDIENT:
*Glyphosate, N-(phosphonomethyl) glycine, in the form of its isopropylamine salt ……………………….……………...……………………..41.0%

INERT INGREDIENTES……………………………………………………...… 59.0%

100.0%

*Contains 480 grams per litre of active ingredient glyphosate, in the form of isopropylamine salt. Equivalent to 356 grams per litre of the acid, Glyphosate.
.

DISTRIBUTED BY:
CAC. Ltda, y Cía. S.C.A.
A.A. 50915,
Tel:(57-1) 288-6012 -- 01 8000916012
Bogota, Colombia

NET CONTENT:
Formulation date:
Expiration date:
Lot number:

TOXICOLOGICAL CATEGORY IV
SLIGHTLY TOXIC
CAUTION

SECTION 3

GENERAL INFORMATION

Product description: This product is a post-emergence, systemic herbicide with no soil residual activity. It gives broad-spectrum control of many annual weeds, perennial weeds, woody bush and trees. It may be applied using most equipments commonly used on farms, after diluting and mixing it well in water or other solvents, according to the label recommendations.

MIXTURE:

Clean thoroughly all parts of application equipment after using this product, rinsing with abundant water.

NOTICE: RESULTS WILL NOT BE OPTIMAL IF DIRTY WATER, OR WATER FROM PONDS AND DRAINS THAT IS NOT CLEAR IS USED.

Mixing with water: This product mixes readily with water. Mix spray solutions of this product as follows: Begin filling the mixing tank or spray tank with the required amount of clean water. Add the recommended amount of this product near the end of the filling process and mix well. Use caution to avoid siphoning back into the carrier source. Use approved anti-back siphoning devices. During mixing and application, foaming of the spray solution may occur. To prevent or minimize foam, avoid the use of mechanical agitators, terminate by-pass and return lines at the bottom of the tank and, if needed, use an approved anti-foaming agent.

Surfactants.

Non-ionic surfactants may be used to improve wetting on foliage. Do not reduce rates of this product when adding surfactant. Read and carefully observe all caution statements and other information on the surfactant label.

WEED CONTROL

Annual weeds

Apply from 2 to 3 litres of GL Y-41 SL per hectare to control the following species:
Amaranthus spp (pigweed)*, Bidens pilosa* (Spanish needle)*, Boerhaavia erecta* (erect spiderling)*, Borreris laevis* (purple-leaved button weed)*, Cenchrus brownii* (Brown's burgrass)*, Commoiina diffusa* (climbing dayflower)*, Cyperus diffuses (*Dwarf Umbrella Grass*), Digitaria sanguinalis (hairy crabgrass), Echinochloa coIonum* (Jungle rice)*, Eleusine indica* (wire grass)*, Euphorbia hirta (*asthma weed), *Fimbrisilys annua* (annual fimbry), *Galinsoga ciliata (*hairy galingosa*), Ipomoea spp (*morning glory*), Ischaemum rugosum (*ribbed muriana grass*)*,
*Jussiaea linifolia, Kallstroemia maxima (*big caltrop*), Oryza sativa* (*Asian rice*),* *Portulaca oleracea (*common purslane*), Physalis angulata (*cutleaf groundcherry*),* *Rottboellia exaltata (*itch grass*), Tradescantia cumanensis* (*spiderwort*).*

Perennial weeds*:* Apply from 4 to 6 litres of GL Y-41 SL per hectare to control the following species:
Andropogon bicomis (West Indian foxtail)*, Axonopus micay* (pasto micael)*, Brachiaria mutica* (para grass), *Cynodon dactylon (*bermudagrass*), Cyperus spp (*papyrus*), Cyperus rotundus* (nutgrass)*, Imperata cilindrica* (cogongrass)*, Panicum maximum* (Embu guinea grass)*, Paspalum conjugatum (*hilograss*), Paspalum fasciculatum* (Mexican crown grass), *Paspalum virgatum* (talquezal)*, Paspalum paniculatum* (arrocillo) Penni setum purpureum (elephant grass), *Pennisetum clandestinum,* (Kikuyograss), *Sorghum halepense* (Johnsongrass),

Herbaceous semi-woody weeds such as Croton leptostachyus (empidonax), globules of Croton (myrtle), edible Randia (cruceto), Myrcia acuminata (smooth myrtle), canescent Cordia (sharpened foliage), Acacia farnesiana (pela, corona de Cristo, aromo), among other difficult to control. Knowing that the ligneous brushes and trees do not grow in the form of ordered plants occupying constant areas, we recommend a solution of 6 % (12 liters of GLY-41 SL per hectare, applying 27 cc of herbicide solution per plant for the control of plants woody shrubs and trees of waxy cuticle. For shrubby weeds plants with leaf area less waxed, the recommendation is a solution of the herbicide from 4% to 5% (8-10 litres of GLY-41 SL) per hectare, applying 22.5 cc per plant.

TECHNIQUES AND EQUIPMENT FOR IMPLEMENTATION:

Sites for implementation: You can use this product, as recommended for:
- Control of annual herbaceous weeds and undesirable perennial and perennial weeds in non cultivated lands,
- Control of semi-ligneous shrubs and small trees
- For burning help, to develop and maintain burning limit, fire perimeters and "black" lines,
- Along the roads and easements of power lines
- Around industrial and parking lots, buildings, fences, etc

Implementation techniques: Always use this product to the higher dose per hectare, within the range recommended, when the growth of weeds is large or dense, or if the weeds are growing up in an area without disturbing.
The control can be reduced when addressing the weeds in terms of stress and little growth as in drought, damage caused by disease or insects. They can also detract the results of control when treated weeds are covered by a layer of dust. When they have been lopped or cut, the weeds must be expected to grow back prior to treat them. For best results, the implementation should be uniform and complete. It is not necessary to spray the foliage of weeds until the solution drains. It may be necessary to repeat the

treatments to control weed that regrow from the roots or runners or when new weeds germinate by seed below the surface of the soil. You can repeat the treatments up to an annual maximum download of 27.7 litres of this product per hectare. You can use the product of 10 to 12 L/has for best results t control perennial weeds, semiligneous shrubs and trees of difficult control, when the plants grow in poor conditions, or when the infestation is dense. Do not apply this product through an irrigation system. THE HERBICIDE SOLUTION WITH WELL MAINTAINED AND CALIBRATED EQUIPMENTS, CAPABLE OF SPRAYING THE DOSES IN DESIRED VOLUMES.

This product can be applied using the following equipments:

Implementation with land equipments: Systems with or without boom and other equipment for the implementation on the ground.

To control annual weeds or perennial with equipment for the implementation on the ground, use the recommended doses per hectare for this product in volumes of 30 to 350 litres of solution. As it increases the population density of the weeds, the volume of implementation must be increased within the range recommended to obtain full coverage with the recommended dose per hectare. Select carefully the nozzle to prevent that the application is too thin and causes drift. For better results in terrestrial application use flat spray nozzle.

Hand-held or high-volume spray equipment. Knapsack and backpack sprayers, pump-up pressure sprayers, handguns, handwands, mistblowers, lances or other hand-held or motorized spray equipment used to direct the spray onto weed foliage.

Apply the spray solution onto vegetation foliage to be controlled. For applications made on a spray-to-wet basis, spray coverage should be uniform and complete. Do not spray to the point of runoff. Use coarse sprays only. Prepare the desired volume of the spray solution by mixing the amount of this product with the volume water, as shown in the following table:

Desired volume	Quantity of GLY-41 herbicide					
	½ %	1%	1½ %	2%	5%	10%
4 L	20 cc	40 cc	60 cc	80 cc	200 cc	400 cc
20 L	100 cc	200 cc	300 cc	400 cc	1 L	2 L
200 L	1 L	2 L	3 L	4 L	10 L	20 L

When using backpack sprayers, it is suggested to mix the recommended quantity of this product with the water volume in a big container separately. Then pour the spray solution into the tank of the spray pump.

Equipment for aerial – fixed wing and helicopter

Use the recommended dose of herbicide in 20 to 140 litres of water volume per hectare, unless otherwise specified on the label. Refer to the recommended volumes, application dose, and additional instructions in the individual sections of use area in the label according to the type of mixture.

Avoid direct application to any body of water. AVOID DRIFT – DO NOT APPLY DURING INVERSION CONDITIONS, WHEN WINDS ARE GUSTY, OR UNDER ANY OTHER CONDITION WHICH FAVORS DRIFT. DRIFT MAY CAUSE DAMAGE TO ANY VEGETATION CONTACTED TO WHICH TREATMENT IS NOT INTENDED. TO PREVENT INJURY TO ADJACENT DESIRABLE VEGETATION, APPROPRIATE BUFFER ZONES SHOULD BE MAINTAINED.

Coarse sprays are less likely to drift; therefore, do not use nozzles or nozzles configurations which dispense spray as fine spray droplets. Do not angle nozzles forward into the airstream and do not increase spray volume by increasing nozzle pressure. Drift control additives may be used. When a drift control additive is used, read and carefully observe the cautionary statements and all other information appearing on the additive label. Ensure uniform application. To avoid streaked, uneven or overlapped application use appropriate marking devices. Thoroughly wash aircraft, especially landing gear, after each day of spraying to remove residues of this product accumulated during spraying or flap spills. PROLONGED EXPOSURE OF THIS PRODUCT TO UNCOATED STEEL SURFACES MAY RESULT IN CORROSION AND POSSIBLE FAILURE OF THE PART. LANDING GEAR ARE MOST SUSCEPTIBLE. The maintenance of an organic coating (paint) which meets aerospace specifications ML-C-38413 may prevent corrosion.

LIMITED WARRANTY AND LIABILITY:

The owner of the Registration ensures that this product meets the label chemical description and that is reasonably designed for specific purposes, when used according to these instructions and under the conditions described for implementing. DO NOT OFFER ANY OTHER EXPRESS OR IMPLIED GUARANTEE AS TO THE SUITABILITY FOR A PARTICULAR PURPOSE OR ITS MERCHANDISING. This warranty is also subject to the conditions and restrictions here stipulated. The buyer and users must notify opportunely this Company any complaint, either based on contract, negligence, strict obligation, injury or otherwise. The buyer and all users are responsible for the loss or damage by use or handling, resulting from conditions outside the control of the Company, including but not limited and incompatibility with products other than the indicated on the label, implementation or contact with desirable vegetation, unusual climate conditions, other than the conditions that are considered normal for the site and during the period of the application, as well as weather conditions other than those specified in the label and other implementation than the explicitly specified in the label. This company does not guarantee any product reformulated or re-packaged from this product, except in accordance with the requirements of this Company and express permission in writing, granted by this Company.

THE WAY OF COMPENSATE THE USER OR THE BUYER DAMAGE AND THE LIABILITY LIMIT OF THIS COMPANY OR ANY OTHER SELLER IN REGARD TO ANY AND ALL THE LOSSES, INJURIES OR DAMAGES RESULTING FROM THE USE OR HANDLING OF THIS PRODUCT (INCLUDING CLAIMS BASED ON CONTRACT, NEGLIGENCE, STRICT OBLIGATION, OTHER DAMAGE, OR OTHERWISE), WILL BE THE PURCHASE PRICE PAID BY THE USER OR THE BUYER FOR THE RESPECTIVE QUANTITY OF THIS PRODUCT OR AS THIS COMPANY OPTION OR ANY OTHER SELLER, THE REPLACEMENT OF THE QUANTITY, IF NOT BOUGHT, THE REPLACEMENT OF THE QUANTITY IN ANY CASE SHALL THIS COMPANY WILL BE RESPONSIBLE OR ANY OTHER SELLER FOR ANY INCIDENTAL, CONSEQUENTIAL OR SPECIAL PREJUDICE Once the product IS open and used, it is understood that the buyer and users have accepted the terms of this limited warranty and liability, which may not be altered by any verbal or written agreement. If these terms are unacceptable, immediately return the product without opening it.

GLY 41 SAFETY DATA SHEET

SALES REGISTRATION 4294

SAFETY DATA SHEET Glyphosate Herbicide

Section 2: IDENTIFICATION OF CHEMICAL PRODUCT: Commercial name: Glyphosate Herbicide Use: Agricultural herbicide, Soluble Liquid Glyphosate N-(phosphonomethyl) glycine, Isopropylamine salt ……480.0 g/l Formulation agents …………………………………………………. C.s.p. 1 L C.A.S No. 38-642-94-0
Section 3: RISKS IDENTIFICATION: Glyphosate herbicide is neither flammable nor explosive. It is irritating when in contact with eyes. Keep in a locked place and keep out of children's reach
Section 4: FIRST AID MEAURES: The person must be taken away from the contamination source and check that he/she is breathing. Artificial breathing must be provided if necessary to ensure that this vital function continues. People in charge of providing first aid must avoid direct contact with the very contaminated clothes or vomit of the victim. Impermeable gloves must be used to decontaminate the hair and skin of the victim. LOOK FOR MEDICAL ASSISTANCE AS SOON AS POSSIBLE If ingested If the person is conscious and aware, give her two glasses of milk or water. An unconscious person or with unusual movements must never be fed or induced to vomit. LOOK FOR MEDICAL ASSITANCE In case of skin contact: Wash the skin immediately with water and soap. If possible, remove the shoes and shoes of the patient. Contaminated clothes must be washed separately before wearing it again. In case of inhaling: Take the person to a fresh air area; if he/she is not breathing, provide artificial breathing and oxygen if necessary. LOOK FOR MEDICAL ASSITANCE In case of contact with the eyes: Keep eyelids open and wash with running water for at least 15 minutes. LOOK FOR MEDICAL ASSITANCE NOTE FOR THE PHYSICIAN Treatment must be based on symptoms. This product does not inhibit

cholinesterase. Atropine and oximes must not be used as an antidote. s open given
Section 5: MEASURES TO EXTINGUISH FIRES Glyphosate herbicide is neither flammable nor explosive. In case of fire, combustion of the product may produce toxic vapors such as carbon oxides and nitrogen. Extinguishing: Containers exposed to heat must be kept cool. It is extinguished with carbon dioxide, foam, dry chemical powder or water spray in limited quantities. Water used to extinguish it must not be allow to flow to superficial water nor must it be allowed to flow to sewage systems. Water must be collected and kept as special residues. Autonomous breathing protection equipment must be used.
Section 6: MEASURES IN CASE OF ACCIDENTAL SPILL Spills are contained with sand or earth dikes. It is pick up by suction or vacuuming or by absorption using dry sand or earth and the material collected is packed in a sealed container duly labeled. The contaminated sites must be decontaminated by washing it with industrial detergent and it is handled as special residues in burning devices or approved safety landfills. Recommended personal protection: See section 8
Section 7: HANDLING AND STORAGE: Handling: Eating, drinking or smoking not allowed during handling or application of this product. Was hands after being in contact with this product. Storage: Keep the product in original packaging and containers. No smoking in the place. Keep out of children and animals' reach. Stored in a ventilated place, away from food, drink, hay, or concentrated food for animals. Compatible materials for storage: Stainless steel, aluminum, fiber glass or plastic.
Section 8: EXPANSION CONTROLS AND PERSONAL PROTECTION: Chemical safety gloves and eye protection must be worn while handling. Occupational health and safety general rules must be observed.
Section 9 PHYSICAL-CHEMICAL PROPERTIES: State: Liquid Appearance and color: Amber viscous liquid, practically odorless Density: 1,17 g/mL pH: 4.99 (Solution at 1%)
Section 10: STABILITY AND REACTIVITY: Glyphosate herbicide is stable under normal storage and manipulation conditions. There is no probability of dangerous reaction in the original containers. It reacts with galvanized steel or soft steel without covering layer, producing hydrogen, a very flammable gas that may cause explosion.
Section 11: TOXICOLOGICAL INFORMATION: ACUTE TOXICITY: It is very unlikely that exposure to glyphosate herbicide poses risk of acute toxicity (LD50 Oral (rats): > 5.000 mg/Kg; LD50 Dermal (rats): > 5.000 mg/Kg. It may cause slight irritation on skin and from moderate to severe in the eyes. CHRONICLE TOXICITY: No chronicle effects on humans have been documented, attributable to chronicle exposure. Mutagenicity and carcinogenicity studies have resulted negative.
Section 12: ECOTOXICOLOGICAL INFORMATION: ECOTOXICITY:

It is not dangerous for aquatic organisms, nor is it toxic to birds. It must not be poured into or near channels, drains, nor water courses or reservoirs.
Section 13: CONSIDERATIONS ON PRODUCT DISPOSAL: Residues resulting from the use of this product cannot be chemically re-used and must be disposed of as special residues in adequate burning devices or approved safety landfills.
Section 14: INFORMATION ON TRANSPORT: It cannot be transported nor stored with food for people or concentrated food for animals, beverages, medicine, nor items for human use such as clothes, blankets or mattresses. Glyphosate herbicide is not classified as dangerous.
ISSUING DATE: August 2005

This information is applicable only to the purposes stated for the product. It complements the technical information on the label but does not substitute it in any matter. It is based on the best information available at the time of issuing; it does not imply insurance or warranty and it is provided on good faith basis.

Annex 135

ANDEAN REGULATION FOR THE REGISTRATION AND CONTROL OF CHEMICAL PESTICIDES FOR AGRICULTURAL USE, ANDEAN COMMUNITY, DECISION 436 OF 2000

(*Norma Andina para el Registro y Control de Plaguicidas Químicos de Uso Agrícola*, Arts. 57- 59; Annex 1 – Glossary, "Mean Lethal Dose, LD 50" (Comunidad Andina, Decisión 436 de 2000). Available at: http://www.comunidadandina.org/normativa/dec/D436.htm (last visited 19 February 2010))

[…]

Article 57.- The information contained in the files of the National Registers of chemical pesticides for agricultural use shall be public. However, the Competent National Authority will refrain from circulating the information received, when the individual or legal entity that has provided such information requested a confidential treatment.

The documents which contain confidential information will be kept separate from the main file.

Article 58.- In no case will the following information be labeled as confidential:

- The name and content of the active substance or substances and the pesticide´s name;

- The name of other substances considered as hazardous;

- The physical and chemical data of the active substance, the formulated product and the additives of toxicological importance;

- The methods used to inactivate the technical-grade active ingredient or the formulated product.

- The summary of the results of the tests to determine the product´s efficacy and its toxicity for human beings, animals, plants and the environment;

- The recommended methods and precautions to reduce the risks of handling, storage, transport, and fire;

- The methods for eliminating the product and its containers;

- The decontamination measures to be adopted in case of accidental spill or leak.

- The first aid and medical treatment to be given in case of bodily injury;

- The data and information that appears on the label and instructions sheet.

Article 59.- The interested party requiring confidential treatment of specific information shall state the reasons for such a request and include a non-confidential summary of such information, or an explanation of any reasons why it is not possible to summarize it.

In case the requesting party does not comply with the aforementioned paragraph or if the information does not qualify as confidential, the Competent National Authority shall give reasoned notification of such circumstance to the requesting party, and grant it a reasonable time-limit so that it may withdraw the documents containing the information subject to the denial. Following that time-limit period the documents will be included in the public record.

[…]

ANNEX 1
GLOSSARY

[…]

Mean Lethal Dose, LD 50, statistical estimate of the minimum dose required to kill fifty percent of a population of laboratory test animals in controlled conditions. It is stated in milligrams of toxic [substance] per kilogram of animal weight indicating the species, gender and age of the animals used for experimenting. It is administrated via oral, dermal, mucosal or parenteral channels.

Annex 136

REPORT OF THE FIFTH MEETING OF VICE-MINISTERS OF FOREIGN AFFAIRS OF THE ANDEAN COMMUNITY, CARACAS, 16-17 OCTOBER 2000

(*Comunidad Andina, Consejo Andino de Ministros de Relaciones Exteriores, Informe de la Quinta Reunión de Viceministros de Relaciones Exteriores de la Comunidad Andina, Caracas, Venezuela, 16-17 October 2000*, 6 November 2000)

Confidential Report

The Vice-Ministers of Foreign Affairs of the five member countries, who met on the 16 and 17 October 2000 in the framework of the Andean Council of Ministers of Foreign Affairs in Caracas, requested the General Secretariat to prepare a Confidential Report about the debate that arose from the 5th point of the Provisional Agenda: "Early warning mechanisms for the detection of biological control agents in the eradication of illicit crops, which affect Andean ecosystems". This point had been removed from the approved agenda.

Referring to this topic, the Colombian Vice-Minister, Clemencia Forero, expressed her gratitude for the welcome given by the government of Venezuela and particularly by Vice-Minister Valero. With regards to the proposed agenda and in reference to point 5, she explained that in the previous days a Note had been sent to the Minister of Foreign Affairs of Venezuela containing preliminary comments about this point. It explained Colombia's point of view that the treatment of this topic belonged to the established forum, namely, that of the Andean Committee of Environmental Authorities.

In that sense, Colombia considered that the Vice-Ministers should not express their direct views on the draft Decision prepared by the Secretary-General which their respective environmental authorities were not acquainted with in great detail. She mentioned that this project could be further studied at the CAAM meeting to be held in Venezuela during the month of November, taking into account that this was a matter of instances and one where the Committee of Environmental Authorities existed.

She requested that the more specific opinions that their environmental authorities may have on this matter be taken into account and, thus, [deemed] it would be difficult to consider supporting or endorsing the draft Decision.

She offered to provide two documents to the General Secretariat containing the response given by the Minister of Foreign Affairs Fernández de Soto to a questionnaire formulated by some Colombian senators. She requested that such document be included in the Confidential Record of this meeting and, hence read the response stating the position of the Colombian government regarding this topic in the following terms:

"The Government of Colombia has stated that it does not approve under any circumstance experimenting with myco-herbicides exogenous to our ecosystems and which may affect the environmental balance and the population's health. In particular, it has rejected experimentation with *fusarium oxysporum*. It is important to clarify that no myco-herbicide is currently being studied."

She pointed out that the position of the Colombian government is unequivocal since the use of chemical and now biological agents for crops eradication has had a long history in the countries that have suffered this scourge.

She stated that Colombia, on several occasions and under intense pressure, has been subject to questioning, and even to demands, in relation to the use of new chemical herbicides. She explained that on each of those occasions, the National Narcotics Council of her country, which gathers all the Ministers involved in the fight against drugs, has publicly referred to the matter and has never allowed the application of any herbicide or biological agent that is harmful to the environment or to health. Thus the answer of the Colombian government to this topic is unequivocal.

She made reference to a public statement by the Minister of Environment, Juan Mayer [sic], in October 2000. It stated that, in relation to the possible experimentation, use or application of *fusarium oxysporum* as a mechanism to eradicate illicit crops in the country, the Ministry of Environment, as supreme environmental authority, did not approve the proposal made by United Nations International Drug Programme [sic] to conduct tests with *fusarium oxysporum,* as it considered that any agent, external to the native ecosystems of the country, could cause serious risks to the environment and to normal health.

She reaffirmed the high sensitivity of this matter for Colombia's Government and that her country is not experimenting with this fungus, nor will it do so in the future, for which reason she reiterated her request for this item not to be considered in the agenda.

On the other hand, the Vice-Minister of Ecuador, Gonzalo Salvador Holguín, expressed his gratitude to the government of Venezuela for the opportunity of having this meeting and, in connection to the issue raised by the Vice-Minister of Colombia, he expressed his full agreement with the removal of this item from the agenda. He further expressed that in the course of the last two months his country has held intensive conversations with Colombia with respect to this matter, the results of which were reflected in a

Presidential Declaration recently signed by the Presidents of both nations, on the occasion of the last visit of President Pastrana to Ecuador.

He stated that complete and absolute assurances were received from the authorities of the Colombian Government to the effect that no use or experimenting with the fungus *fusarium oxysporum* or any other type of myco-herbicide will be undertaken for the illicit crops eradication programs. Thus, the Government of Ecuador deems it unnecessary to bring this issue to the next meeting of the Council.

In turn, the Vice-Minister of Bolivia, Ana María Solares, thanked the Government of Venezuela, through its Vice-Minister, for its hospitality, and in relation to the discussed issue, reiterated that the Government of her country opposes any type of practice or uses of this nature. But in any case, she requested further details of the background of this draft Decision to the General Secretariat.

Likewise the Vice-Minister of Peru, José Antonio Arróspide, took the floor and thanked Ambassador Valero for the invitation and pleasant opportunity of being in Caracas for such an important meeting. He recalled the topics that had been the subject of work between the Presidency of Peru and the General Secretariat and, with regards to the subject, he stated that he fully shared the position of Colombia.

He expressed that in the case of Peru, his country has a legal norm that prohibits the use of any kind of biological agent of this type and therefore, he considered that the matter had no direct link with the work of the Ministers of Foreign Affairs. Like Colombia, he stated his preference for the item not to be included in the Council's Agenda.

He further recalled that a written communication had been sent to the Ministry of Foreign Affairs of Venezuela with regards to another item of the agenda, i.e. item 4, on the Latin-American Monetary Fund.

The meeting's secretary, Carlos Longa, explained that the draft Decision initially referred to, came from the Andean Committee of Environmental Authorities, and that the idea of the Committee in bringing this proposal to the Vice-Ministers' meeting had the purpose of assessing the possibility of submitting it to the Ministers of Foreign Affairs. That Committee considered the advisability of developing an early warning mechanism for possible uses of biological control agents and, given that such Committee is an advisory body with no power to adopt binding decisions in the framework of the Agreement, it chose to submit this proposal to determine the feasibility of adopting this mechanism by Decision of the Ministers of Foreign Affairs.

Vice-Minister Solares deemed it important to continue dialogue on this early warning mechanism once the issue is more evolved and stated her wish to continue receiving information about this sort of sectional topics, such as those coordinated by other organs of the System or other bodies of the [Andean] Community, which would allow for their adequate treatment by the Andean Council of Ministers of Foreign Affairs and the Presidents.

Annex 137

ANDEAN COOPERATION PLAN FOR THE CONTROL OF ILLEGAL DRUGS AND RELATED OFFENSES, ANDEAN COMMUNITY, DECISION 505 OF 2001

(Andean Community, Decision 505 of 2001)

Decisions

Decision 505
Andean Cooperation Plan for the Control of Illegal Drugs and Related Offenses

THE ANDEAN COUNCIL OF FOREIGN MINISTERS,

HAVING SEEN: Article 16 of the Cartagena Agreement and Decision 458 "Common Foreign Policy Guidelines";

BEARING IN MIND: The agreement approved by the Presidents of the Andean Countries at the meeting held on April 17, 2001 in Cartagena, Colombia;

WHEREAS: Illegal drug production, traffic, and consumption, asset laundering, diversion and smuggling of chemical precursors, and arms trafficking seriously threaten the development and security of the Andean countries;

The efforts being made today by the Andean countries under their respective national programs for the control of illegal drugs and related offenses can be significantly boosted and supplemented through an Andean Cooperation Plan to intensify national, bilateral, and Community measures in this area;

The international community can wage an integrated campaign against the worldwide illegal drug problem that could cover all of the aspects involved in illegal drug production, traffic, and consumption and related offenses, based on the principle of shared responsibility;

The Andean strategy for the control of illegal drugs and related offenses, as well as international efforts in this area, should be carried out with full respect for national law and sovereignty.

DECIDES:

Sole article. – To approve the Andean Cooperation Plan for the Control of Illegal Drugs and Related Offenses set out in the document attached to this Decision.

Signed in the city of Valencia, Venezuela, on the twenty-second of June of two thousand and one.

ANDEAN COOPERATION PLAN FOR THE CONTROL OF ILLEGAL DRUGS AND RELATED OFFENSES

Principles and Objectives

The Andean Cooperation Plan for the Control of Illegal Drugs and Related Offenses:

1. Is grounded in the conviction that illegal drug production, trafficking, and consumption is a worldwide problem that seriously threatens the development

and security of the Andean countries and of the international community. Recognizes that this is one of the most harmful and dangerous forms of organized transnational crime, that makes use of the globalizing logic of the markets, disrupts the social dynamic, distorts the economy, undermines the state of law, and subverts the public order.

2. Is comprehensive and encompasses all of the aspects of the worldwide drug problem and related offenses: prevention, interdiction, reduction of illicit crops, and alternative development, as well as the control of the diversion of chemical precursors, asset laundering, and the traffic in arms, ammunition, and explosives.

3. In this connection, it is based on the shared responsibility of each and every one of the actors involved in creating the problem and, as a result, in the search for solutions to it at both the Andean Subregional level and the South American, hemispheric, and world levels.

4. Is respectful of national legislation and territorial sovereignty and integrity, as well as of the strict observance of International Law and is implemented through cooperation and solidarity. That cooperation is inherent to the shared nature of the problem and, consequently, should be mutual, voluntary and not subject to limitations or requirements that set conditions on the unhampered involvement of the wills of the parties. The solidarity, for its part, is an expression of the recognition that national and Subregional drug control efforts should be accompanied by international cooperation in order to reinforce democracy and the exercise of human rights and at the same time promote the sustainable economic and social development of the Andean Countries.

5. Seeks to strengthen and step up national programs in each of the Andean Countries through coordination, cooperation, and the exchange of experiences among the Member Countries and by taking joint action in dealing with third countries and in international forums.

6. Is a key issue of Andean political cooperation that links up the common foreign policy, Community border integration and development policy, sustainable development policy, the Andean Social Agenda, and security and confidence-building efforts in the Subregion, as applicable.

7. It is proposed that the Andean Community be consolidated as the moving force for a South American and hemispheric strategy for the control of illegal drugs and related offenses.

Mechanisms

1. The Andean Council of Foreign Ministers is the body responsible for defining, coordinating, and following up the Andean Cooperation Plan for the Control of Illegal Drugs and Related Offenses.

2. An Executive Committee will be set up, formed of high-level officials of the Ministries of Foreign Affairs and the national officers responsible for controlling illegal drugs and related offenses, including representatives of the security bodies.

3. The Executive Committee may establish subcommittees and working groups specializing in the different aspects of the Andean Plan. The Subcommittees and working groups may be made up of two or more Member Countries and will be open to the participation of the others.

4. The Andean Community General Secretariat will act as the Executive Committee's Technical Secretariat.

Program of Action

1. The Program of Action will be approved by decision of the Andean Council of Foreign Ministers and will cover a two-year period.

2. The Executive Committee will draw up the Operating Plans for carrying out the Program of Action and every two years will propose the updating of that program to the Andean Council of Foreign Ministers.

3. It will be the Executive Committee's responsibility to coordinate, oversee, and evaluate the Program of Action, with the assistance of the General Secretariat.

PROGRAM OF ACTION

I. REINFORCEMENT OF NATIONAL STRATEGIES

A. Control of the production, smuggling, and diversion of chemical precursors

1. Implement the mechanism for reporting the export of controlled chemical substances prior to their shipment and the timely answers from the intended country of destination, pursuant to article 12 of the 1988 Vienna Convention.

2. Reinforce the monitoring of enterprises that produce, use, and/or sell controlled chemical substances in order to avoid their diversion for the production of illegal drugs.

3. Strengthen the mechanisms for detecting controlled chemical substances and train the pertinent officials to identify those substances.

4. Make the measures for controlling the illegal production and smuggling of controlled chemical substances stronger.

5. Set up and/or reinforce the mechanisms for controlling the transport and diversion of chemical substances in the national territory through the following, among other things:

   a) The use of customs documents containing the generic name and corresponding tariff code for trade in the controlled chemical substances.

   b) The establishment of a system of labeling and safety sealing that would make it difficult to divert packaged or bottled products by replacing them.

6. Create and/or update the national register of firms that import and export controlled chemical substances. That information will be made available to whoever asks for it.

7. Identify the needs of the legitimate industries dealing with potassium permanganate, acetic anhydride, and the substances included in the Andean Community's control operations.

8. Develop inter-sector coordination for the purpose of identifying new substances used in drug production for possible inclusion on the list of controlled substances following a study of their level of use.

B. Technical eradication of illegal crops

1. Build up national capacities to implement programs for the technical eradication of illegal crops by hand or by air, in the countries that need it, keeping in mind the environmental standards established by the competent authorities.

2. Identify illegal crop growing areas, their size, evolution, features, zones of influence, and any other relevant information.

3. Contribute to the coordination between the authorities responsible for execution of the eradication programs and those in charge of the alternative development programs.

4. Promote the establishment of agreements between local communities and public authorities as a means of reducing crops grown for illegal purposes and introducing alternative products.

C. Alternative Development.

1. Create the necessary economic, social, and cultural conditions to make it feasible to replace the illegal crop production-based economy and to bring farmers into the legal economy.

2. Identify and establish the characteristics of the populations of the illegal crop growing areas and their zones of influence.

3. Design and put into use financial, economic, and technological instruments for supporting national alternative development programs, including private investment promotion, market opening, and the incorporation into alternative production of products with a larger value added.

4. Boost the strengthening of grass-roots organizations and give them support through consciousness-raising, training, and communication processes.

5. Step up the national capacity to offer basic social services and develop the economic infrastructure in the illegal crop growing areas and their zones of influence.

6. Design and implement social communication strategies to discourage the involvement of farm and native families with illegal crops and promote alternative crops.

D. Dismantling of the production and transport infrastructure and organizations

1. Reinforce the mechanisms for coordination among the police and military forces and state security bodies, the Public Ministry and/or the Attorney General's Office, and the Judiciary.

2. Build up the capacity for action of the intelligence units specialized in the control of drug trafficking and ensure the timely exchange of information among the various competent national authorities.

3. Increase the human, material, financial, and technological resources allocated to the specialized units responsible for controlling drug trafficking organizations.

4. Strengthen the mechanisms for detecting illegal drug production laboratories and hidden airstrips.

5. Buttress the system for controlling illegal drug trafficking by sea, river, air,

and land.

6. Create and/or reinforce the control mechanisms in order to impede illegal trafficking in arms, ammunition, explosives, and other similar materials.

E. Asset laundering

1. Establish and/or build up the national intelligence and financial analysis units.

2. Identify the existing types or methods of asset laundering and create the corresponding control mechanisms.

3. Train specialized personnel in the agencies responsible for detecting and controlling asset laundering operations.

4. Investigate the sectors capable of use for activities connected with asset laundering and link them up with the intelligence and financial analysis units.

5. Design and implement mechanisms for administrative control of international currency transactions.

6. Criminalize asset laundering as an autonomous offense, so that it will encompass other criminal behavior (vehicle theft, extortion, kidnapping, white slavery, trafficking in human organs, and arms trafficking).

7. Strengthen the application of provisions on the seizure of goods procured as a result of drug trafficking or related offenses.

8. Establish regulations on the prevention of asset laundering in free trade areas and at free ports.

F. Reduction of the demand

1. Put a stop to the rising trend in illegal drug consumption, especially among children and young people, with schooling or not, through programs targeting the family, community, and school.

2. Develop a mass media strategy to inform, sensitize, and educate young people about the consequences of drug consumption, giving special emphasis to the synthetic or designer drugs that have recently appeared on the scene.

3. Incorporate more information about prevention in the curriculums at the different educational levels and educate parents and educational agents in the new trends in illegal drug consumption.

4. Promote programs for the rehabilitation and social reinsertion of drug-dependent individuals.

5. Implement mechanisms for overseeing and evaluating programs to cut down the demand for drugs.

6. Design and launch programs to give human resources preparation and training in prevention and rehabilitation.

7. Boost and support the participation of civil organizations in prevention and rehabilitation activities.

II. REINFORCEMENT OF BINATIONAL STRATEGIES

1. Evaluate the existing bilateral drug control agreements, update and perfect

them, and put them into force.

2. Promote and strengthen bilateral mechanisms, such as the mixed commissions, border workshops, and neighborhood committees, in order to draw up border action plans for:

a. Controlling the traffic in drugs and controlled chemical substances.
b. Giving border authorities training in subjects connected with drug control.
c. Carrying out combined interdiction operations.
d. Stepping-up the exchange of information and coordination of logistics among border authorities.
e. Controlling the illegal traffic in firearms, ammunition, and other similar materials.

3. Incorporate alternative development projects in the Border Integration Zones and include them in the Project Bank to be set up as part of the Andean Integration and Development Policy.

4. Institute effective mechanisms to control trafficking in illegal drugs, controlled chemical substances, arms, ammunition, and other related materials, through the National and Binational Border Service Centers (NBSC and BBSC).

5. Periodically examine and evaluate the execution and efficiency of the binational cooperation measures that are carried out under this Andean Cooperation Plan.

III. COMMUNITY STRATEGY

1. Establish an Andean mechanism for exchanging information through the Andean Community website about the methods of trafficking in and diversion of controlled chemical substances, use of new substances, successful control operations, updated national registers of enterprises that import and export controlled chemical substances, and changes in the importance and use of border crossings for the illegal trafficking in those substances, and promote the use of other national, regional and international computerized systems, such as *Unidos contra Drogas (UCD)* and the Venezuelan, inter-American, and European drug observatories.

2. Step up the exchange of intelligence among the competent authorities of the Andean countries, among others, making more use of existing communication mechanisms, such as the Regional Liaison Offices of the World Customs Organization (RILO) and the Inter-American Telecommunications Network for Drug Control (RETCOD), in order to back regional efforts to control drugs, related offenses, and the arms traffic.

3. Establish closer coordination among the national authorities responsible for drug control in the Member Countries, among others, by appointing national liaison officers in the respective institutions and assigning new duties to the police and military attachés' offices, as applicable, to support this Andean Cooperation Plan.

4. Promote the training in common of national drug control officials through, among others, the Andean Community's Regional Antidrug Intelligence School (ERCAIAD), ensuring its appropriate funding and adjusting its curriculum to the priorities of the Andean Strategy, and supporting the establishment and activation of the Andean Anti-drug Canine Training School.

5. Contribute to the signing of legal assistance agreements on criminal matters and step up the execution of existing agreements, including procedures for the

extradition of defendants accused of drug trafficking or related offenses under the existing accords.

6. In each Member Country, appoint as liaison officers investigating judges who are empowered to answer requests for reciprocal legal assistance in drug trafficking cases or to remit them to the competent authorities for compliance.

7. Contribute to harmonizing national criminal and procedural legislation through periodic meetings of the Ministers of Justice of the Andean Community, bearing in mind the work that is being done under the aegis of the mechanism between the European Union and the Andean Community on coordination and cooperation in drug matters.

8. Promote the exchange of experiences and undertake joint actions to back alternative development programs, incorporating for that purpose the Andean Committee for Alternative Development (CADA) as the Andean Cooperation Plan's specialized body on the subject and supporting its efforts.

9. Reinforce cooperation in order to prevent and control asset laundering at the Andean level through the exchange of experiences and interlinkage of the Financial Intelligence Analysis Units of the countries in the Subregion and other competent bodies.

10. Implement the guidelines established by the Inter-American System of Standardized Drug Consumption Data (SIDUC) and entrust the analysis to the Hipólito Unanue Convention (CONHU), so that the Andean Community can have data on which it can draw to prepare prevention strategies that are attuned to its situation.

11. Develop a joint strategy for preventing drug consumption and production and controlling synthetic and designer drugs.

12. Identify the international technical cooperation requirements and capacities and establish a mechanism for horizontal cooperation among the Member Countries.

13. Design and carry out joint strategies for mobilizing international technical and financial cooperation to support the measures provided for in the Andean Strategy for the control of drugs and related offenses, as well as debt-for-alternative development program support swaps.

14. Apply for the renewal and expansion of the programs of trade preferences in support of drug control that benefit the Member Countries and obtain conditions for preferential access to other markets and the removal of restrictions on their full use.

15. Promote the mobilization of international cooperation for programs to prevent and alleviate the environmental impact of the illegal drug problem, including the recovery of ecosystems and conservation of the biodiversity.

16. Further international cooperation, in particular through the organization of donor groups in order to boost alternative development, create jobs in production, and alleviate poverty in illegal drug crop growing areas, in areas from which labor is migrating, and in areas that are highly prone to use for drug cultivation.

17. Coordinate joint drug control positions in dealing with third countries and in international forums and organizations as part of the Andean Common Foreign Policy.

18. Update the "Rodrigo Lara Bonilla" Convention on cooperation for preventing

drug abuse and for suppressing the illegal traffic in narcotic drugs and psychotropic substances, in order to adjust it to the needs created by this Andean Cooperation Plan.

19. Examine and evaluate, as a Community, the implementation and effectiveness of the measures that are carried out under this Andean Cooperation Plan.

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Annex 138

COSMO-FLUX® 411-F TECHNICAL DATA SHEET

(Cosmoagro, June 2002)

COSMO-FLUX® 411-F
Adjuvant for Agrochemicals Application

Specifications

Classification	Additive for spraying		
Chemical description	Mixture of Mineral oil and non-ionic specialized surfactants with coupling agents.		
Active Ingredient	Mixture of Exitane esters: Linear alcohol + aryl ethoxylate Mixture of non-ionic tensoactive stereospecific, linear alcohol ethoxylate propoxylate with small quantities of aryl ethoxylate	17%	EPA regulation: Tolerance exempt under 40 CFR 180.1001 (c), (e) regulation
Additive ingredients	Liquid isoparafins isoparafin oil of high purity, with very low toxicity, very low aromatic content and low superficial tension that improves humidibility which reinforces efficacy of active ingredients.	83%	EPA regulation: Tolerance exempt under 40 CFR 180.1001 (c), (e) regulation

General Characteristics

Appearance at 25 ^{o}C	Amber liquid
Flash point	Above 149 ^{o}C
Specific gravity	0.84

Viscosity at 25 ^{o}C	40 cP
Product pH at 10%	6.0-8.0
Superficial tension	25-28 dynes/cm

Solubility

Mineral Oils	Soluble
Vegetable oils	Soluble
Organic solvents	Soluble
Water	Dispersible, forming a rapid emulsion

Characteristics of the Mixtures Created with COSMO-FLUX® 411-F

Homogeneity	Excellent
Persistence	Over 24 hours
Compatibility with active ingredients	Excellent (See ANNEX "Evaluation of physical compatibility …"
Mixing speed	Rapid
Adherence	Excellent

Toxicological Summary

Classification as Poison	Not classified
Irritation in rabbit's eyes (According to the Kay D. Calandra Application)	Practically non irritating
Irritation of rabbit's skin	After applying it for 24 hours undiluted produced slight irritation
Sensitivity on human skin	It does not cause irritation, nor is it a skin sensitizer of human skin
Biodegradability (OECD method for Non-ionic tensoactives)	Non-ionic components of COSMO-FLUX® 411-F have a biodegradability above 98%

First Aid

¡In any case see a physician!

Contact with skin	Wash with water and soap
Contact with eyes	Wash immediately with abundant clean water or with eye wash solution for 15 minutes
Inhaling	Symptom-based Treatment
Ingestion	Do not induce vomit. Drink milk or water, symptom-based treatment. See a physician and show the label.

Transport, Storage, and Handling

Safety category according to I.S.G. (International Shipping of Goods)	Not applicable
Caution measures in personal protection:	[ ] Breathing mask [X] Gloves [X] Eye protection Other:
Technical precautions	There are no special requirements
Storage conditions	There are no special requirements
Fire and explosion risk	It is not classified as flammable, its decomposition products are CO and CO_2
Means for extinguishing	Water mist Dry chemical CO_2 foam
Spills	Absorb with sand, earth, sawdust or a similar absorber

Disclaimer

The information in this safety data sheet is provided in good faith and represents what is known about the product at the time of publishing.
Recommendations for its use and application are based on tests conducted by COSMOAGRO, but its use and application in each specific case must be evaluated to determine the appropriateness of its use.

COSMOAGRO guarantees that the physical-chemical characteristics of the product correspond to those listed on the label, and that through opinion on efficacy No. 2186 of 19 April 1993, issued by ICA (Colombian Agriculture and Livestock Institute), it was verified that it is suitable for the purposes recommended therein, in accordance with the specifications for use, but assumes no liability for how it may be used, since its handling is beyond its control.
This product must be used with the recommendation of an Agricultural Engineer or a Technical Assistant.

COSMOAGRO and COSMO-FLUX 411F are registered trademarks of COSMOAGRO.
COSMO-FLUX is a product with the technological support of ICI – Specialty Chemicals

Annex 139

PRESS ITEM: "ECUADOR ACCEPTS SPRAYINGS TO CONTINUE", *EL COMERCIO* (ECUADORIAN NEWSPAPER), QUITO, 4 AUGUST 2004

(*El Comercio, Ecuador acepta que las fumigaciones continúen,* available at: http://www.elcomercio.com/solo_texto_search.asp?id_noticia=100416&anio=2004&mes=8&dia=4 (last visited 19 February 2010))

[…]

The diplomatic authorities from Ecuador are in question.

This time because they accepted Colombia to continue with its antidrug fumigations in the border line "taking the necessary precautions to avoid effects among the Ecuadorian population".

Thus, the Ecuadorian Foreign Ministry abandoned the thesis that the Government of Bogotá was to refrain from carrying out sprayings with glyphosate in a strip of 10-km from the border line. The agreement was reached yesterday, during the closing of the fourth meeting of the Technical Scientific Commission in Quito.

The announcement was made after Vice-Minister Edwin Johnson announced he would request Colombia to carry out the fumigations "at a low altitude". And, also, because he anticipated that if they agree to that request "there is no need to ask them to stop spraying in the area of 10-km".

[...]

Annex 140

US Department of State, Bureau for International Narcotics and Law Enforcement Affairs, Memorandum of Justification Concerning the Secretary of State's 2002 Certification of Conditions Related to the Aerial Eradication of Illicit Coca in Colombia, Washington D.C., 2002

(Available at: http://www.state.gov/p/inl/rls/rpt/aeicc/13232.htm (last visited 8 March 2010), p. 1)

Memorandum of Justification Concerning Determination on Health, Environmental, and Legal Aspects of Coca Eradication in Colombia

The Kenneth M. Ludden Foreign Operations, Export Financing and Related Programs Appropriations Act, 2002 (P.L. 107-115) ("FOAA") lays out conditions under which assistance using funds appropriated under the FOAA may be made available for the purchase of chemicals for the aerial eradication of coca in Colombia. The legislation?s requirements and the Administration?s summarized responses are below.

1. That the coca spraying is being carried out in accordance with regulatory controls required by the Environmental Protection Agency as labeled for use in the United States:

Tab 2 of the report illustrates that the glyphosate formulation used to spray coca in Colombia is used in accordance with the EPA label instructions for non-agricultural use. In Tab 3 of the report, a letter from EPA Assistant Administrator Johnson EPA confirms that application rates are within the parameters listed on U.S. glyphosate labels.

2. That the coca spraying is in accordance with Colombian laws:

Tab 6 of the report includes a letter from the Ministry of Foreign Affairs of the Government of Colombia confirming that the spraying is being carried out in accordance with each and every applicable Colombian law.

3. That the chemicals used in the coca spraying, in the manner in which they are applied, do not pose unreasonable risks or adverse effects to humans or the environment:

USDA?S assessment (Tab 5) opines that the spray program poses no unreasonable health or environmental risks. Upon examining the chemicals that used in Colombia, EPA notes the potential for acute eye toxicity, due to an inert ingredient in the particular glyphosate formulation used by the program. EPA?s response points out that the Department did not provide to the EPA the results of INL-commissioned toxicological tests performed on the spray mixture, as promised in a briefing (note: these tests had not been completed at the time EPA submitted its response). EPA replies that because of its inability to review such tests, it is unable to evaluate the toxicity of the spray mixture that we are using in Colombia. In the absence of these testing results, EPA recommended that the Department consider using an alternative glyphosate product with lower potential for acute toxicity.

Until a lower toxicity glyphosate formulation could be made available for use in Colombia, we have continued to spray with the higher toxicity glyphosate product. According to the EPA report, the risks of eye damage from the current formulation are limited principally to the handlers and mixers of the concentrated formulation as opposed to the general public. The concentrated glyphosate formulation is diluted when mixed with water for use in the spray program; approximately 75 percent of the end use product is water. Furthermore, several safeguards are in place to minimize human exposure to the spray mixture. Pilots are carefully selected and trained and are instructed to avoid spraying near people, homes, or occupied buildings. The permissible spray parameters of flight speed, aircraft height, and wind conditions are rigidly monitored and complied with. The Embassy is working with the GOC to warn local citizens in areas where we spray (through radio and newspaper advisory messages) to avoid the spray mist and inform them of precautions to take in case of possible incidental contact with the spray mixture.

The Department now has the results of the eye irritation test of the spray mixture that would have bolstered EPA?s analysis, but we did not receive these results in final form until after receipt of EPA?s response. This test determined that the spray mixture currently used in Colombia would be rated Category III on EPA?s scale of I-IV, with I being the most toxic. Congress is aware that this testing is underway and as we have notified in the addendum to the report, we will provide the testing results as soon as all of the testing is completed.

In addition, INL now has an alternative glyphosate product with lower potential for acute toxicity available for use in Colombia. This formulation, registered in July 2002, is less toxic to the eyes because it uses a different inert ingredient and is also known to have as low or lower toxicity ratings in all other categories, as well. Although this alternative formulation has only recently been approved in Colombia, it has been extensively tested and widely used elsewhere, and is registered for non-agricultural use in the U.S. by the EPA. Because this alternative formulation addresses EPA?s recommendation that the Department switch to a less toxic formulation, the Department plans to switch to it for use in Colombia as soon as it can be manufactured, purchased, and delivered. INL expects to place an order for the new product early in September 2002. The Department?s notification to Congress will indicate our intention to make this switch, in response to EPA?s concerns.

Based on the above information, we do not believe that EPA?s reservation about the risk of eye irritation rises to the threshold of "unreasonable risks" or "adverse effects" to humans or the environment identified in the statute.

4. That procedures are available to evaluate claims of local citizens that their crops were damaged by such aerial coca fumigation, and to provide fair compensation for meritorious claims:

Tab 7 of the report outlines the procedures to evaluate claims of damage to legal crops from aerial eradication and to provide fair compensation for meritorious claims. This includes an English language version of the Colombian National Drug Council?s Resolution 0017, which formalized the new process. Complaints are being received, logged, investigated, verified, and compensation is being

Annex 141

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY (EPA), *ADDENDUM TO MEMORANDUM. SUBJECT: DESCRIPTION OF GLYPHOSATE USED IN THE U.S. AS A BASIS FOR COMPARISON TO GLYPHOSATE USED IN COLOMBIA FOR COCA ERADICATION,* FROM: VIRGINIA WERLING AND TIMOTHY KIELY (EPA, BEAD BIOLOGICAL AND ECONOMIC ANALYSIS DIVISION) TO JAY ELLENBERG (EPA, BEAD BIOLOGICAL AND ECONOMIC ANALYSIS DIVISION), 21 AUGUST 2002

(Available at: www.epa.gov/opp00001/foia/reviews/103601/103601-2002-08-21a.pdf (last visited 2 October 2009))

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AUG 21 2002

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

ADDENDUM TO MEMORANDUM

SUBJECT: Description of Glyphosate Use in the U.S. as a Basis for Comparison to Glyphosate Use in Colombia for Coca Eradication

FROM: Virginia Werling, Biologist
Herbicide and Insecticide Branch
Virginia Werling 08/19/02

Timothy Kiely, Economist
Economic Analysis Branch
Biological and Economic Analysis Division (7503C)
Stephen Smearman for Timothy Kiely 08/19/02

TO: Jay Ellenberger, Associate Director
Field and External Affairs Division (7506C)

THRU: Arnet W. Jones, Chief
Herbicide and Insecticide Branch
Biological and Economic Analysis Division (7503C)

BEAD would like to report additional information on the use of glyphosate in domestic forestry applications and in international sites found through research subsequent to issuance of the original memo (dated June 28, 2002).

BEAD was asked to report on the use of glyphosate in forestry sites since it seemed similar to the use pattern for coca eradication. However, it is not clear how closely this use approximates that for coca eradication. Glyphosate is typically applied to forestry sites using helicopters at air speeds of 50-70 knots (about 60-80 miles per hour). Application to forestry sites by fixed wing aircraft, if practiced at all, is extremely rare (1). The recommended rate of application for pine release (conifer release) is 1.5 to 2 pounds active ingredient per acre.

Aerial application to other sites comprises less than one percent of the total amount of glyphosate applied in the United States (3).

In addition to surfactants, drift control agents may be added to the spray mixture for forestry uses in an effort to prevent drift to off target sites. BEAD has not investigated the prevalence of use or the effectiveness of these products.

BEAD estimates total global use of glyphosate to be between 350 and 360 million pounds of glyphosate per year. Annual use in the United States is approaches 100 million pounds of active ingredient and an estimated 250 to 260 million pounds of glyphosate is used outside of the United States. Use of glyphosate in Colombia accounts for between four and five million pounds of this use. Primary sites in Colombia include coffee, bananas, pasture-land and rice (3).

REFERENCES:

(1) Personal communication between Virginia Werling, United States Environmental Protection Agency and John Taylor, United States Forest Service on August 9, 2002.

(2) Hamilton, R.A. "2002 North Carolina Agricultural Chemicals Manual - Chemical Weed Control In Forest Stands" Extension Forest Resources Department, North Carolina State University. Available on-line at http://ipmwww.ncsu.edu/agchem/chptr8/821.pdf

(3) United States Environmental Protection Agency Proprietary Data.

Annex 142

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY (EPA), *DETAILS OF THE CONSULTATION FOR THE DEPARTMENT OF STATE:* USE OF PESTICIDES FOR COCA AND POPPY ERADICATION PROGRAM IN COLOMBIA, AUGUST 2002

(In: United States Department of State, Bureau of International Narcotics and Law Enforcement Affairs, *Report on issues Related to the Aerial Eradication of Illicit Coca in Colombia,* December 2003 (partially included as EM, Vol. III, Annex 143). Available at: http://www.state.gov/p/inl/rls/rpt/aeicc/26991.htm (last visited 27 February 2010), pp. 2, 4, 5, 8, 9, 10, 13, 23, 39)

Details of the Consultation for Department of State: Use of Pesticide for Coca Eradication Program in Colombia

Report on Issues Related to the Aerial Eradication of Illicit Coca in Colombia
BUREAU OF INTERNATIONAL NARCOTICS AND LAW ENFORCEMENT AFFAIRS
December 2003

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

The Honorable Colin L. Powell, Secretary
U.S. Department of State
Washington, D.C. 20520

Dear Secretary Powell:

We are enclosing our consultation review as per your request to Environmental Protection Agency (EPA) Administrator Christine Todd Whitman, for consultation on the potential human health and environmental effects of the aerial coca eradication program in Colombia, pursuant to the Foreign Operations, Export Financing, and Related Programs Appropriation Act (P.L 107-115). Administrator Whitman has asked me to respond on her behalf because my office has primary oversight responsibility for pesticides, and the nature of this consultation centers around the technical aspects of chemicals used in the aerial fumigation of coca.

The Foreign Operations, Export Financing, and Related Programs Appropriation Act specifically requires the Department of State to consult with EPA on whether (1) "aerial coca fumigation is being carried out in accordance with regulatory controls required by the EPA as labeled for use in the United States .... ; and (2) whether the chemicals used in the aerial fumigation of coca, in the manner in which they are being applied, do not pose unreasonable risks or adverse effects to humans or the environment..."

As part of our consultation review, we considered the full range of available scientific information from laboratory and field testing and incident reports. Our consultation review evaluates the potential impact to human health and the environment from the eradication program, based on information provided by Department of State, on the pesticide used (glyphosate), inert ingredients, and the application rates and methods, In addition, Agency scientists reviewed scientific studies on glyphosate, conducted a limited literature search for human health incidents related to glyphosate use, and examined information on glyphosate use conditions in the United States. We also considered information provided by non-governmental organizations, concerning effects reportedly connected to coca eradication in Colombia.

Glyphosate is widely used in the United States. Based upon EPA reviews of domestic use conditions, glyphosate appears to be one of the most safely-used pesticides in the U.S. EPA's regulatory authority for domestic pesticide use allows significant controls through pesticide labeling and compliance and enforcement infrastructure implemented with the states and other federal agencies. Recognizing that these mechanisms are not available to EPA in Colombia, the Agency has evaluated potential risks associated with the coca eradication program and identified areas where Department of State should pay particular attention to minimize the potential for adverse effects.

I trust that the attached document will assist you in preparing your response to Congress. Please let me know if you have additional questions concerning this consultation review.

Sincerely,

Stephen L. Johnson
Assistant Administrator

U.S. Environmental Protection Agency Office of Pesticide Programs

Details of the Consultation for Department of State Use of Pesticide for Coca Eradication Program in Colombia, August 2002

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EPA has reviewed information provided by Department of State concerning the pesticide formulation applied (combination of the pesticide active ingredient, glyphosate, and inert ingredients), and application rates and methods. According to the most recent figures (1999 sales and usage) glyphosate is the most widely used conventional pesticide in the United States. The Agency evaluates all pesticides used in the U.S. to determine whether they meet the U.S. safety standard of no unreasonable adverse effects. Consequently, EPA has a significant amount of information about glyphosate from a health and environmental standpoint because of our reviews of use conditions in the U.S. In the U.S., the Agency can assure significant controls on use and potential health and environmental impacts through the pesticide label, and through a state infrastructure which governs label compliance to address issues such as drift and worker and bystander exposure.

Based on a comparison of the glyphosate use pattern in Colombia, as described by the Department of State, and use in the U.S., EPA determined that the most equivalent U.S. uses of glyphosate would be forestry or rights-of-way. The glyphosate product which has been identified to us as used in Colombia is registered in both the U.S. and Colombia, although it has never been marketed in the U.S. The Agency found application rates described as used in Colombia to be within the parameters listed on U.S. labels. The addition of a spray adjuvant (to facilitate the formulation adhering to and penetrating the coca plant) is also in keeping with U.S. practice. While the specific spray adjuvant product identified as that used in Colombia is not sold in the U.S., similar substances and products are commonly used. Most U.S. labels for forestry and right-of-way use of glyphosate suggest application by helicopter. Since application in Colombia is done by fixed-wing aircraft, it is likely conducted at a higher speed and from a greater altitude, than would be typical in the U.S. Department of State has assured the Agency that mixers/loaders and applicators of the glyphosate formulation receive training comparable to U.S. label requirements for glyphosate products including the use of personal protective equipment such as gloves and goggles.

As for potential human health effects of the coca eradication program, there are no risks of concern for glyphosate, *per se*, from dermal or inhalation routes of exposure, since toxicity is very low. There is concern for acute eye toxicity due to an inert ingredient in the glyphosate formulated product used to treat coca. The potential eye effects are related to an inert ingredient, not the glyphosate itself, and greatest potential for exposure is expected for workers mixing and loading the concentrated glyphosate product. The components of the spray adjuvant, Cosmoflux 411F, are substances with low oral and dermal toxicity that have been approved for use in/on food by EPA and the Food and Drug Administration. There are no expected toxicological effects of concern for acute (short-term) or chronic (long-term) dietary exposure through food and water from the coca eradication program. Incident data from Colombia involving humans, livestock, mammals and birds, are based on potential exposure to glyphosate from fumigation of poppy fields, which may differ from use of and exposure to glyphosate from coca eradication, so conclusions should be made cautiously.

Relative to the potential environmental effects of the spraying program based on U.S. data, phytotoxicity to non-target plants outside of the application zone would be expected, since glyphosate is a broad spectrum herbicide. Given the application method described by Department of State, offsite exposure from spray drift is probable, as it would be under similar uses in the U.S. This proposed use of glyphosate itself does not appear to pose a significant direct risk to terrestrial or aquatic animals, although secondary adverse effects from the temporary loss of habitat in the spray area could occur. EPA would not expect any risk to birds and mammals, including livestock, based on dietary exposure to the active ingredient glyphosate. Anticipated effects to animals are based on an extrapolation of data related to North American species. Glyphosate does not have a high potential to leach to ground water or reach surface water as dissolved runoff but does have potential to contaminate surface water as a result of residues suspended in runoff water. A more refined assessment is difficult due to uncertainty regarding the exact formulation of the spray solution.

As part of its consultation, EPA reviewed available scientific studies and information on the human health and environmental effects of glyphosate and the inert ingredients and on exposure pathways; conducted a literature search for human health incidents related to glyphosate use in the U.S.; and summarized use patterns for glyphosate in the U.S., including use sites, methods and rates of application, and differing formulations. In addition, the Agency considered information, provided by non-governmental sources, concerning adverse effects reportedly connected to the eradication program.

Details of the Agency?s findings are provided in the attached document.

SECTION 1. Description of Glyphosate Use in the U.S. for Comparison to Use in Colombia for Coca Eradication

INTRODUCTION: The Biological and Economic Analysis Division (BEAD) within the Office of Pesticide Programs, Environmental Protection Agency, has been asked to describe the use of glyphosate within the United States with a more detailed description of its use in forestry sites so that methods of use in the United States may be used as a basis for comparison for coca eradication in Colombia (1).

SUMMARY: Glyphosate is the herbicide most widely used in the United States[1] (2). In agriculture this popularity is due, in large glyphosate for use in glyphosate-tolerant soybeans.

Table Two. Allowed Rate of the Isopropylamine Salt of Glyphosate Per Application in Tolerant Soybeans

Maximum for Application Timing	Quarts of Product/Acre	Pounds of Active Ingredient/Acre	Kilograms of Active Ingredient/Hectare
For Entire Season	8	8	9
Before Crop Emergence	5	5	5.6
In Crop	3	3	3.4
Up to Two Weeks Prior to Harvest	1	1	1.1

NON-AGRICULTURAL USES INCLUDING FORESTRY: BEAD has been asked to describe the use of glyphosate in U.S. forestry sites since that use most closely corresponds to the use of glyphosate in Colombia for coca control. For simplicity this document only refers to Accord? which is intended specifically for forestry use (6). This product contains the isopropylamine salt of glyphosate (41.5%), and is labeled for non-agricultural uses including Forestry Site Preparation and Utility Rights-of Way, Forestry Site Conifer and Hardwood Release, and Wetland Sites in the U.S. Table Three describes the rates at which it may be used. It is recommended for use in site preparation prior to planting any tree species, including Christmas tree and silvicultural nursery sites (7). Specific methods of application for forestry uses include: aerial spraying; spraying from a truck, backpack or hand-held sprayer; wipe application; frill treatment; cut stump treatment (7).

For forestry site preparation it may be applied using either ground or aerial equipment at rates from 2 to10 pounds glyphosate active ingredient per acre which is equivalent to 2.2-11.2 kilograms of active ingredient per hectare (Table Three). It may also be applied using hand-held equipment. Product instructions specify that a non-ionic surfactant be added to the spray mixture for all forestry uses at a rate of 0.5 to 1.5 percent by spray volume (2 to 6 quarts of surfactant per 100 gallons of spray solution). It may also be combined with certain residual herbicides to extend the period of weed control beyond that obtained with glyphosate alone.

The isopropylamine salt of glyphosate may also be used in forestry conifer and hardwood release as a directed spray or by using selective equipment. This product may also be used in or around wetland sites generally at no more than 5 quarts of product per acre (5 lbs isopropylamine salt of glyphosate per acre which is equal to

5.6 kg/ha) using over-water broadcast application (5).

Table Three. Rate of Isopropylamine Salt of Glyphosate Per Application For Certain Use Sites

Use Site	Quarts of Product/Acre	Pounds of Active Ingredient/Acre	Kilograms of Active Ingredient/Hectare
Forestry Site Preparation and Utility Rights-of Way	2-10	2-10	2.2-11.2
Forestry Site Conifer and Hardwood Release	2-10	2-10	2.2-11.2
Wetland Sites	2-5	2-5	2.2-5.6

PROPERTIES OF GLYPHOSATE: Glyphosate is a foliar-active herbicide; to exert herbicidal properties it must enter the plant through foliage (or in some cases, the stem). Glyphosate applied to foliage is absorbed by leaves and rapidly moves through the plant. It acts by preventing the plant from producing an essential amino acid. This reduces the production of protein in the plant, and inhibits plant growth.

Glyphosate has systemic activity, meaning that it circulates through the plant?s vascular system; affecting the entire plant, not just the treated foliage. Other foliar-active herbicides, like paraquat for example, are contact herbicides; affecting only the portion of the plant onto which they are applied. After treatment with a contact herbicide, a plant may then regrow from untreated portions, often necessitating re-treatment for complete control. The advantage to a systemic herbicide is that if applied at an appropriate dose, it can kill an entire plant, thus preventing regrowth from an untreated plant part such as a root.

Glyphosate has no residual activity, once adsorbed to soil it quickly becomes unavailable to plants and no longer has herbicidal activity. This means that a plant that would ordinarily be susceptible to glyphosate can be planted shortly after an application of glyphosate; this is common practice in U.S. agriculture. In contrast, some herbicides have month-long or even year-long residual activity which limits the plants that may be grown following their use.

Glyphosate is non-selective. Some herbicides are selective in their action, controlling only grassy weeds in a broadleaf crop like soybeans, for example. However, glyphosate exerts herbicidal action on a variety of plants; it is active on grasses, herbaceous plants including deep rooted perennial weeds, brush, some broadleaf trees and shrubs, and some conifers. However, glyphosate does not control all broadleaf woody plants. Plants vary in their susceptibility to glyphosate, so the treatment of dose in important. Plants of certain species and older plants are less susceptible to glyphosate Timing is critical for effectiveness on some broadleaf woody plants and conifers.

FORMULATIONS OF GLYPHOSATE: Glyphosate and four salts of the parent glyphosate molecule are currently used as active ingredients in registered pesticide products in the U.S.(9). These products are registered with the U.S. EPA for use in the U.S. in many different crop, non-crop, industrial and residential sites.

Table Four. Number of Products and Sites for Different Formulations of Glyphosate

Active Ingredient	Number of Products	Number of Sites
Glyphosate acid	28	more than 250
Ethanolamine salt	2	more than 200
Ammonium salt	16	more than 300
Isopropylamine salt	237	more than 400
Trimesium salt	6	more than 100
Sesquisodium salt	no currently active products	no active sites

GLYPHOSATE USED WITH SURFACTANT FOR FOLIAR ABSORPTION: Since glyphosate is only effective if absorbed by plant foliage, glyphosate is combined with a surfactant to facilitate its absorption. Many herbicide concentrates, including glyphosate, are mixed with water before application. Without a surfactant, the aqueous spray mixture is repelled by the plant?s waxy cuticle layer ("beads up"), and quickly runs off the plant?s surface, preventing absorption.

Surfactants are commonly used as wetting agents with herbicides and in other products such as laundry and dishwashing detergent. Non-ionic surfactants, which are comprised of alcohols or fatty acids and considered an all-purpose surfactant are commonly used with glyphosate-containing products. Surfactants are frequently added during manufacture of the herbicide concentrate. If not, a non-ionic surfactant is generally mixed with the herbicide and water before spraying to enable the liquid to make better contact with the waxy cuticle of the plant. These glyphosate products, which are formulated without a surfactant, are considered "non-loaded" (10).

A short description of international usage of glyphosate, including Colombia, appears after the following references to the above program in Colombia is being carried out in accordance with regulatory controls required by the EPA as labeled for use in the United States, and the chemicals used, in the manner in which they are being applied, do not pose unreasonable risks or adverse effects to humans and or the environment. According to information provided by DoS, the eradication program, includes the use of a spray mixture of a glyphosate containing pesticide product, an adjuvant (Cosmo-Flux 411F) and water. The glyphosate tank mixture is applied in an over the top aerial foliar application in certain provinces within Colombia. To facilitate the request, the DoS met with members of OPP on April 18 and sent a written request, dated May 8, 2002, with documentation on the coca eradication program, including a description of the pesticide spray mixture components, application methods, target site identification, and potential exposures. DoS also supplied EPA with incident reports for aerial eradication of illicit poppy in Colombia.

The Field and External Affairs Division (FEAD) of OPP, which has the responsibility of managing the EPA?s role of providing technical information and assistance to DoS for this program, forwarded the DoS request to Health Effects Division (HED), the Environmental Fate and Effects Division (EFED), and the Biological and Economics Assessment Division (BEAD) for scientific assessments. The HED of OPP is charged with estimating the risk to human health from exposure to pesticides. Registration Action Branch 1 (RAB1), Reregistration Branch 1 (RRB1) and the Chemistry and Exposure Branch (CEB) of HED as a team have performed the assessment requested by the Department of State and have evaluated the potential hazard, exposure, and risk to human health from the U.S. supported coca eradication program Colombia.

A summary of the findings and an assessment of human risk resulting from the use of glyphosate in Colombia to eradicate coca is provided in this document.

Unless otherwise specified, all information pertaining to the U.S. supported coca eradication program in Colombia was provided to the Agency from two sources: (1) Department of State (DoS) Presentation, DoS Coca Eradication Program, 4/18/02, (2) DoS document entitled Chemicals Used for the Aerial Eradication of Illicit Coca in Colombia and Conditions of Application.

II EXECUTIVE SUMMARY

USE PATTERN

According to the State Department, the glyphosate tank mixture is applied as an over the top aerial foliar application to coca in certain provinces within Colombia. The tank mixture sprayed for eradication of coca in Colombia contains 55% water, 44% of glyphosate herbicide product, and 1% adjuvant (Cosmo-Flux 411F). Up to two *included as it may be entitled to confidential treatment)* determines its biological properties, and, thus, its toxicity. The lower molecular weight *(information not included as it may be entitled to confidential treatment)* tend to be more toxic than the higher-weighted *(information not included as it may be entitled to confidential treatment)* and are absorbed by the digestive tract and excreted in the urine and feces, while the higher molecular weight *(information not included as it may be entitled to confidential treatment)* are absorbed more slowly or not at all *(study citation not included as it may be entitled to confidential treatment)*. *(information not included as it may be entitled to confidential treatment)* have low acute and chronic toxicity in animal studies. No significant adverse effects have been noted in inhalation toxicology studies, carcinogen testing, or mutagen assays. High oral doses have resulted in toxic effects to the kidneys and loose feces *(study citation not included as it may be entitled to confidential treatment)*. Topical dermal application of *(information not included as it may be entitled to confidential treatment)* to burn patients with injured skin has resulted in toxicity *(study citation not included as it may be entitled to confidential treatment)*.

Cosmo - Flux 411F (**Adjuvant)**

The Cosmo-Flux 411F adjuvant product used in the glyphosate tank mix is produced by a Colombian company and is not sold in the U.S. The Agency is not in possession of toxicity data from direct dosing of test animals with Cosmo-Flux 411F. However, the Agency has made a hazard assessment based on the toxicity of the individual components. As stated above, sale or use of spray adjuvant products in the U.S. are generally not regulated by EPA. However, the DoS has provided the EPA with a copy of this product?s label and a description of the product ingredients. To be able to provide an opinion on hazard characterization of the Cosmo-flux ingredients, the EPA relied on available technical information from various sources. Cosmo-Flux 411F consists mainly of *(information not included as it may be entitled to confidential treatment)* with a nonionic surfactant blend primarily composed of *(information not included as it may be entitled to confidential treatment)*. All ingredients of this product are substances that are not highly toxic by oral or dermal routes. They may cause mild eye and skin irritation. All components of the adjuvant have been approved for use in/on food by EPA (40 CFR 180.1001, Letter from R.Forrest/EPA, to R.Woolfolk/DoS, 7/30/2001).

Components of Cosmflux

1. *(information not included as it may be entitled to confidential treatment)*. The *(information not included as it may be entitled to confidential treatment)* can cause dermal and ocular irritation and, in high doses orally, can cause significant toxicity. However, small amounts are not a concern and these substances have been protected from aerial spray applications. This reviewer agrees with the conclusion that "the twenty-one clinical histories . . . reveals that any relationship between aerial eradication with the herbicide glyphosate (tank mixture) and the skin conditions treated in Aponte is unlikely".

In summary, the evidence collected and presented in this report cannot confirm that the glyphosate tank mixture used in Colombia as the likely cause of illness in the surrounding community. There is suggestive evidence in the form of reported increases of morbidity and reports from municipalities that some cases of relatively mild complaints could have occurred in relation to the spraying eradication program. Some of the reports appear to be similar to those reported in the literature and by California. These cases report irritation to skin, eyes, and respiratory passages and suggest that the Cosmo-Flux 411F added to the glyphosate product in Colombia has little or no effect on the overall toxicity of the formulated product.

Rather than review incomplete medical records, it would be better to collect information prospectively. For example, if pesticide poisoning is a mandatory reporting condition, a form documenting the exposure, health effects and medical data on each case could be designed and used to establish whether any particular conditions might be related to spraying the glyphosate tank mixture. Without prospective collection of data and follow up, it is difficult to evaluate potential health effects of the glyphosate tank mixture sprayed in Colombia. Better records of the time of exposure relative to the onset of symptoms would also enhance interpretation of the incidence data.

X RISK CHARACTERIZATION

Risk characterization combines the assessments of the first three steps to develop a qualitative or quantitative estimate of the probability, that under the assumed conditions or variables of the exposure scenario, that harm will result to an exposed individual. Risk is equal to hazard multiplied by exposure. For the scenarios that are relevant to the subject use, the Agency has not identified toxic effects attributable to a single oral exposure, short- or intermediate-term dermal, or short- or intermediate-term inhalation exposures (TXR No. 0050428, W. Dykstra, 22-JAN-2002). Therefore, no quantification of exposure or risk was performed. Nonetheless, it is appropriate to qualitatively characterize the potential for risk concerns for this use.

From the review of glyphosate product incident reports for the use on poppy, it should be emphasized that the spraying reported to have occurred in 2000 and not in 1999 suggests, that the overwhelming majority (95%) of the illnesses reported would be background incidents unrelated to the spraying of herbicide. The

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US DEPARTMENT OF STATE, BUREAU FOR INTERNATIONAL NARCOTICS AND LAW ENFORCEMENT AFFAIRS, *MEMORANDUM OF JUSTIFICATION CONCERNING THE SECRETARY OF STATE'S 2003 CERTIFICATION OF CONDITIONS RELATED TO THE AERIAL ERADICATION OF ILLICIT COCA IN COLOMBIA*, WASHINGTON D.C., 2003

(Available at: http://www.state.gov/p/inl/rls/rpt/aeicc/27484.htm (last visited 8 March 2010), p. 4)

U.S. DEPARTMENT OF STATE
DIPLOMACY IN ACTION

Memorandum of Justification Concerning the Aerial Eradication of Coca and Opium Poppy in Colombia

Report on Issues Related to the Aerial Eradication of Illicit Coca in Colombia

BUREAU OF INTERNATIONAL NARCOTICS AND LAW ENFORCEMENT AFFAIRS

December 2003

The Andean Counterdrug Initiative section of the Foreign Operations, Export Financing, and Related Programs Appropriations Act, Division E, Consolidated Appropriations Resolution, 2003, (P.L. 108-7) (?FOAA?) lays out conditions under which assistance using funds appropriated under the FOAA may be made available for the procurement of chemicals for use in aerial eradication of illicit crops. In particular, the FOAA provides:

> That not more than 20 percent of the funds appropriated by this Act that are used for the procurement of chemicals for aerial coca and poppy fumigation programs may be made available for such programs unless the Secretary of State, after consultation with the Administrator of the Environmental Protection Agency (EPA), certifies to the Committees on Appropriations that (1) the herbicide mixture is being used in accordance with EPA label requirements for comparable use in the United States and any additional controls recommended by EPA for this program, and with the Colombian Environmental Management Plan for aerial fumigation; (2) the herbicide mixture, in the manner it is being used, does not pose unreasonable risks of adverse effects to humans or the environment; (3) complaints of harm to health or licit crops caused by such fumigation are evaluated and fair compensation is being paid for meritorious claims; and such funds may not be made available for such purposes unless programs are being implemented by the United States Agency for International Development, the Government of Colombia, or other organizations, in consultation with local communities, to provide alternative sources of income in areas where security permits for small-acreage growers whose illicit crops are targeted for fumigation.

This memorandum lays out the justification for the Secretary of State?s Determination that the conditions in The Andean Counterdrug Initiative section have been met as required.

On April 9, 2003, the Secretary of State wrote U.S. Environmental Protection Agency (EPA) Administrator Whitman to request written consultation concerning the U.S.-supported Colombia eradication program. This letter is included as Attachment 1. Specifically, EPA was asked to advise the Department of State about whether the herbicide mixture is being used in accordance with EPA label requirements for comparable use in the United States and any additional controls recommended by EPA for this program; and about the risks of adverse effects to humans or the environment from the herbicide mixture, in the manner it is being used.

In 2002, EPA provided the Department of State a thorough technical review of the Department of State?s glyphosate use in the Government of Colombia?s coca spray program. The Department of State and EPA determined that EPA should use the EPA?s 2002 analysis as a foundation for the 2003 consultation. The Department?s working level consultations with EPA preceded the Secretary?s letter and continued into June. The Department met with EPA to brief EPA on changes in the eradication program since the 2002 EPA Analysis and to discuss opium poppy eradication, which Congress did not ask EPA to address in 2002. The Secretary?s April 9 letter provided EPA with a written document -- ?Department of State Updated Report on Chemicals used in the Colombian Aerial Eradication Program? -- that provided further information on the issues discussed in the briefing. This document is included as Attachment 2.

On June 9, EPA Assistant Administrator Stephen Johnson responded to the Secretary of State on behalf of EPA Administrator Whitman with the results of EPA?s consultation review. That letter, and the attached document ?Office of Pesticide Programs Details of the 2003 Consultation for the Department of State Use of Pesticide for Coca and Poppy Eradication Program in Colombia? (?EPA 2003 Analysis?) are included as Attachment 3.

1. (A) The herbicide mixture is being used in accordance with EPA label requirements for comparable use in the United States

EPA does not draft the label requirements for pesticide use in the United States, although it reviews and approves recommendations for use that are written by pesticide manufacturers. The aerial spray mixtures currently used in the U.S.-supported program of aerial eradication of both coca and opium poppy in Colombia contain three components: water, an EPA-registered formulation of the herbicide glyphosate, and a surfactant (Cosmo-Flux 411F).

The commercial glyphosate formulation used in the spray mixture is registered with EPA for sale in the United States for non-agricultural use. Although EPA does not regulate the use of adjuvant products not labeled as pesticides, EPA?s Office of Pesticide Programs reviewed the complete chemical constituents of Cosmo-Flux 411F, at the request of the Department of State, in 2001. This allowed the Department of State to better assess safety concerns related to the use of this product in the spray program. EPA determined in September 2001 that all of the ingredients of Cosmo-Flux 411F are exempt under 40 CFR 180.1001 from the requirement of tolerances when included in pesticides applied to food, feeds, and livestock.

During 2003 consultations with EPA, the Department of State reported to EPA the breakdown of the spray mixtures used for spraying coca and opium poppy and the application rates used in each operation (Attachment 2, p. 5). EPA responded that ?EPA has determined that application rates for both coca and opium poppy eradication in Colombia are within the parameters listed on U.S. labels? (Attachment 3, Executive Summary). This determination meets the criteria for the Secretary to certify that the herbicide mixture is being used in accordance with EPA label requirements for comparable use in the United States.

1. (B) The herbicide mixture is being used in accordance with any additional controls recommended by the EPA for this program

The Government of Colombia and the Department of State have implemented several changes in the program to address issues raised by the 2002 EPA analysis. For reference, the 2002 EPA analysis, entitled: ?Office of Pesticide Programs Details of the Consultation for Department of State: Use of Pesticide for Coca Eradication Program in Colombia? (?2002 EPA Analysis?) is enclosed as Attachment 4. The 2002 EPA recommendations and the Department of State responses are outlined below.

EPA recommendation to change glyphosate product used by the program:

The EPA made one direct recommendation to the Department of State related to spray program controls in the 2002 EPA Analysis. EPA recommended

Executive Summary, p. ii).

The Department will continue drift control efforts as EPA recommends. Based on responses to EPA?s 2002 and 2003 recommendations on herbicide use, human health tracking, and spray drift, the Department of State believes that the herbicide mixture is being used in accordance with any additional controls recommended by the EPA for this program.

1. (C) The herbicide mixture is being used in accordance with the Colombian Environmental Management Plan for aerial fumigation

The GOC?s Environmental Management Plan for aerial eradication (EMP) was drafted and implemented by the Ministry of the Environment (MINAMB) in 2001. The EMP was designed to be a living document, and it was modified by several MINAMB resolutions at the end of the previous administration. As written, the EMP was impossible to execute and lacked clear lines of responsibility for the GOC line agencies that were required to carry out aspects of the EMP.

In 2003, the GOC recognized that further refinement was necessary to achieve greater efficiencies, and formed an inter-institutional technical committee to revise the EMP. This committee, which first met on May 8, 2003, was composed of representatives from the Ministry of the Environment (MINAMB), the National Directorate for Dangerous Drugs (DNE), the Antinarcotics Police (DIRAN), the Ministry of Health, the Ministry of Agriculture (ICA), MINAMB's laboratory (IDEAM), and the U.S. Embassy Bogota Narcotics Affairs Section (NAS).

The revisions recommended by the committee were briefed to Colombian environmental groups following formal publication. After a fifteen-day period, during which no adverse comments were received, the revisions were incorporated into the EMP by MINAMB Resolution 1054 on September 30, 2003. An English language version of the revised EMP is enclosed as Attachment 8.

The most significant change in the EMP is the inclusion of multiple agencies in the monitoring process. Under the EMP as modified, environmental monitoring is an inter-agency process, with clear roles and responsibilities for each party. INL technical and equipment assistance provided to a wide range of EMP participants has given these agencies an ability to actively participate in monitoring of the spray program and to carry out the roles required of them. With Department of State-donated laboratory equipment, the GOC Institute of Geography will conduct soil sampling and the Ministry of Health will conduct water sampling to determine the persistence of glyphosate in sprayed areas. Similarly, with assistance from the Department of State, the GOC?s Ministry of Health is training health care providers in areas where spraying takes place to recognize different forms of chemical poisoning. Once trained, they will be able to differentiate between glyphosate-derived illness and the other forms of chemical poisoning that commonly afflict people who process raw materials into finished drugs in their homes. NAS has allocated $3 million from the eradication budget for environmental improvements ranging from physical upgrades at bases to the provision of training and equipment to GOC line agencies for EMP purposes.

INL Principal Deputy Assistant Secretary Paul Simons visited Bogota during November 5-7 to meet with NAS Bogota and participating GOC EMP agencies to discuss their roles under the new EMP. All of these agencies were appreciative of the Department of State?s assistance that is now allowing them a seat at the table under a functioning EMP. In addition to providing assistance to Colombia?s EMP agencies, NAS Bogota has hired four personnel to strengthen oversight of the eradication program and related initiatives to ensure continued compliance with environmental guidelines, including the EMP. The added positions include a U.S. contractor Environmental Advisor, a Colombian Environmental Advisor, and a Colombian lawyer to assist with complaint investigations and adjudication, and a Colombian toxicologist.

Due to the limited time between the approval of the modifications to the EMP (September 30) and the submission of this report, INL has been unable to fully comply with one provision. This provision (Attachment 8, specification No. 4), calls for sewage and industrial wastewater treatment facilities to be installed at all aerial eradication forward operating locations (FOL?s). NAS Bogota has designed and ordered the necessary equipment, but there will be some lag time pending delivery and installation. This is inevitable, as spraying moves into new areas and new FOL?s are developed. Although this aspect of the EMP has not been completed, we believe that in progress implementation of the program complies with both the spirit and the letter of the EMP sufficiently so that the Secretary?s certification is appropriate at this time.

Attachment 9 is a letter dated November 5 from the Government of Colombia?s Vice Minister of Environment certifying that the spray program is being carried out in compliance with the Government of Colombia?s Environmental Management Plan. The Government of Colombia?s Environmental Ministry has over-arching responsibility for supervision of the Environmental Management Plan.

2. The herbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment

The Secretary of State certified last year that the herbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment. Since the 2002 certification, the Department has responded to EPA recommendations (per the above) with adjustments that have strengthened spray program controls and ensure increased protection against adverse effects to humans and the environment.

After consultations with the Department of State in 2003, EPA offered the following assessment of human health concerns related to the spraying of coca and opium poppy in Colombia: ?As for human health concerns, EPA concludes there are no risks of concern from dietary, mixer/loader/applicator or field workers, or bystanders (including children). The concerns for mixer/loader eye irritation discussed in the Agency?s 2002 findings have been mitigated by switching to the lower toxicity product? (Attachment 3, Executive Summary, p. ii).

EPA also concluded that the eradication program lowered its potential risks to wildlife and takes appropriate measures to minimize off target drift: ?EPA concludes that the switch to a lower toxicity product will pose less risk of acute poisoning to wildlife. The Agency believes that the potential for spray drift phytotoxicity is still a factor for both coca and poppy spraying. EPA recognizes that the Department of State is employing Best Management Practices to minimize drift and encourages them to continue these efforts.? (Attachment 3, Executive Summary, p. ii).

The Department of State believes that improvements over the last year have decreased the likelihood of adverse impacts of eradication program on humans and the environment and that the herbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment.

3. (A) Complaints of harm to health or licit crops caused by such fumigation are evaluated and fair compensation is being paid for meritorious claims

On October 4, 2001, the GOC formally instituted a new process to compensate growers for legal crops sprayed in error. Since that date, the Government of

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US DEPARTMENT OF STATE, BUREAU FOR INTERNATIONAL NARCOTICS AND LAW ENFORCEMENT AFFAIRS, *MEMORANDUM OF JUSTIFICATION CONCERNING THE SECRETARY OF STATE'S 2004 CERTIFICATION OF CONDITIONS RELATED TO THE AERIAL ERADICATION OF ILLICIT COCA IN COLOMBIA*, WASHINGTON D.C., 2004

(Available at: http://www.state.gov/p/inl/rls/rpt/aeicc/57012.htm (last visited 8 March 2010), pp. 3, 4)

Memorandum of Justification Concerning the Secretary of State's 2004 Certification of Conditions Related to the Aerial Eradication of Illicit Coca and Opium Poppy in Colombia

Other Releases
BUREAU FOR INTERNATIONAL NARCOTICS AND LAW ENFORCEMENT AFFAIRS
Washington, DC
2004

The Andean Counterdrug Initiative section of the Consolidated Appropriations Act, 2004 (Public Law 108?199) lays out conditions under which assistance using funds appropriated under the Andean Counterdrug Initiative may be made available for the procurement of chemicals for use in aerial eradication of illicit crops. In particular, Public Law 108?199 provides:

> "That not more than 20 percent of the funds appropriated by this Act that are used for the procurement of chemicals for aerial coca and poppy fumigation programs may be made available for such programs unless the Secretary of State, after consultation with the Administrator of the Environmental Protection Agency (EPA), certifies to the Committees on Appropriations that: (1) the herbicide mixture is being used in accordance with EPA label requirements for comparable use in the United States and any additional controls recommended by the EPA for this program, and with the Colombian Environmental Management Plan for aerial fumigation; and (2) the herbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment: *Provided further,* That such funds may not be made available unless the Secretary of State certifies to the Committees on Appropriations that complaints of harm to health or licit crops caused by such fumigation are evaluated and fair compensation is being paid for meritorious claims: *Provided further,* That such funds may not be made available for such purposes unless programs are being implemented by the United States Agency for International Development, the Government of Colombia, or other organizations, in consultation with local communities, to provide alternative sources of income in areas where security permits for small-acreage growers whose illicit crops are targeted for fumigation:?."

This memorandum provides justification for the Secretary of State?s determination and certification to Congress that the above conditions have been met as required. In 2002 and 2003, the Secretary of State determined and certified to Congress on similar conditions concerning human health and environmental safety issues related to the Colombia spray program. These certifications were based on, among other information: all available scientific data on glyphosate, the herbicide used by the program; toxicological tests of the spray mixture (water, glyphosate, and a surfactant); active field verifications and complaint investigations; comprehensive human health monitoring; and thorough verbal and written consultations on the spray program with USDA and EPA. Because the Colombia aerial eradication program has not made any changes in the chemical formulation or application methods used for eradication of coca and opium poppy since the Department of State last submitted documents to EPA for the 2003 consultation (April 9, 2003), these prior certifications serve as the foundation for the 2004 certification. These certifications and attachments can be found on the Internet at the following address: **http://www.state.gov/p/inl/rls/rpt/aeicc/**.

On **September 27, 2004**, the Secretary of State wrote U.S. Environmental Protection Agency (EPA) Administrator Leavitt to request written consultation concerning the U.S.-supported Colombia eradication program. This letter is included as **Attachment 1**. Specifically, EPA was asked to advise the Department of State about whether the herbicide mixture employed by the U.S.-supported program of aerial eradication of coca and opium poppy in Colombia is being usec in accordance with EPA label requirements for comparable use in the United States and any additional controls recommended by the EPA for this program; whether the herbicide mixture is being used in accordance with the Colombian Environmental Management Plan for aerial fumigation; and whether this herbicide mixture, in the manner it is being used, poses unreasonable risks or adverse effects to humans or the environment.

The Department met with EPA on **September 6, 2004** to brief EPA on the expanded monitoring of possible environmental and human health issues related to the program since the 2003 EPA Analysis. The Secretary of State?s **September 27, 2004** letter provided EPA a written document -- "2004 Department of State Report to EPA on Human Health and Environmental Monitoring Related to the Colombian Illicit Crop Eradication Program" -- with further information on the issues discussed in the briefing. This document is included as **Attachment 2**.

On **November 17, 2004**, EPA Administrator Michael O. Leavitt responded to the Secretary of State with the results of EPA?s consultation review. That letter and the attached document from the Office of Pesticide Programs, "Details of the 2004 Consultation for the Department of State Use of Pesticide for Coca and Poppy Eradication Program in Colombia" are included as **Attachment 3**. The next six sections directly address the requirements and concerns of Public Law 108-199.

1. The herbicide mixture is being used in accordance with EPA label requirements for comparable use in the United States.

EPA told the Department of State in its recent 2004 report that "Application rates for both coca and poppy eradication in Colombia are within the parameters listed on labels of glyphosate products registered by EPA for use in the United States." (**Attachment 3, Section B**). This is the same finding they reached in the 2003 report, when the EPA stated, "EPA has determined that application rates for both coca and poppy eradication in Colombia are within the parameters listed on U.S. labels." This determination meets the criteria for the Secretary to certify that the herbicide mixture is being used in accordance with EPA label requirements for comparable use in the United States.

2. The herbicide mixture is being used in accordance with any additional controls recommended by the EPA for this program.

The Government of Colombia and the Department of State have implemented several changes in the program to address EPA?s recommendations made in the 2003 EPA analysis as evidenced by the EPA?s statement in its 2004 report, "The DoS and the Government of Colombia made modifications and enhancements to the spray program as EPA recommended in its prior assessments." In 2003, the EPA recommended in its Executive Summary, "that the Department of State continue programs for investigating health complaints. The Agency also requested that the Department of State improve its definition of

20-22 April Arauca City	1,572 farm animals treated on 49 farms
15 May Arauquita	1,105 civilian patients
15-16 May Monta?ita	2,800 civilian patients
22-23 May Saravena	1,915 civilian patients
5 June La Antioquena	687 civilian patients
12-13 June Florencia	3,493 civilian patients
9-10 July	1,668 civilian patients
14-15 Aug	2,354 civilian patients
21-22 Aug	1,089 civilian patients
18-19 Sept	1,599 civilian patients
Totals	22,263 civilian patients 1,572 farm animals

The only changes suggested by the EPA in its 2004 report are minor and relate to improving the data collection form used to collect information on reports of damage to human health. They are as follows:

- **General Data**: Record date and contact information about the health care provider (who fills out the form) in case follow-up consultation is needed
- **Characterization of the Exposure**: Record more information about the location of exposure and any description about the proximity to the spraying (how far away) or amount of exposure (e.g. amount of skin exposed, eyes exposed, etc.).

The NAS in the U.S. Embassy in Bogota will be following up with the appropriate GOC officials to ensure that these suggestions are incorporated into the overall Aerial Eradication Program.

3. The herbicide mixture is being used in accordance with the Colombian Environmental Management Plan for aerial fumigation

On July 26, 2004 the Minister of the Environment, Housing, and Territorial Development, the Government of Colombia entity charged with supervision of the Environmental Management Plan for aerial eradication (EMP), ruled that the illicit crop eradication program is being conducted in compliance with the EMP. That Ruling No. 707, an English version of which is enclosed as **Attachment 5**, reads:

> "The entities responsible for executing the Illicit Crop Eradication Program Using Aerial Spraying with the Herbicide Glyphosate ? PECIG ? are currently complying with the measures established in the Environmental Management Plan imposed by this Ministry, the purpose of which is preventing, mitigating, controlling, offsetting, and correcting any possible negative environmental effects or impacts which might result from eradicating illicit crops (p. 26)."

The Department of State provided EPA the English language version of the EMP in late 2003. EPA responded to the Department of State in a February 23, 2004 letter: "We believe the Plan contains appropriate types of activities for a pesticide spray program. The information in the EMP is generally in agreement with information provided to EPA for the previous consultations and discussed in EPA?s 2002 and 2003 written assessments." This letter is found in **Attachment 6.**

The Government of Colombia?s Ministry of the Environment, Housing, and Territorial Development?s ruling meets the criteria for the Secretary to certify that the herbicide mixture is being used in accordance with the Colombian Environmental Management Plan for aerial fumigation.

4. The herbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment

The Secretary of State determined and certified in 2002 and 2003 that the herbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment. Since the 2003 certification, the Department has responded to EPA recommendations (per section 2) with adjustments that have strengthened spray program controls to ensure increased protection against adverse effects to humans and the environment.

In the 2004 EPA report, EPA offers the following assessment of human health concerns related to the spraying of coca and opium poppy in Colombia: "Despite an aggressive search for cases, there does not appear to be any evidence that glyphosate aerial spraying has resulted in any adverse health effects among the population where this spraying takes place." EPA also concluded, "that an aggressive program to identify glyphosate poisoning has been implemented in the areas of Colombia where illicit crop eradication spraying programs are prevalent." A significant number of health care providers have received training and additional training is under way or planned.

As recognized in the 2003 report, the eradication program lowered its potential risks to wildlife and has responded appropriately to minimize off target drift. However, in the 2004 report the Agency stated, "Spray drift and potential side effect down wind of the target sites are common, universal factors in most if not all pesticide applications from aerial or ground applications for all uses." In 2003, EPA recognized that the Department of State was employing "Best Management Practices to minimize drift." The Department of State continues to follow these Best Management Practices and is ever vigilant regarding the manner in which the herbicide is applied.

The Government of Colombia regularly conducts studies to assess the spray program's environmental impact through ground truth verifications to estimate spray drift and the accuracy of the spray mixture application, and during verification of all legitimate complaints about alleged spraying of crops or vegetation that are not coca or opium poppy. After the most recent verification, the Government of Colombia?s Ministry of Environment, Housing, and Territorial Development characterized spray drift in the following fashion:

> The drift effects that were observed in areas visited on a random basis were temporary in nature and small in extent, and basically consisted of partial defoliation of the canopy of very high trees. No complementary collateral damage from spraying activities was observed at the sites selected and verified. In sprayed areas that were subsequently abandoned, it was noted that vegetation was starting to grow again, the predominant types being grasses and a number of herbaceous species (**Attachment 5**, p. 4)

As part of the spray program?s compliance with the Government of Colombia?s Environmental Management Plan for the Aerial Eradication of Illicit Crops (EMP), NAS and the Government of Colombia conduct analyses of soils and water in areas where coca is sprayed. The purpose of these studies is twofold. Initial tests determine the levels of glyphosate and AMPA (amino-methyl phosphonic acid - the principal metabolite of glyphosate and an indicator of the natural degradation of that herbicide in soils) to understand the persistence of glyphosate in the Colombian soil and water in sprayed areas. In addition, further studies assess the physio-chemical properties of the samples (percentages of sand, clay, and mud, pH level, percentage of interchangeable acid saturation, total phosphate and useable phosphate content, percentage of organic material, total nitrogen level, catatonic interchange capacity, mineralization index, and nitrate, ammonium, calcium, magnesium, potassium, and sodium content).

These studies increase the public?s understanding of glyphosate?s transformation and rate of decay in Colombian soil and help answer questions about any significant modification of the properties of the soil associated with the spray program. The soil analyses determined that soils contained acceptable levels of glyphosate and AMPA even shortly after spraying, that glyphosate degrades over time in Colombian soils, and that there are no appreciable significant changes in the properties of the soil due to the glyphosate used by the spray program.

Soil and water samples were collected in the field by an inter-agency committee of Government of Colombia agencies, including the Ministry of Environment, Housing, and Territorial Development (MMA), the Institute of Agriculture and Husbandry (ICA), the National Directorate of Dangerous Drugs (DNE), and the Colombian National Police (CNP). The laboratory studies were conducted by three different labs: the USDA Agricultural Research Service (USDA-ARS) laboratory at the University of Mississippi conducted glyphosate and AMPA analysis in soils; the Government of Colombia?s August?n Codazzi Geographic Institute (IGAC) National Soils Laboratory Division conducted physio-chemical analysis of soil samples, and the Government of Colombia?s National Institute of Health (INS) conducted glyphosate and AMPA analysis of water samples.

After review of the test results and protocols for soil and water sampling, EPA responded in 2004 by saying, "similar to the results of previous Agency assessments, no risks are predicted for aquatic animals and plants, based on exposure to residual glyphosate or AMPA in water bodies contiguous to or near coca crops."

For the 2003 Spray Certification, the Department had laboratory toxicity tests performed on the entire spray mixture, which tested at an acceptable Category III for eye irritation and Category IV for all other categories (on EPA's scale of I-IV with IV being the least toxic). Since that time, the spray program has increased its environmental and human health monitoring program and the Government of Colombia?s Environmental Ministry has determined that the spraying complies with the Ministry's Environmental Management Plan for aerial eradication.

The Department of State believes that improvements over the last year have significantly decreased the likelihood of adverse impacts of eradication program on humans and the environment and that theherbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment.

5. Complaints of harm to health or licit crops caused by such fumigation are investigated, and fair compensation is being paid for meritorious claims

The methodology for investigations into human health problems allegedly tied to spraying is covered in section 3 above. Therefore, this section focuses exclusively on complaints of spray damage to legal crops. The Government of Colombia is investigating and resolving these complaints more swiftly than in past years and continues to compensate all meritorious claims fairly.

On October 4, 2001, the GOC formally instituted a new process to compensate growers for legal crops sprayed in error. Since that date, the Colombian National Police, Anti-Narcotics Directorate (DIRAN), the Government of Colombia agency responsible for complaint investigations, has received 5,065 such complaints.

In 2004, the DIRAN?s complaint investigations unit and other GOC entities that play a role in complaint investigations made substantial progress in eliminating the existing backlog of cases to be investigated and resolved. In calendar year 2004, although only 632 new complaints were received (through October), 2,725 complaint investigations were completed. Of these investigations in 2004, only four complaints were found to be valid and compensation payments were made, for a total of $3,846. Four more cases of compensation are due to be paid in November. To date, the spray program has compensated growers in 12

Annex 145

ANDEAN REGULATION FOR THE CONTROL OF CHEMICAL SUBSTANCES USED IN THE ILLEGAL MANUFACTURE OF NARCOTIC DRUGS AND PSYCHOTROPIC SUBSTANCES, ANDEAN COMMUNITY, DECISION 602 OF 2004

(Andean Community Decision 602 of 2004)

Decisions

Decision 602
Andean Regulation for the Control of chemical substances used in the illegal manufacture of narcotic drugs and psychotropic substances

THE ANDEAN COUNCIL OF MINISTERS OF FOREIGN AFFAIRS, IN AN EXTENDED MEETING WITH THE PRINCIPAL REPRESENTATIVES TO THE ANDEAN COMMUNITY COMMISSION,

HAVING REVIEWED: The first paragraph b) in Article 3 and Article 16 of the Cartagena Agreement; Articles 6 and 12 of the Regulations of the Andean Council of Foreign Affairs Ministers; and Decisions 477 (International Customs Traffic, in place of Decision 327), 478 (Mutual Assistance and Cooperation between Customs Authorities of Andean Community Member Countries), 505 (Andean Cooperation Plan for Fighting Against Illegal Drugs and Associated Crimes), 562 (Directives for the preparation, adoption and application of Technical Regulations in Andean Community Member Countries and at Community level) and 574 (Andean Customs Control System); and,

WHEREAS:

The Andean Community is determined to reinforce the application of the control and surveillance procedures currently being used by its Member Countries, concerning the traffic of chemical substances which are likely to be used for the production of illicit drugs, cocaine and heroin in particular;

In an effort to protect the Community's customs territory against eventual diversion of chemical substance imports or exports for use in the manufacture of illicit drugs, it is essential to establish in the Community an early warning mechanism on the export of such chemical substances between Member Countries, as a complement to any mechanisms in place between each Member Country and other countries;

While the efforts individually made by the Member Countries to control and monitor the chemical substances included in Tables I and II of the 1988 United Nations Convention Against the Illicit Traffic in Narcotic Drugs and Psychotropic Substances, are recognized, there is a need to prepare a basic harmonized list of controlled chemical substances for Community use, which can be gradually updated based on the experience gathered in the Andean Community and the possibilities of effective international surveillance;

The Member Countries that have signed the 1988 United Nations Convention Against the Illicit Traffic in Narcotic Drugs and Psychotropic Substances, abide by the recommendations of the Model Regulations for the Control of Chemical Substances Used in the Illicit Manufacture of Narcotic Drugs and Psychotropic Substances issued by the Organization of American States (CICAD/OEA); and the United Nations Manual for the Transport of Hazardous Goods;

The Member Countries, in the Third Meeting of the Executive Committee of the Andean Cooperation Plan for Fighting against Illegal Drugs and Associated

Crimes, resolved to carry out mutual cooperation actions to enhance the parameters applicable to the control and surveillance of import, export, transport and any other type of transactions at the Andean level and from other countries, of chemical substances which could be possibly used in the production of cocaine and heroin;

Abiding by the recommendation of the Third Meeting of the Executive Committee of the Andean Cooperation Plan for Fighting against Illegal Drugs and Associated Crimes, the General Secretariat has submitted Proposal 125/Rev. 1 on the adoption of "Andean Regulations for the Control of Chemical Substances Used in the Illicit Manufacture of Narcotic Drugs and Psychotropic Substances";

The representatives to the Andean Community Commission have reviewed the said Proposal and have issued a favorable opinion for adoption thereof on the terms set forth in Proposal 125/Rev. 1;

DECIDES:

CHAPTER I
PURPOSE AND SCOPE OF APPLICATION

Article 1.- The purpose of this Regulation is to enhance control and surveillance of import, export, transport and any other type of transactions at the Andean level and from other countries, of the chemical substances included in the Basic Harmonized List for Community Use, identified in

annex Annex I hereof, which are frequently used in the illicit production, manufacture, preparation or extraction of narcotic drugs and psychotropic substances, cocaine and heroin in particular.

Article 2.- This Regulation shall be applicable in the entire territory of the Member Countries. Under no circumstances shall the rules and procedures set forth in this Regulation imply:

a) The creation of unnecessary restrictions on free trade or free border movement, pursuant to the provisions of the Cartagena Agreement or of bilateral or multilateral Agreements or Treaties;

b) A limitation on the application in each Member Country of the provisions of Article 12 of the 1988 United Nations Convention Against the Illicit Traffic in Narcotic Drugs and Psychotropic Substances;

c) An attempt to ignore the authority of each Member Country to regulate surveillance of all stages of trading, including production, storage and distribution, among others, in accordance with the stipulations of this Regulation.

Any cases not prescribed by this Regulation shall be governed by the internal regulations of each Member Country with respect to matters related to the monitoring of the chemical substances listed in Annex I hereof, and by the 1988 United Nations Convention Against the Illicit Traffic in Narcotic Drugs and Psychotropic Substances.

CHAPTER II
DEFINITIONS

Article 3.- For the purposes of this Regulation, the following definitions shall apply:

Competent Administrative Authorities: They are the national entities listed in Annex V hereof, with jurisdiction to deal with matters related to licenses, registration, permits and authorizations, or to issue early warning on the import, export, customs traffic or transport, at the Andean level and from other countries, of the controlled chemical substances identified in Annex I hereof.

CAS: Chemical Abstract Service.

Andean Community: Comprised of the sovereign States of Bolivia, Colombia, Ecuador, Peru and Venezuela, and by the organizations and institutions forming part of the Andean Integration System established in the Cartagena Agreement.

Andean Council of Foreign Affairs Ministers: Comprised of the Foreign Affairs Ministers of Andean Community Member Countries, with authority to adopt Decisions which are binding on the Member Countries.

Concentration: Physical magnitude expressing the quantity of a controlled substance, by volume unit.

Dilution: Lowering of the concentration of a controlled substance in water.

Import and Export: Respectively, the legal entry or exit of goods to or from customs facilities, including special customs regimes and free trade zones.

Mix: This is the product into which one or more controlled substances are combined, and which may be used in full or in part, in the extraction and/or refining or synthesis of natural or man-made drugs.

NANDINA: Common Nomenclature of the Andean Community Member Countries.

Controlled Chemical Substances: Chemical substances listed in Annex I and in Tables I and II of the 1988 United Nations Convention Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances, included in Annex II hereof.

Transfer: Transfer of controlled chemical substances, performed under the control of a single customs facility, from one transport or freight unit to another, or to the same unit in a different journey, including unloading to land, with the purpose of continuing to the place of destination.

International Customs Traffic: Customs regime, according to which, the goods are carried under customs control, from a departure customs facility to an arrival customs facility, in the same operation and in the course of which, one or more borders are crossed.

Harmonized System: World Customs Organization's Basic Harmonized Commodity Description and Coding System .

CHAPTER III
BASIC COMMON LIST OF CONTROLLED CHEMICAL SUBSTANCES

Article 4.- For the purposes of effective monitoring at the Community level, the controlled chemical substances listed in Annex I shall be identified by their generic and chemical names, the CAS Code and their respective numerical codes assigned in the Harmonized System – NANDINA classification.

Article 5.- The Chemical Substances Subcommittee shall study and recommend the application of additional measures required for greater effectiveness of the control exercised over the substances included in Annex I, as well as the physical and chemical parameters required to establish control of any mix, concentration or dilution.

CHAPTER IV

IMPORT, EXPORT, TRAFFIC AND TRANSFER REQUIREMENTS

Article 6.- Anyone importing or exporting controlled chemical substances must present, notwithstanding compliance with requirements pertaining to registration, qualification, license and filing, pursuant to the internal regulations of each Member Country (as well as with the relevant foreign trade regime), any authorizations or permits issued by the Competent Administrative Authorities to import or export and for international traffic under the International Customs Traffic Declaration defined in Decision 477.

Article 7.- Anyone importing or exporting the chemical substances included in Annex I hereof and those listed in the corresponding legislation of each Member Country, shall be subject to a control system consisting of authorizations, licenses and similar procedures to be followed pursuant to the internal regulations of each Member Country.

Article 8.- Applications for authorization and permits must be filed by the importer or exporter with the competent national authority, within the terms stipulated in the internal regulations of each Member Country in the case of imports. An authorization or permit may only be used once and it may not cover future imports of substances of a different nature.

Said authorizations and permits shall expire 180 calendar days from their date of issue. If this term has elapsed without the respective import or export having been performed, a new authorization or permit must be sought.

Applications for a permit or authorization must include the following information:

a) Name, address, classification, license or registration number, telephone and fax number and/or electronic mail of importer and exporter;

b) Name, address, telephone and fax number and/or electronic mail of import or export agent and of the shipping agent, as the case may be;

c) Names, NANDINA subheading and CAS name for each chemical substance listed in Annex I of this Regulation, as well as the description found on the label of each piece, package and/or container;

d) Net weight or volume of the product, in kilograms or liters, with their respective fractions;

e) Amount and gross weight of pieces or packages;

f) Number e identification of containers, if applicable;

g) Proposed date for shipping and import or export. Place of origin, shipping points, stopovers, ports of entry and destination; and

h) Transport means and identification of carrier.

Article 9.- The Competent Administrative Authorities may deny authorization or permit, or suspend the operation whenever they have well grounded reasons to believe that the substances may be used in the illicit production, manufacture, extraction or preparation of narcotic drugs and psychotropic substances.

Article 10.- International transport of controlled chemical substances within the Andean Community may only be performed using the methods and under the terms set forth by the competent authorities on transport matters, pursuant to the provisions of Article 28 of Decision 477 on Customs Traffic.

CHAPTER V

ADMINISTRATIVE MEASURES FOR REGISTRATION AND INFORMATION

Article 11.- For the purposes hereof, notwithstanding the provisions of domestic legislation, the Competent Administrative Authorities shall keep a record of individuals or legal entities authorized to import or export controlled chemical substances, including the consignees, as well as authorizations granted, rejected or revoked. The Competent Administrative Authorities must keep the confidentiality of any information classified as industrial, business, trade or professional secret.

Article 12.- The records must include the following information about the importer or exporter; and when applicable, about the consignee:

a) Name and address, telephone, telex and fax number and/or electronic mail address;

b) License or registration type and number, including issue and expiry dates; and,

c) The main industrial activity and the chemical substances listed in Annex I used in the industrial process.

Importers and exporters must report to the Competent Administrative Authorities any changes in the information supplied, within thirty (30) calendar days following the date when the change takes place.

Taking into consideration the recommendations made by the Technical Subcommittee on Chemical Substances, the Member Countries shall centralize the information included in the aforementioned records, on the Andean Community General Secretariat's web site. The General Secretariat shall set forth the most adequate security procedures for such information, as well as the most suitable mechanisms to facilitate information inquiries by the competent national entities.

The information must be forwarded to the General Secretariat at least once a year, preferably during the month of February.

Article 13.- Anyone importing or exporting controlled chemical substances must keep and maintain records for a period of no less than two (2) years. Such records must be complete, accurate and up to date, concerning each operation associated with those substances, including the following information:

a) Amounts imported and exported, with specific details on:

- Transaction date;
- Name, address, telephone, fax, electronic mail, and license or registration number for each and every one of the parties involved in the operation and the ultimate consignee, if other than one of the parties involved in the operation;
- Name, NANDINA subheading, amount, unit of measurement, form of presentation and type of package containing the chemical substance; and
- Transportation means and carrier identification.

b) Amounts sold internally;

c) Quantity in stock; and

d) Quantities lost or destroyed and drops caused by shrinkage or other causes such as accidents and theft. The competent authorities must be informed of any losses or unusual or significant amounts missing with respect to chemical substances under their control. Once the information is confirmed, the competent authorities must notify the authorities of the country of origin, destination or transit, as soon as possible, providing them with as much detail as may be available.

Article 14.- Importers and exporters shall keep individual files containing records for each authorized transaction and a record of stock balances of the chemical substances included in the respective permit, for a period equal to that indicated in the preceding article.

Article 15.- The Competent Administrative Authorities may propose to the General Secretariat, the inclusion or exclusion of controlled chemical substances in Annex I of this Regulation. To this effect, they shall forward a request to the General Secretariat using the Technical Sheet found in Annex III hereof, including the reasons supporting their proposal.

Article 16.- The following is the procedure to be used for inclusion or exclusion of controlled chemical substances:

a) The request submitted by the interested Member Country shall be forwarded to the rest of the Member Countries through the General Secretariat;

b) The General Secretariat shall forward the request to the national representatives of the rest of Member Countries accredited to the Chemical Substances Subcommittee, within five (5) business days from the receipt of the said request;

c) The members of the Chemical Substances Subcommittee shall issue a response to the request within a term of no greater than thirty (30) business days counted as from the date of the notice forwarded by the General Secretariat, unless a Member Country asks for a term extension;

d) The extension referred to in paragraph c) above shall be granted only once and shall be authorized for a maximum term of fifteen (15) business days; and

e) The General Secretariat shall issue a Resolution incorporating or excluding the substance into or from Annex I hereof, provided the consensus of the Member Countries is obtained; otherwise, Annex I shall not be modified.

CHAPTER VI
INTERNATIONAL SURVEILLANCE AND COOPERATION

Article 17.- The Member Country from which territory any of the substances listed in Annex I hereof is exported, prior to the export being carried out and through its competent authorities, shall give prior notice of such export to the competent authority of the importing Member Country, using the form prepared by the International Narcotics Control Board (INCB).

Article 18.- Once the prior notice is given, the importing Member Country must acknowledge receipt thereof and within fifteen (15) business days, it must respond to the competent authority of the exporting Member Country stating conformity or otherwise with respect to the transaction. If the exporting Member Country has not received a response from the competent authority of the importing Member Country within the aforementioned term, it shall mean that the transaction has been accepted.

The Member Countries agree to timely give each other every details concerning the follow up on the information supplied and to cooperate to provide each other with all the information relative to any presumed illicit operations.

Article 19.- The imports shall be suspended whenever, in the opinion of the importing Member Country, there are reasonable signs to assume that the controlled chemical substances may be subject of diversion for the illicit manufacture of narcotic drugs or of psychotropic substances, or whenever the exporting Member Country requests it.

The Member Countries shall cooperate to afford each other any and all information relative to the presumed illicit operations.

Article 20.- A Member Country receiving the information subject matter hereof, must maintain confidentiality with regard to any information classified as industrial, business, trade or professional secret, as well as any other additional details, in accordance with its internal regulations and international commitments in place.

Article 21.- Any individuals and legal entities importing, exporting, trading or transporting controlled chemical substances, must immediately report to the Competent Administrative Authorities the transactions or proposed transactions they are involved in, whenever there are reasonable signs to believe that such substances could be used in the illicit production, manufacture, extraction or preparation of narcotic drugs, psychotropic or other substances with similar effects.

Among other cases, reasonable signs shall be considered to exist whenever the traded amount of the chemical substances contained in Annex I, the form of payment, or the characteristics of the buyer, are extraordinary, unusual or do not correspond to the company’s business or industrial endeavor.

Article 22.- Whenever an inspection is to be made during the transport **of** controlled chemical substances in an international customs traffic operation, as well as whenever a fault, infraction or a crime occurs during such traffic, the procedures established in Decision 477 concerning International Customs Traffic shall be followed.

Article 23.- The Member Countries shall endeavor to adopt measures for cooperation with any private sector entities undertaking activities related to the scope of application of this Regulation, particularly with regard to the supply of information and records to the competent authorities, prior notification procedures and timely information with regard to suspicious and unusual operations.

All information supplied shall be treated confidentially and shall not be disclosed, except in the case of a court order.

CHAPTER VII
MARKING AND LABELING

Article 24.- In order to enhance surveillance over international trade between Member Countries, each shipment of controlled chemical substances must bear the “Standard Andean Label” in a visible place on the original packages, including details of their designation as “controlled chemical substances”. The operators shall make sure that the Standard Andean Label is placed before shipping.

The aforementioned label shall be designed by the Technical Subcommittee for Chemical Substances Control, in accordance with technological progress and based on the enclosed model found in Annex IV of this Regulation, with the following features:

a) It must be easily visible and legible;

b) It must be capable of remaining on the wind and weather without its information being notably deteriorated;

c) It must be placed on the surface of the piece, package or container; and

d) It must allow for the marking of information identifying the exporter or the consignee, or both.

CHAPTER VIII
ADMINISTRATIVE DEFAULT

Article 25.- Notwithstanding the provisions of the Cartagena Agreement and of the Treaty for the Creation of the Andean Community Court of Justice, non-compliance with the following provisions of this Regulation shall be considered faults or violations subject to administrative sanctions applied in accordance with the internal legislation of each Member Country:

a) Individuals or legal entities not obtaining, updating or renewing registration;

b) Individuals or legal entities not requesting import or export authorization within the required time;

c) The information contained in the special records is not updated, or it is not accurate; and

d) Transactions are carried out with companies which have not been duly registered.

CHAPTER IX
TECHNICAL SUBCOMMITTEE FOR CHEMICAL SUBSTANCES

Article 26.- The Technical Subcommittee for Chemical Substances is the body responsible for issuing non-binding technical opinions on matters related to controlled chemical substances. Its set up and organization shall be determined by the Executive Committee of the Andean Cooperation Plan for Fighting Against Illegal Drugs and Associated Crimes, and it shall be responsible for the following duties:

a) Adopt a mechanism for permanent evaluation and follow up on compliance with the provisions contained herein, in order to propose the adjustments required in view of the constant changes occurring in the diversion methods used, in such a way that the effectiveness hereof is not lost;

b) Conduct periodic specialized studies to provide advice to national administrative authorities and the General Secretariat, to identify any trends and methods observed in the Andean Region in matters pertaining to:

i. Production, manufacture, preparation, transformation, storage, import, export, customs traffic, trade and transport of controlled chemical substances;

ii. Final disposal of controlled chemical substances, taking into account environmental protection measures, whenever such disposal implies the technical destruction of the seized substances;

iii. Transfer of controlled chemical substances, including the permanent re-export of the seized substances;

iv. Domestic and international diversion of controlled chemical substances for illicit purposes;

v. Determination of acceptable levels of variation in the weight or measurement of the imported controlled chemical substances, produced during the period involving their transport and storage, in order to recommend the competent national authorities on the adoption of corrective action and investigation of any diversion of partial quantities of the said substances;

vi. Introduction of new substances into the illicit production chain, as well as trends on illicit drug production; and

c) Prepare the essential technical studies that will make it possible to determine the control of the mixtures, concentrations and dilutions.

The Technical Subcommittee for Chemical Substances shall keep permanent contact to study the problem relating to the identification, investigation and verification of the existence of crimes, so as to recommend the most appropriate course of action.

Article 27.- This Regulation shall come into force as from the date of its publication in the Official Gazette of the Cartagena Agreement.

FINAL PROVISIONS

FIRST.- For the purpose of compliance with the provisions hereof, a close work relationship must be established between the Competent Administrative Authorities and the Andean Committee on Customs Affairs, and with the Committee Against Fraud.

At the national level, each Member Country must design and implement an inter-institutional coordination mechanism.

TWO.- The Member Countries must adapt their national laws so as to define as a crime, any activity associated with the diversion of chemical substances likely to be used in the production of illicit drugs.

THREE.- To resolve on the qualification, registration, filing and granting of licenses, authorizations or similar permits, the Member Countries shall establish minimum requirements such as: verification of criminal record and police record with regard to illicit drug traffic and associated crimes of the shareholders and/or legal representatives, and a physical and legal verification of the existence of the company. Such circumstances may also be taken into account for revoking or suspending any permits and authorizations granted, all of the above in accordance with their internal legal system.

TEMPORARY PROVISIONS

ONE.- The Technical Subcommittee for Chemical Substances shall propose to the Executive Committee of the Andean Cooperation Plan for Fighting Against Illegal Drugs and Associated Crimes, the model and contents of the Standard Andean Label referred to in Article 25 hereof. Once the Standard Andean Label has been approved by the Executive Committee, it shall be forwarded to the General Secretariat for publication by way of Resolution.

TWO.- The Member Countries hereby agree to report to the General Secretariat, through their respective Ministries of Foreign Affairs, any changes to the list of

Competent Organizations mentioned in Annex V hereof, within a term of no more than thirty (30) calendar days counted as from the date when such modification is decided at the national level. Within the following five (5) business days, the General Secretariat shall notify the Member Countries of the corresponding modifications.

Given in the City of Cusco, Peru, on December 6, 2004.

ANNEX I

Basic Common List of the chemical substances that are subject to additional specific control measures within the Andean Community territory

NANDINA	CAS NUMBER[1]	GENERIC NAME	CHEMICAL NAME	
2914.11.00	67-64-1	Acetone	Dimethyil ketone / 2-propanone	*
2806.10.00	7647-01-0	Hydrochloric Acid	Muriatic Acid	*
2807.00.10	7664-93-9	Sulfuric Acid	Sulfuric Acid	*
2814.10.00	7664-41-7	Anhydrous Ammonia	Anhydrous Ammonia	
2814.20.00	1336-21-6	Aqueous Ammonia	Ammonium Hydroxide	
2915.24.00	108-24-7	Acetic Anhydride	Acetic Anhydride	*
2836.20.00	497-19-8	Sodium Carbonate	Sodium Carbonate	
2909.11.00	60-29-7	Ethyl Ether	Diethyl Oxide	*
2914.12.00	78-93-3	Ethyl Methyl Ketone	Butanone	*
2841.61.00	7722-64-7	Potasium Permanganate	Potasium Permanganate	*
2707.20.00	108-88-3	Toluene (with no defined chemical structure)	Toluene	*
2902.30.00		Toluene (HC derivative, with defined chemical structure)	Toluene	

***** Substances found in Tables I and II of the 1988 United Nations Convention Against the Illicit Traffic in Narcotic Drugs and Psychotropic Substances, which are included by the Andean Community in Annex I due to their importance in the region in matters relating to industrial development, and particularly with regard to their diversion for use in the illicit production of natural origin drugs.

[1] Chemical Abstract Substance.

ANNEX II

Tables I and II
of the 1988 United Nations Convention Against
Illicit Traffic in Narcotic Drugs and Psychotropic Substances

TABLE I	**S.A.**	**CAS**		**TABLE II**	**S.A.**	**CAS**
N-acetyilanthranylic acid	2924.29	89-52-1		Acetone	2914.11	67-64-1
Lysergic acid	2939.63	82-58-6		Anthranilic acid	2922.43	118-92-3
Acetic anhydride	2915.24	108-24-7		Hydrochloric acid	2806.10	118-92-3
Ephedrine	2939.41	299-42-3		Phenylacetic acid	2916.34	103-82-2
Ergometrine	2939.61	60-79-7		Sulfuric acid	2807.00	7664-93-9
Ergotamine	2939.62	113-15-5		Ethyl ether	2909.11	60-29-7
1-phenyl-2-propanone	2914.31	103-79-7		Ethyl methyl ketone	2914.12	78-93-3
Isosafrole	2932.91	2932.91		Piperidine	2933.32	110-89-4
3,4-methylene dioxyphenyl-2-propanone	2932.99	2932.92		Toluene	2902.30	108-88-3
Potasium Permanganate	2841.61	2841.61				
Piperonal	2932.93	2932.93				
Safrole	2932.94	2932.94				
Seudoephedrine	2939.42	2939.42				

ANNEX III

Technical Sheet

1. Name or corporate name of the institution

2. Justification

— Legal framework applied

— Type of companies or industries in which such diversion has been confirmed

— Reports submitted by at least two laboratories on the product's chemical analysis.

— Statistics supporting product diversion.

3. Date of shipment and date of receipt of the request at the General Secretariat.

4. Signature of person responsible at the competent national authority.

ANNEX IV

Standard Andean Label Model

General provisions

General format

Color

Symbols

Ecuador proposes the following suggested model label:

ANDEAN COMMUNITY
CONTROLLED SUBSTANCE
SUBSTANCE NAME
SHIPPING COUNTRY / ORIGIN / EXPORTER
DESTINATION COUNTRY / IMPORTER

ANNEX V

Competent Organizations

Bolivia

Dirección General de Sustancias Controladas
(General Bureau on Controlled Substances)
Viceministerio de Defensa Social
(Office of the Vice-Minister of Social Defense)
Ministry of Government

Colombia

Dirección Nacional de Estupefacientes
(National Narcotic Drugs Bureau), entity attached to the Ministry of the Interior and Justice
Fondo Nacional de Estupefacientes del Ministerio de la Protección Social
(National Narcotic Drugs Fund), entity forming part of the Ministry of Social

Protection
Dirección de Impuestos y Aduanas Nacionales (DIAN)
(National Tax and Customs Bureau)

Ecuador

Dirección Técnica Nacional de Control y Fiscalización
(National Control and Monitoring Technical Bureau)
CONSEP

Peru

Dirección de Insumos Químicos y Productos Fiscalizados
(Controlled Chemical Inputs and Products Bureau)
Ministry of Production

Bolivarian Republic of Venezuela

Dirección de Control y Fiscalización de Sustancias Químicas
(Chemical Substances Control and Monitoring Bureau)
CONACUID

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US DEPARTMENT OF STATE, BUREAU FOR INTERNATIONAL NARCOTICS AND LAW ENFORCEMENT AFFAIRS, *MEMORANDUM OF JUSTIFICATION CONCERNING THE SECRETARY OF STATE'S 2005 CERTIFICATION OF CONDITIONS RELATED TO THE AERIAL ERADICATION OF ILLICIT COCA IN COLOMBIA*, WASHINGTON D.C., 2005

(Available at: http://www.state.gov/p/inl/rls/rpt/aeicc/52411.htm (last visited 8 March 2010) pp. 1, 2)

U.S. DEPARTMENT OF STATE
DIPLOMACY IN ACTION

Information Package on the Certification of the Aerial Eradication of Illicit Coca and Opium Poppy in Colombia

Other Releases
BUREAU FOR INTERNATIONAL NARCOTICS AND LAW ENFORCEMENT AFFAIRS
Washington, DC
April 22, 2005

Memorandum of Justification Concerning the Secretary of State?s 2005 Certification of Conditions Related to the Aerial Eradication of Illicit Coca and Opium Poppy in Colombia

The Andean Counterdrug Initiative sectionof the Foreign Operations, Export Financing and Related Programs Appropriations Act, 2005 (Division D, P.L. 108-447) lays out conditions under which assistance using funds appropriated under the heading Andean Counterdrug Initiative may be made available for the procurement of chemicals for use in aerial eradication of illicit crops. In particular, the legislation provides:

> "That not more than 20 percent of the funds appropriated by this Act that are used for the procurement of chemicals for aerial coca and poppy fumigation programs may be made available for such programs unless the Secretary of State certifies to the Committees on Appropriations that: (1) the herbicide mixture is being used in accordance with EPA label requirements for comparable use in the United States and with Colombian laws; and (2) the herbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment: *Provided further,* That such funds may not be made available unless the Secretary of State certifies to the Committees on Appropriations that complaints of harm to health or licit crops caused by such fumigation are evaluated and fair compensation is being paid for meritorious claims: *Provided further,* That such funds may not be made available for such purposes unless programs are being implemented by the United States Agency for International Development, the Government of Colombia, or other organizations, in consultation with local communities, to provide alternative sources of income in areas where security permits for small-acreage growers whose illicit crops are targeted for fumigation?."

This memorandum provides justification for the Secretary of State?s determination and certification to Congress that the above conditions have been met as required. In 2002, 2003, and 2004, the Secretary of State determined and certified to Congress on similar conditions concerning human health and environmental safety issues related to the Colombia spray program. These certifications were based on, among other information: all available scientific data on glyphosate, the herbicide used by the program; toxicological tests of the spray mixture (water, glyphosate, and a surfactant); active field verifications and complaint investigations; comprehensive human health monitoring; and thorough verbal and written consultations on the spray program with USDA and EPA. Because the Colombia aerial eradication program has not made any changes in the chemical formulation or application methods used for eradication of coca and opium poppy since the Secretary of State last certified to Congress on the Colombia spray program (November 29, 2004), these prior certifications serve as the foundation for the 2005 certification. These certifications and attachments can be found on the Internet at the following address: **http://www.state.gov/p/inl/rls/rpt/aeicc/**.

1. The herbicide mixture is being used in accordance with EPA label requirements for comparable use in the United States and with Colombian laws.

EPA told the Department of State in previous consultations that application rates for both coca and poppy eradication in Colombia are within the parameters listed on labels of glyphosate products registered by EPA for use in the United States. Since neither the application rates used by the Colombia eradication program nor the EPA-registered label recommendations have changed since 2004, the Secretary can certify to Congress that the herbicide mixture continues to be used in accordance with EPA label requirements for comparable use in the United States.

With respect to accordance with Colombian laws, the Colombian Minister of the Environment, Housing, and Territorial Development determined in July 2004 that the illicit crop eradication program is being conducted in compliance with the Environmental Management Plan for aerial eradication (EMP). Since that determination, there have been no substantive changes in the execution of the illicit crop eradication or the EMP.

The spray program?s compliance with other Colombian laws governing aerial eradication was reconfirmed by the October 19, 2004 final resolution of a class action suit filed in 2002 against the aerial eradication program on environmental and human health grounds. The Colombian Administrative Tribunal, Colombia?s highest administrative court, upheld the Government of Colombia?s appeal of a 2003 lower court?s ruling to halt aerial eradication.

The Colombian Administrative Tribunal ruling (an English language translation of which is included as Attachment 1) concluded that:

> It cannot be accurately inferred from the evidence outlined that glyphosate causes irreversible damage to the environment when it is used for eradicating illicit crops; on the other hand, a number of facts lead to the conclusion that sprayed areas regenerate in a relatively short period of time and that many hectares of forest are destroyed when trees are felled by growers of illicit crops. (p. 10)

Accordingly, the Administrative Tribunal reversed a lower court?s finding, and ordered that the Ministry of the Environment, Housing and Regional Development, Ministry of Social Protection, and National Directorate of Dangerous Drugs continue their oversight of the spray program. This finding represents a decisive legal endorsement of the methods used for spraying illicit crops in Colombia and of the integrity of existing environmental oversight mechanisms.

2. The herbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment

The Secretary of State determined and certified in 2002, 2003, and 2004 that the herbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment. After previous consultations with EPA, the Department and the Government of Colombia have incorporated all EPA recommendations to strengthen spray program controls and ensure increased protection against adverse effects to humans and the environment. The Department of State is not aware of any new evidence of risks or adverse effects to humans or the environment that have surfaced since the 2004 certification. Included below is a brief review of the conditions that allow the Secretary to recertify to Congress in 2005 that the herbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment.

In the 2004 EPA report, EPA offered the following assessment of human health concerns related to the spraying of coca and opium poppy in Colombia: "Despite an aggressive search for cases, there does not appear to be any evidence that glyphosate aerial spraying has resulted in any adverse health effects among the population where this spraying takes place." EPA also concluded, "that an aggressive program to identify glyphosate poisoning has been implemented in the areas of Colombia where illicit crop eradication spraying programs are prevalent." A significant number of health care providers have received training and additional training is under way or planned.

As recognized in the 2003 report, the eradication program lowered its potential risks to wildlife and has responded appropriately to minimize off target drift. However, in the 2004 report the Agency stated, "Spray drift and potential side effect down wind of the target sites are common, universal factors in most if not all pesticide applications from aerial or ground applications for all uses." In 2003, EPA recognized that the Department of State was employing "Best Management Practices to minimize drift." The Department of State continues to follow these Best Management Practices and is ever vigilant regarding the manner in which the herbicide is applied.

The Government of Colombia regularly conducts studies to assess the spray program's environmental impact through ground truth verifications to estimate spray drift and the accuracy of the spray mixture application, and during verification of all legitimate complaints about alleged spraying of crops or vegetation that are not coca or opium poppy. After one recent verification, the Government of Colombia?s Ministry of Environment, Housing, and Territorial Development characterized spray drift in the following fashion:

> The drift effects that were observed in areas visited on a random basis were temporary in nature and small in extent, and basically consisted of partial defoliation of the canopy of very high trees. No complementary collateral damage from spraying activities was observed at the sites selected and verified. In sprayed areas that were subsequently abandoned, it was noted that vegetation was starting to grow again, the predominant types being grasses and a number of herbaceous species (Attachment 2)

The Department of State believes that the program?s rigid controls and operational guidelines have decreased the likelihood of adverse impacts of the eradication program on humans and the environment and that theherbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment.

This conclusion was recently confirmed by an objective, independent scientific study that evaluated the Colombia illicit crop eradication program and its potential human health and environmental considerations. The Inter-American Drug Abuse Control Commission (CICAD) section of the **Organization of American States (OAS)** commissioned a two-year risk assessment of human health and environmental effects related to aerial eradication of illicit crops in Colombia. The final report to CICAD is enclosed as Attachment 3 and can also be found at the following Internet Address: **http://www.cicad.oas.org/en/glifosateFinalReport.pdf**. This study examined not just the possible human health and environmental effects of glyphosate, but the specific manner in which glyphosate is applied in Colombia to eradicate illicit crops, and reached the following conclusion: "(b)ased on all evidence and information presented above, the Panel concluded that the risk to humans and human health from the use of glyphosate and Cosmo-flux in the eradication of coca and poppy were minimal." (Conclusions, 6.1, p. 90). Similarly, with respect to potential risks to the Colombian environment, the panel concluded that "the risks to the environment from the use of glyphosate and Cosmo-Flux in the eradication of coca and poppy in Colombia were small in most circumstances." (Conclusions, 6.2, p. 90).

3. Complaints of harm to health or licit crops caused by such fumigation are investigated, and fair compensation is being paid for meritorious claims

The Government of Colombia continues to compensate all meritorious claims fairly. On October 4, 2001, the GOC formally instituted a new process to compensate growers for legal crops sprayed in error. From that date through the end of March 2005, the Colombian National Police?s Antinarcotics Directorate (DIRAN), the Government of Colombia agency responsible for complaint investigations, has received 5,270 such complaints.

Since the Secretary?s 2004 spray certification to Congress, the DIRAN complaint investigations unit and other GOC entities that participate in complaint investigations have made substantial progress in eliminating the existing backlog of cases to be investigated and resolved. In October 2004, 1,063 cases were still under investigation. By the end of March 2005, 208 new cases had been received, 925 cases were under investigation, and 346 investigations had been completed. To date, of the 5,270 cases received, 4,345 investigations have been completed. During 2004, only four complaints were found to be valid and compensation payments were made, for a total of $3,846. The spray program has compensated a total of 12 cases, amounting to almost $30,000 in compensation.

The 925 outstanding complaints are currently being processed and verified by an interagency group including the DIRAN, agronomists from the Colombian Institute of Agriculture and Husbandry (ICA), the Ministry of Environment, and the Office of Dangerous Drugs (DNE). Flight database and on-site investigations continue, and compensation is being paid for all cases with merit after analysis of all considerations. Typically, compensation hinges on very basic issues, such as whether planes sprayed in the vicinity of the complainant?s property within a five-day window of the alleged date of spraying; whether the complainant owns the allegedly sprayed property; whether the legal crop sprayed was intermixed with illegal crops; and whether the affected crop suffered damage from the spray mixture, as opposed to fungus, insects, or other causes. If the spray pilots have erred and accidentally sprayed licit crops, compensation is paid to the farmer for the loss of the crop, based on current market value of the crop.

Field verification is extremely dangerous and resource intensive; and it is an unavoidably methodical process. Because of the high risks involved for all personnel who conduct site visits, the primacy of security will dictate the pace of investigations in the future. Although logistical considerations (security concerns, personnel availability, and helicopter resources) are part of the reason why complaints cannot be resolved in the field more quickly, the greatest

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US Department of State, Bureau for International Narcotics and Law Enforcement Affairs, *Memorandum of Justification Concerning the Secretary of State's 2006 Certification of Conditions Related to the Aerial Eradication of Illicit Coca in Colombia*, Washington D.C., 2006

(Available at: http://www.state.gov/p/inl/rls/rpt/aeicc/70974.htm (last visited 8 March 2010) pp. 1, 2)

U.S. DEPARTMENT OF STATE
DIPLOMACY IN ACTION

Information Package on the Certification of the Aerial Eradication of Illicit Coca and Opium Poppy in Colombia

Other Releases
BUREAU FOR INTERNATIONAL NARCOTICS AND LAW ENFORCEMENT AFFAIRS
Washington, DC
August 22, 2006

Memorandum of Justification Concerning the Secretary of State?s 2006 Certification of Conditions Related to the Aerial Eradication of Illicit Coca and Opium Poppy in Colombia

The Andean Counterdrug Initiative sectionof the Foreign Operations, Export Financing and Related Programs Appropriations Act, 2006 (P.L. 109-102) lays out conditions under which assistance using funds appropriated under the heading Andean Counterdrug Initiative may be made available for the procurement of chemicals for use in aerial eradication of illicit crops. In particular, the legislation provides:

> "That not more than 20 percent of the funds appropriated by this Act that are used for the procurement of chemicals for aerial coca and poppy fumigation programs may be made available for such programs unless the Secretary of State certifies to the Committees on Appropriations that: (1) the herbicide is being used in accordance with EPA label requirements for comparable use in the United States and with Colombian laws; and (2) the herbicide, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment including endemic species: *Provided further,* That such funds may not be made available unless the Secretary of State certifies to the Committees on Appropriations that complaints of harm to health or licit crops caused by such fumigation are evaluated and fair compensation is being paid for meritorious claims: *Provided further,* That such funds may not be made available for such purposes unless programs are being implemented by the United States Agency for International Development, the Government of Colombia, or other organizations, in consultation with local communities, to provide alternative sources of income in areas where security permits for small-acreage growers whose illicit crops are targeted for fumigation?."

This memorandum provides justification for the Secretary of State?s determination and certification to Congress that the above conditions have been met as required. In 2002, 2003, 2004, and 2005 the Secretary of State determined and certified to Congress on similar conditions concerning human health and environmental safety issues related to the Colombia spray program. These certifications were based on, among other information: all available scientific data on glyphosate, the herbicide used by the program; toxicological tests of the spray mixture (water, glyphosate, and a surfactant); active field verifications and complaint investigations; comprehensive human health monitoring; and thorough verbal and written consultations on the spray program with USDA and EPA.

Because the Colombia aerial eradication program has not made any changes in the chemical formulation or application methods used for eradication of coca and opium poppy since the Secretary of State last certified to Congress on the Colombia spray program (July 30, 2005), these prior certifications serve as the foundation for the 2006 certification. These certifications and attachments can be found on the Internet at the following address: **http://www.state.gov /p/inl/rls/rpt/aeicc/c15752.htm**

1. The herbicide is being used in accordance with EPA label requirements for comparable use in the United States and with Colombian laws.

EPA told the Department of State in previous consultations that application rates for both coca and poppy eradication in Colombia are within the parameters listed on labels of glyphosate products registered by EPA for use in the United States. Since neither the application rates used by the Colombia eradication program nor the EPA-registered label recommendations have changed since 2004, the Secretary can certify to Congress that the herbicide mixture continues to be used in accordance with EPA label requirements for comparable use in the United States.

With respect to accordance with Colombian laws, the Colombian Minister of the Environment, Housing, and Territorial Development determined in July 2004 that the illicit crop eradication program is being conducted in compliance with the Environmental Management Plan for aerial eradication (EMP). Since that determination, there have been no substantive changes in the execution of the illicit crop eradication or the EMP.

The spray program?s compliance with other Colombian laws governing aerial eradication was reconfirmed by the October 19, 2004 final resolution of a class action suit filed in 2002 against the aerial eradication program on environmental and human health grounds. The Colombian Administrative Tribunal, Colombia?s highest administrative court, upheld the Government of Colombia?s appeal of a 2003 lower court?s ruling to halt aerial eradication.

The Colombian Administrative Tribunal ruling (an English-language translation of which is included as Attachment 1) concluded that:

> It cannot be accurately inferred from the evidence outlined that glyphosate causes irreversible damage to the environment when it is used for eradicating illicit crops; on the other hand, a number of facts lead to the conclusion that sprayed areas regenerate in a relatively short period of time and that many hectares of forest are destroyed when trees are felled by growers of illicit crops. (p. 10)

Accordingly, the Administrative Tribunal reversed a lower court?s finding and ordered that the Ministry of the Environment, Housing and Regional Development, Ministry of Social Protection, and National Directorate of Dangerous Drugs continue their oversight of the spray program. This finding represents a decisive legal endorsement of the methods used for spraying illicit crops in Colombia and of the integrity of existing environmental oversight mechanisms.

2. The herbicide, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment including endemic species.

The Secretary of State determined and certified in 2002, 2003, 2004, and 2005 that the herbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment. After previous consultations with EPA, the Department and the Government of Colombia have incorporated all EPA recommendations to strengthen spray program controls and ensure increased protection against adverse effects to humans and the environment. The Department of State is not aware of any new evidence of risks or adverse effects to humans or the environment that have surfaced since the

2005 certification. Included below is a brief review of the conditions that allow the Secretary to recertify to Congress in 2006 that the herbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment, including endemic species.

In the 2004 EPA report, EPA offered the following assessment of human health concerns related to the spraying of coca and opium poppy in Colombia: "Despite an aggressive search for cases, there does not appear to be any evidence that glyphosate aerial spraying has resulted in any adverse health effects among the population where this spraying takes place." EPA also concluded, "that an aggressive program to identify glyphosate poisoning has been implemented in the areas of Colombia where illicit crop eradication spraying programs are prevalent." A significant number of health care providers have received training and additional training is under way or planned.

As recognized in the 2003 report, the eradication program lowered its potential risks to wildlife and has responded appropriately to minimize off target drift. However, in the 2004 report the EPA stated, "Spray drift and potential side effect down wind of the target sites are common, universal factors in most if not all pesticide applications from aerial or ground applications for all uses." In 2003, EPA recognized that the Department of State was employing "Best Management Practices to minimize drift." The Department of State continues to follow these Best Management Practices and is ever vigilant regarding the manner in which the herbicide is applied.

The Government of Colombia regularly conducts studies to assess the spray program's environmental impact through ground truth verifications to estimate spray drift and the accuracy of the spray mixture application and during verification of all legitimate complaints about alleged spraying of crops or vegetation that are not coca or opium poppy. After one recent verification, the Government of Colombia?s Ministry of Environment, Housing, and Territorial Development characterized spray drift in the following fashion:

> The drift effects that were observed in areas visited on a random basis were temporary in nature and small in extent, and basically consisted of partial defoliation of the canopy of very high trees. No complementary collateral damage from spraying activities was observed at the sites selected and verified. In sprayed areas that were subsequently abandoned, it was noted that vegetation was starting to grow again, the predominant types being grasses and a number of herbaceous species (Attachment 2, p. 4)

The Department of State believes that the program?s rigid controls and operational guidelines have decreased the likelihood of adverse impacts of the eradication program on humans and the environment and that theherbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment.

This conclusion was confirmed by an objective, independent scientific study that evaluated the Colombia illicit crop eradication program and its potential human health and environmental considerations. The Inter-American Drug Abuse Control Commission (CICAD) section of the **Organization of American States (OAS** commissioned a two-year risk assessment of human health and environmental effects related to aerial eradication of illicit crops in Colombia. The final report to CICAD is enclosed as Attachment 3 and can also be found at the following Internet Address: **http://www.cicad.oas.org/en/glifosateFinalReport.pdf**

<>This study examined not just the possible human health and environmental effects of glyphosate, but the specific manner in which glyphosate is applied in Colombia to eradicate illicit crops, and reached the following conclusion: "(b)ased on all evidence and information presented above, the Panel concluded that the risk to humans and human health from the use of glyphosate and Cosmo-flux in the eradication of coca and poppy were minimal." (Conclusions, 6.1, p. 90). Similarly, with respect to potential risks to the Colombian environment, the panel concluded that "the risks to the environment from the use of glyphosate and Cosmo-Flux in the eradication of coca and poppy in Colombia were small in most circumstances." (Conclusions, 6.2, p. 90).

This study also concluded that the "Risks of direct effects in terrestrial wildlife such as mammals and birds were judged to be negligible as were those to beneficial insects such as bees." (Conclusions, 6.2, p. 90). This is a far-reaching and important judgment which addresses the risk from the spray program faced by all terrestrial fauna potentially exposed to the spray: not only those species endemic to Colombia, but any introduced species present as well.

This does not mean that the spraying of glyphosate poses zero risk. The study goes on to state that "Moderate risks to some aquatic wildlife may exist in some locations where shallow and static water bodies are located in close proximity to coca fields and are accidentally over-sprayed. However, when taken in the context of the environmental risks from other activities associated with the production of coca and poppy, in particular, the uncontrolled and unplanned clearing of pristine lands in ecologically important areas for the purposes of planting the crop, the added risks associated with the spray program are small." (Conclusions, 6.2, p. 91).

Despite the limited risk represented by the spray program, the Department of State, in consultation with Congress, is supporting further CICAD research to better understand the level of risk that could be posed to Colombia?s aquatic amphibians as a result of potential overspray of amphibian habitat. Preliminary results of this continued study confirm that the glyphosate mixture as used in Colombia has low toxicity for aquatic amphibians. The Department will submit to Congress a separate report on this work when the study has been completed.

These studies, as well as third-party research on glyphosate, warrant a certification by the Secretary of State that the spray program does not pose unreasonable risks or adverse affects to Colombia?s endemic species.

3. Claims of harm to health or licit crops caused by such fumigation are investigated, and fair compensation is being paid for meritorious claims

The Government of Colombia continues to compensate all meritorious claims fairly. On October 4, 2001, the Government of Colombia formally instituted a new process to compensate growers for legal crops sprayed in error. From that date through the end of March 2006, the Colombian National Police?s Antinarcotics Directorate (DIRAN), the Government of Colombia agency responsible for complaint investigations, has received 5,974 such claims. Of these, 5,511 investigations were completed as of March 31, 2006.

Claims are processed and verified by an interagency group including the DIRAN, agronomists from the Colombian Institute of Agriculture and Husbandry (ICA), the Ministry of Environment, and the Office of Dangerous Drugs (DNE). In 2005, 12 claims were found to be valid and $123,000 was paid as compensation. To date, the spray program has paid $160,000 compensation in 28 cases.

The 462 outstanding claims are being processed and verified by the interagency claims investigations group. Flight database and on-site investigations continue, and compensation is being paid for all cases with merit after analysis of all considerations. Typically, compensation hinges on basic issues, such as whether planes sprayed in the vicinity of the claimant's property within a five-day window of the alleged date of spraying; whether the claimant owns the allegedly sprayed property; whether the legal crop sprayed was intermixed with illegal crops; and whether the affected crop suffered damage from the spray mixture, as opposed to fungus, insects, or other causes. If the spray pilots have erred and accidentally sprayed licit crops, compensation is paid for the loss of the crop, based on current market value of the crop.

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PRESS ITEM: "DEFENCE MINISTER WELCOMES THE NEW SUPER TUCANO AIRPLANES OF THE AIR FORCE", 14 DECEMBER 2006

(Web page of the Colombian Ministry of National Defence, *Mindefensa da la bienvenida a los nuevos aviones Super Tucano de la FAC,* available at: http://alpha.mindefensa.gov.co/index.php?page=181&id=4875&PHPSESSID=f6066769e3962dd24ba0d9aa49969c7b , (last visited 20 February 2010), pp. 1,2)

[…]

"We explained to the Ecuadorian authorities, President Uribe spoke to President Palacio, I spoke to the Minister of Defence of Ecuador, and we explained to them why we are taking that step. We cannot allow the production of coca plants to keep growing, or the proliferation of processing laboratories, or the presence of the guerrillas and the increase in violence in that zone of the country".

[…]

Annex 149

US Department of State, Bureau for International Narcotics and Law Enforcement Affairs, *Memorandum of Justification Concerning the Secretary of State's 2007 Certification of Conditions Related to the Aerial Eradication of Illicit Coca in Colombia*, Washington D.C., 2007

(Available at: http://www.state.gov/p/inl/rls/rpt/aeicc/111210.htm (last visited 8 March 2010), p. 2)

U.S. DEPARTMENT OF STATE
DIPLOMACY IN ACTION

Memorandum of Justification Concerning the Secretary of State's 2007 Certification of Conditions Related to the Aerial Eradication of Illicit Coca in Colombia

August 10, 2007

Bureau for International Narcotics and Law Enforcement Affairs
Washington, DC
August 10, 2007

The Andean Counterdrug Initiative sectionof the Foreign Operations, Export Financing and Related Programs Appropriations Act, 2006 (P.L. 109-102) lays out conditions under which assistance using funds appropriated under the heading Andean Counterdrug Initiative may be made available for the procurement of chemicals for use in aerial eradication of illicit crops. FY 2006 conditions also apply for FY 2007 under the Revised Continuing Appropriations Resolution, 2007 (P.L. 110-5)(CR). In particular, the legislation provides:

> "That not more than 20 percent of the funds appropriated by this Act that are used for the procurement of chemicals for aerial coca and poppy fumigation programs may be made available for such programs unless the Secretary of State certifies to the Committees on Appropriations that: (1) the herbicide mixture is being used in accordance with EPA label requirements for comparable use in the United States and with Colombian laws; and (2) the herbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment including endemic species: *Provided further,* That such funds may not be made available unless the Secretary of State certifies to the Committees on Appropriations that complaints of harm to health or licit crops caused by such fumigation are evaluated and fair compensation is being paid for meritorious claims."

This memorandum provides justification for the Secretary of State's determination and certification to Congress that the above conditions have been met as required as well as a further condition imposed by the legislation: "that such funds may not be made available for such purposes unless programs are being implemented by the United States Agency for International Development, the Government of Colombia, or other organizations, in consultation with local communities, to provide alternative sources of income in areas where conditions exist for successful alternative development and where security permits for growers and communities whose illicit crops are targeted for fumigation. In 2002, 2003, 2004, and 2005 the Secretary of State determined and certified to Congress similar conditions concerning human health and environmental safety issues related to the Colombia spray program. In 2006, the Secretary of State determined and certified to Congress identical conditions concerning human health and environmental safety issues, including endemic species. These certifications were based on, among other information: all available scientific data on glyphosate, the herbicide used by the program; toxicological tests of the spray mixture (water, glyphosate, and a surfactant) as well as comparative soil and water samples before and after spray; active field verifications and complaint investigations; comprehensive human health monitoring; and thorough verbal and written consultations on the spray program with USDA and EPA. Because the Colombia aerial eradication program has not made any changes in the chemical formulation or application methods used for eradication of coca since the Secretary of State last provided certification to Congress on the Colombia spray program on August22, 2006, these prior certifications serve as the foundation for the 2007 certification. The only change since previous certifications is that there has been no aerial eradication of illicit poppy crops since August 2006, and there are no current plans to restart aerial eradication of poppy in the coming year. These certifications and attachments can be found on the Internet at the following address: **http://www.state.gov/p/inl/rls/rpt/aeicc/**.

1. The herbicide mixture is being used in accordance with EPA label requirements for comparable use in the United States and with Colombian laws.

EPA informed the Department of State in previous consultations that application rates for coca eradication in Colombia are within the parameters listed on labels of glyphosate products registered by EPA for use in the United States. Since neither the application rates used by the Colombia eradication program nor the EPA-registered label recommendations have changed since 2004, the Secretary certifies to Congress that the herbicide mixture continues to be used in accordance with EPA label requirements for comparable use in the United States.

With respect to Colombian laws, the Colombian Minister of the Environment, Housing, and Territorial Development determined in July 2004 that the illicit crop eradication program is being conducted in compliance with the Environmental Management Plan for aerial eradication (EMP). Since that determination, there have been no substantive changes in the execution of the illicit crop eradication or the EMP.

The spray program's compliance with other Colombian laws governing aerial eradication was reconfirmed by the October 19, 2004 final resolution of a class action suit filed in 2002 against the aerial eradication program on environmental and human health grounds. The Colombian Administrative Tribunal, Colombia's highest administrative court, upheld the Government of Colombia's appeal of a 2003 lower court's ruling to halt aerial eradication.

The Colombian Administrative Tribunal ruling (an English language translation of which is included as Attachment 1) concluded that:

> It cannot be accurately inferred from the evidence outlined that glyphosate causes irreversible damage to the environment when it is used for eradicating illicit crops; on the other hand, a number of facts lead to the conclusion that sprayed areas regenerate in a relatively short period of time and that many hectares of forest are destroyed when trees are felled by growers of illicit crops. (p. 10)

Accordingly, the Administrative Tribunal reversed a lower court's finding, and ordered that the Ministry of the Environment, Housing and Regional Development, Ministry of Social Protection, and National Directorate of Dangerous Drugs continue their oversight of the spray program.

On February 21, 2007, the State Council upheld this decision in a ruling on a class action suit filed in May 2006 against the aerial eradication program on environmental grounds. The ruling (an English translation of which is included in Attachment 2) concluded that the aforementioned case decided in 2004 was too similar to warrant a separate decision on this case. The ruling states that:

> In view of the foregoing, this Division shall declare proven the *res judicata* plea and shall reject the claims made in the suit, in view of the fact that it was

> not feasible for the plaintiffs to pursue a new action in order to revive petitions that have already been resolved. (p.5)

Both of these findings represent a decisive legal endorsement of the methods used for spraying illicit crops in Colombia and of the integrity of existing environmental oversight mechanisms.

2. The herbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment, including endemic species.

The Secretary of State determined and certified in 2002, 2003, 2004, 2005, and 2006 that the herbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment. After previous consultations with EPA, the Department of State and the Government of Colombia have incorporated all EPA recommendations to strengthen spray program controls and ensure increased protection against adverse effects to humans and the environment. The Department of State is not aware of any published scientific evidence of risks or adverse effects to humans or the environment that have surfaced since the 2006 certification. Included below is a brief review of the conditions that allow the Secretary to recertify to Congress in 2007 that the herbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment.

In the 2004 EPA report, EPA offered the following assessment of human health concerns related to the spraying of coca in Colombia: "Despite an aggressive search for cases, there does not appear to be any evidence that glyphosate aerial spraying has resulted in any adverse health effects among the population where this spraying takes place." EPA also concluded "that an aggressive program to identify glyphosate poisoning has been implemented in the areas of Colombia where illicit crop eradication spraying programs are prevalent." A significant number of health care providers have received training and additional training is under way or planned.

As recognized in the 2003 report, the eradication program lowered its potential risks to wildlife and has responded appropriately to minimize off-target drift. However, in the 2004 report the Agency stated, "Spray drift and potential side effect down wind of the target sites are common, universal factors in most if not all pesticide applications from aerial or ground applications for all uses." In 2003, EPA recognized that the Department of State was employing "Best Management Practices to minimize drift." The Department of State continues to follow these Best Management Practices and is ever vigilant regarding the manner in which the herbicide is applied.

In 2003, 2004, 2005 and 2006, the U.S. Narcotics Affairs Section (NAS) and the Colombia National Police (CNP) collected and analyzed a total of almost 80 water and 180 soil samples drawn from sprayed areas throughout Colombia in order to determine the impact of glyphosate and AMPA (Amino-Methyl Phosphonic Acid) on the environment. AMPA is a product of glyphosate degradation by natural microbial and environmental activity. In accordance with the Colombian Environmental Management Plan, these samples were taken before, immediately after, and 60 days after spray in two different fields during various aerial eradication campaigns. These studies (the results of which are included as Attachment 3) determined that glyphosate and AMPA residue did not adversely impact the soil of the sprayed coca plots. Nor did the glyphosate or AMPA residue adversely impact the water taken from streams adjacent to sprayed coca crops.

In analyzing the soil and water samples, NAS and CNP (through private laboratories) use the High Pressure Liquid Chromatography (HPLC) method of analysis for glyphosate and AMPA. The HPLC standards conform to EPA standards, and this method is widely accepted as sufficiently accurate to measure and monitor the impact of glyphosate on human health and the environment.

Soil analysis reveals a 108 day half-life for glyphosate after spray application, and a maximum persistence in the environment of 217 days. This analysis does not differentiate between the glyphosate from the aerial spray program and that commonly used by coca growers. However, total residual levels in all these analyses were not found to be of environmental concern. The maximum amount of glyphosate found was close to one part per million (1 mg of glyphosate for each kilogram of dry soil).

Analysis reveals that glyphosate residue levels in water have never approached the "Maximum Contaminant Level" (MCL) as set by the US "Safe Drinking Water Act" at 700 micrograms per litre (0.7 milligrams per litre) for glyphosate residuals.

The Government of Colombia regularly conducts studies to assess the spray program's environmental impact through ground truth verifications to estimate spray drift and the accuracy of the spray mixture application, and during verification of all legitimate complaints about alleged spraying of crops or vegetation that are not coca. After one recent verification, the Government of Colombia's Ministry of Environment, Housing, and Territorial Development characterized spray drift in the following fashion:

> The drift effects that were observed in areas visited on a random basis were temporary in nature and small in extent, and basically consisted of partial defoliation of the canopy of very high trees. No complementary collateral damage from spraying activities was observed at the sites selected and verified. In sprayed areas that were subsequently abandoned, it was noted that vegetation was starting to grow again, the predominant types being grasses and a number of herbaceous species (Attachment 4, p. 4)

The Department of State believes that the program's rigid controls and operational guidelines have decreased the likelihood of adverse impacts of the eradication program on humans and the environment and that theherbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans or the environment, including endemic species.

This conclusion was confirmed by an objective, independent scientific study that evaluated the Colombia illicit crop eradication program and its potential human health and environmental considerations. The Inter-American Drug Abuse Control Commission (CICAD) of the **Organization of American States (OAS)** commissioned a two-year risk assessment of human health and environmental effects related to aerial eradication of illicit crops in Colombia. The final report to CICAD can be found at the following internet address: **http://www.cicad.oas.org/en/glifosateFinalReport.pdf**.

In 2007, this study was peer reviewed and published in volume 190 of the scientific journal Reviews of Environmental Contamination and Toxicology.

This study examined not just the possible human health and environmental effects of glyphosate, but the specific manner in which glyphosate is applied in Colombia and the specific glyphosate mixture used to eradicate illicit crops, and reached the following conclusion: "(b)ased on all evidence and information

Annex 150

PRESS ITEM: "ECUADOR WILL SUE COLOMBIA OVER SPRAYINGS IN THE BORDER", *REVISTA CAMINOS*, 2 JULY 2007

(*Revista Caminos, Demandará Ecuador a Colombia por fumigaciones en la frontera,* available at: http://ecaminos.org/leer.php/4745, (last visited 20 February 2010))

President Correa and foreign minister Espinosa received the report of the Ecuadorian scientific commission about the effects on the Ecuadorian border of Plan Colombia's fumigations

[…]

"We have also implemented a legal way, preparing a case that Ecuador will bring against Colombia before the International Tribunal at The Hague" insisted the Minister of Foreign Affairs.

Maria Fernanda Espinosa vetted the report, after stating that the government's policy has been supplemented "by the scientific way".

[...]

President Correa reiterates that the report is basis for compensations sought by Ecuador for those affected.

[…]

Annex 151

COLOMBIAN ASSOCIATION OF AUTONOMOUS REGIONAL CORPORATIONS (ASOCARS), "SHARED RESPONSIBILITY: THE WORLD DRUG PROBLEM FROM A GREEN PERSPECTIVE", *PERIÓDICO VIRTUAL*, ISSUE N° 14, 2008

(*Asociación colombiana de Corporaciones Autónomas Regionales (ASOCARS), "Responsabilidad Compartida: El Problemas Mundial de las Drogas A Través de Una Perspectiva Verde,* Periódico Virtual, Edición No. 14, 2008. Available at: http://www.asocars.org.co/periodico/14edicion/responsabilidad/RESPONSABILIDADCOMPARTIDAAsocars_2.pdf (last visited 25 February 2010))

[Page 1]

[…]

The Silent Catastrophe

Colombia, located in the Northeast of South America, has two coasts and is the final point of the great Andes. This creates a wide range of climates in the country. Its territory has one of the highest levels of rain in the world and encompasses a land equivalent to France and Spain together.

Less than 6% of the Earth's total surface is covered by tropical jungle, and three fourths of the planet's biodiversity are to be found in this region. The tropical jungle of the Amazons, responsible for 15% of the world's oxygen, covers 40% of South America and 35% of Colombia, one of the ten nations with more primary forests in the world.

Colombia is, after Brazil, the country with more biodiversity in the planet. It holds 18% of the world's bird species and is the richest country in amphibians.

[Page 2]

Moreover, Colombia has a higher potential for water production than countries of the size of the continental United States or India.

Today there are 257 protected natural zones, a number which is likely to increase in the near future, with a total area larger that Holland, Belgium and Denmark together.

Unfortunately, cocaine production geared by consumption threatens the conservation of this environment and places unique species of fauna and flora at risk. The majority of the 78,000 hectares of coca in Colombia are located in or near the Amazon's tropical jungle.

As an aggravating factor, the Colombian Anti-Narcotics Police estimates that for each hectare of coca cultivated, three hectares of forest are cut down. Taking into account the frequency with which coca plantations are relocated to avoid detection, 200,000 hectares of Colombian tropical jungle are burned and cut down each year to grow coca. This burning process is the main cause for pollution in the Colombian jungle zones.

In total, it is estimated that over the last 20 years 2.2 million hectares of Colombian jungle have been deforested.

[…]

Annex 152

EMBASSY OF THE UNITED STATES IN BOGOTÁ, FACT SHEET 2008, "COCAINE PRODUCTION AND CULTIVATION: COLOMBIA", 6 NOVEMBER 2009, ENCLOSURE TO PRESS ITEM: "OFFICIAL U.S. COLOMBIA SURVEY SHOWS SHARP DROP IN COCA CULTIVATION AND COCAINE PRODUCTION"

(Press item is available at: http://bogota.usembassy.gov/pr_75_061109.html and fact sheet is available at: http://bogota.usembassy.gov/root/pdfs/factsheet2008cocaineproductioncultivationeng.pdf (last visited 25 February 2010))

FACT SHEET

2008 COCAINE PRODUCTION AND CULTIVATION: COLOMBIA

- According to the most recent crop estimate from the CNC, potential cocaine production in Colombia dropped fully 39 percent between 2007 and 2008.
- The potential production of pure cocaine fell from an estimated 485 metric tons in 2007 to 295 metric tons in 2008.
- Further, the area under cultivation dropped 29 percent during the same time frame.
- The coca crop declined from an estimated 167,000 ha in 2007 to only 119,000 ha in 2008.
- The current estimate provides a genuinely comparable number to the previous year, given that the "search area" for the estimate was substantially equivalent to that of the previous year.

FACTORS AFFECTING THE DECLINE

- The cumulative effect of steadfast eradication pressure delivered against the primary Colombian growing areas diminished not only the size of the coca fields, but further the ability of remaining fields to produce normal amounts of coca leaf.
- Increased government presence and the deployment of security forces in select growing regions were instrumental in preventing coca cultivation and production.
- Successful operations against drug trafficking organizations kept them under constant pressure and reduced their control over the cocaine industry.

ERADICATION FACTORS

- Combined aerial spraying and manual eradication for 2008 was 227,605 ha.

	2001	2002	2003	2004	2005	2006	2007	2008
Cultivation	**169,800**	**144,450**	**113,850**	**114,100**	**144,000**	**157,200**	**167,000**	**119,000**
Spray (Air)*	**84,251**	**122,695**	**127,112**	**131,824**	**134,474**	**164,119**	**148,435**	**129,876**
Erad (Man)	**1,745**	**2,762**	**4,220**	**6,232**	**37,540**	**42,110**	**64,979**	**95,731**

2008 COCAINE PRODUCTION AND CULTIVATION IN THE ANDES: PERU, BOLIVIA, AND COLOMBIA

- Peru and Bolivia were found to have increased their potential cocaine production for 2008, Peru by a slight 2 percent (to 215 metric tons), while Bolivian production was re-calculated due to increased efficiency converting coca leaf to cocaine, providing a surge of 50 percent increased productive potential in 2008 to 195 metric tons pure cocaine.
- All told, cocaine potential production in the three Andean nations in 2008 was no more than 705 metric tons pure, a figure last seen this low in 1997, and represents a decline from the peak year of production (2001, with an estimated potential production of 1055 metric tons pure) of fully 33 percent.
- Importantly, with the steep drop in Colombia, there has not been an appreciable upsurge of coca cultivation in either Peru or Bolivia.
- Peruvian cultivation experienced a small uptick of 14 percent (from 36,000 ha in 2007 to 41,000 ha in 2008). Even with that uptick Peruvian cultivation remained below where it stood in 2006.

- Bolivia experienced no more than an 8 percent increase in cultivation (from 29,500 ha in 2007 to 32,000 ha in 2008).
- These modest increases in cultivation were more than offset by the steep decline of 48,000 ha in Colombian cultivation.

DOMESTIC INDICATORS SHOW IMPACT ON U.S. STREETS DURING A TIME PERIOD THAT EXPERIENCED COCAINE DISRUPTION

- The most recent National Survey on Drug Use and Health data showed that 18-25 year old past-month cocaine prevalence dropped 32 percent between 2006 and 2008. Past year initiates for cocaine among persons aged 12 and older dropped 26% over the same period.
- Workplace positive rates, as measured by Quest Diagnostics, for cocaine dropped 42% percent from 0.72% in 2006 to 0.42% in 2008..
- DEA STRIDE data on cocaine price and purity show that from the first quarter of 2007 through 2nd quarter of 2009, the price per pure gram of cocaine increased 77.1%, from $99.48 to $176.14, while the purity decreased 27.4%, from 67% to 49%.
- DEA Cocaine Signature Program data on arrival-zone seized cocaine show a drop in purity of cocaine bricks arriving in the U.S. ports-of-entry, dropping from 83% to 85% purity (over the 5-year period mid-2003 to mid-2008) to 75% by mid-2009.
- Cocaine seizures along the Southwest Border dropped 37% from a quarterly average of 7,300 kilograms in the 1st quarter of 2007 to 4,600 kilograms in the 3rd quarter of 2009.

Embassy of the United States

News

Official U.S. Colombia Survey Shows Sharp Drop in Coca Cultivation and Cocaine Production

The U.S. Government has completed the 2008 annual estimate of coca cultivation and potential cocaine production for Colombia. Results showed that the area actually cultivated fell 29% in a single year, from 167,000 hectares in 2007 to 119,000 hectares in 2008. New productivity data show that in 2008 Colombia's maximum potential production dropped sharply from 485 metric tons of pure cocaine to 295 metric tons, a 39% drop. This drop in cocaine production for the second year in a row is likely a major contributor to increase in price and decrease in purity of cocaine in the U.S. – Colombia is the source of an estimated 90 percent of cocaine in the U.S.

According to analysts, the principal reasons for the decline were steadfast aerial and manual eradication pressure delivered against the primary Colombian growing areas, increased government presence and security forces in select growing regions and successful operation against drug trafficking organizations. Violence between trafficking groups and economic disruptions that affect farmers' planting decisions were also a factor. Eradication pressure, as measured by field-based scientific surveys of the impact of eradication on coca productivity, diminishes not only the size of the coca fields but the ability of remaining fields to produce normal amounts of coca leaf.

The Government of Colombia increased its focus on manual eradication efforts in all major coca growing areas last year. In all, 95,000 hectares were manually eradicated, well above the 66,000 hectares reported in 2007. In addition, high levels of aerial eradication were sustained covering more than 133,000 hectares. Very little cultivation was found outside of 2008 growing areas.

The annual estimate is produced by a scientific sampling of coca fields taken by aerial imagery to represent the known growing areas in Colombia. The survey areas were virtually unchanged from 2007 to 2008.

Bogota D.C., November 6, 2009

Fact Sheet

Annex 153

ARIAS V. DYNCORP, PLAINTIFFS' MOTION TO DISMISS THREE INDIVIDUAL PLAINTIFFS, 23 DECEMBER 2009

(United States District Court for the District of Columbia, Case No. 1:01-cv-01908-RWR-DAR, Document 171)

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

ARIAS, et al., **Plaintiffs,** **v.** **DYNCORP, et al.,** **Defendants.**	**Case No.1:01cv01908-RWR-DAR**
QUINTEROS, et al., **Plaintiffs,** **v.** **DYNCORP, et al.,** **Defendants.**	**Case No.1:07cv01042-RWR-DAR** **(Cases Consolidated for Case Management and Discovery)**

PLAINTIFFS' MOTION TO DISMISS THREE INDIVIDUAL PLAINTIFFS[1]

Plaintiffs hereby move, pursuant to Rule 41(a)(2), for an order dismissing without prejudice the claims of David Mestanza Bosquez, Victor Mestanza Bosquez, and Ercilia Veronica Mestanza Bosquez. In support of this Motion, Plaintiffs state as follows:

1. A Plaintiffs' Questionnaire was completed on behalf of David Mestanza Bosquez (Case No. 2551), a minor, in late 2008.

2. A Plaintiffs' Questionnaire was completed on behalf of Victor Mestanza Bosquez (Case No. 2552), a minor, in late 2008.

[1] The statement of points and authorities is included herein.

3. A Plaintiffs' Questionnaire was completed on behalf of Ercilia Veronica Mestanza Bosquez (Case No. 2548), a mentally impaired adult, in late 2008.

4. Each of the Plaintiffs' Questionnaires referenced above claimed exposure to chemicals sprayed from airplanes.

5. Around the time of the deposition of Edy Mestanza (Case No. 2550), which was held on November 11, 2009, Plaintiffs' counsel learned that the exposure claimed by David Mestanza Bosquez and Victor Mestanza Bosquez did not occur.[2] Following that deposition, Plaintiffs' counsel also learned that the exposure claimed by Ercilia Veronica Mestanza Bosquez did not occur.

6. After learning this information, Plaintiffs' counsel promptly contacted DynCorp and proposed that David Mestanza Bosquez and Victor Mestanza Bosquez be dismissed in a joint filing. Some time later, Plaintiffs' counsel then wrote to request the same treatment for Ercilia Veronica Mestanza Bosquez. DynCorp refused to agree to the proposed dismissals of the first two plaintiffs, and has not responded as to the third plaintiff.

7. Plaintiffs' counsel do not have first-hand knowledge of whether these inaccurate questionnaire responses were caused by technological problems that arose in processing and producing nearly 3,000 individual responses, whether the person completing each questionnaire fabricated or embellished facts, or whether some other factor was the cause. Plaintiffs' counsel are, however, conducting an investigation into these inaccuracies and will take appropriate action if the problem causing the inaccuracies in these three plaintiffs' questionnaire responses led to similar issues in other responses.

[2] Around the same time, Plaintiffs' counsel learned that Edy Mestanza's claim of personal exposure in his Plaintiffs' Questionnaire was inaccurate. Mr. Mestanza has, however, other types of valid claims (e.g., property damage claims). Plaintiffs are willing to provide an amended Plaintiffs' Questionnaire for Mr. Mestanza should the Court find it appropriate.

8. In addition, Plaintiffs' counsel can confirm that when these inaccuracies were discovered, they quickly contacted DynCorp in an attempt to dismiss these claims without Court involvement. Because DynCorp has not affirmatively agreed to dismiss the three plaintiffs at issue pursuant to a Rule 41(a)(1)(A)(ii) joint stipulation of dismissal, Plaintiffs seek an order dismissing them pursuant to Rule 41(a)(2).

9. In light of the above-described information regarding the claims of these three plaintiffs, only recently discovered by Plaintiffs' counsel, dismissal of those claims is appropriate.

WHEREFORE, Plaintiffs respectfully request that the Court dismiss without prejudice the claims of David Mestanza Bosquez, Victor Mestanza Bosquez, and Ercilia Veronica Mestanza Bosquez.

Respectfully submitted,

Dated: December 23, 2009

/s/ Terry Collingsworth

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Counsel for Plaintiffs

CERTIFICATE OF SERVICE

I hereby certify that, on this 23rd day of December 2009, a copy of the foregoing Motion and a proposed Order filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of Electronic Filing and a copy will be sent by U.S. mail to all non-registered parties.

/s/ Eric J. Hager

Eric J. Hager

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

ARIAS, ***et al.*****,** **Plaintiffs,** v. **DYNCORP,** ***et al.*****,** **Defendants.**	**Case No.1:01cv01908-RWR-DAR**
QUINTEROS, ***et al.*****,** **Plaintiffs,** v. **DYNCORP,** ***et al.*****,** **Defendants.**	**Case No.1:07cv01042-RWR-DAR** **(Cases Consolidated for Case Management and Discovery)**

[PROPOSED] ORDER

On consideration of Plaintiffs' Motion to Dismiss Three Individual Plaintiffs ("Motion"), Defendants' response thereto, any reply in support, and the entire record herein, it is, this

_________ day of ___________________, 2010, hereby:

ORDERED that the Motion is **GRANTED**; and it is

FURTHER ORDERED that the claims of David Mestanza Bosquez, Victor Mestanza Bosquez, and Ercilia Veronica Mestanza Bosquez are dismissed without prejudice.

IT IS SO ORDERED.

Honorable Richard W. Roberts
U.S. District Court Judge, District of Columbia

Annex 154

ARIAS V. DYNCORP, DEFENDANTS' RESPONSE, 6 JANUARY 2010

(United States District Court for the District of Columbia, Case No. 1:01-cv-01908-RWR-DAR, Document 172)

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA**

Venancio Aguasanta Arias, *et al.*, Plaintiffs, v. DynCorp, *et al.* Defendants.	Case Number: 1:01cv01908 (RWR-DAR)
Nestor Ermogenes Arroyo Quinteros, *et al.*, Plaintiffs, v. DynCorp, *et al.* Defendants.	Case Number: 1:07cv01042 (RWR-DAR) (Cases Consolidated for Case Management and Discovery)

DEFENDANTS' RESPONSE TO PLAINTIFFS'
<u>MOTION TO DISMISS THREE INDIVIDUAL PLAINTIFFS</u>

On December 23, 2009, the plaintiffs moved for the dismissal without prejudice of three individual plaintiffs who now concede – despite sworn Questionnaire responses providing specific details of alleged exposures to and injuries from Plan Colombia spraying – that they were *not* exposed or injured (and who, in fact, were 275 miles away from the alleged spraying events). (*See* Pls.' Mot. at 2 ¶ 5.) The evidence of these false Questionnaire responses emerged during the deposition testimony of several test plaintiffs, including Mr. Edy Mestanza, who is an immediate family member of the three individual plaintiffs whose dismissal is requested. Like the three plaintiffs addressed in the December 23 motion, Edy Mestanza also was not exposed to any spraying operations (because he too was living 275 miles away from the border), *id.* at 2, n.2, even though Edy's Questionnaire response contains similarly detailed and false representations about his alleged exposure and personal injuries. Plaintiffs do not seek the dismissal of Edy Mestanza's claims, however, asserting that the Court should still credit his allegations of *property* damages, which were separately set forth in his Questionnaire response. *Id.*

The DynCorp defendants do not object to the dismissal of the three individual plaintiffs identified in the plaintiffs' December 23, 2009 motion, although they oppose the plaintiffs' odd request that the dismissals be *without* prejudice. As plaintiffs acknowledge, the three individual plaintiffs provided false responses in their sworn Questionnaire responses and have no claims to be preserved. They accordingly should be dismissed *with prejudice*. Defendants also object to the plaintiffs' suggestion that the false Questionnaire responses might be due to "technological problems" (*id.* at 2 ¶ 7) and to the plaintiffs' apparent hope that the Court will address these false statements as isolated or technical problems. To the contrary, the depositions of the 20 test plaintiffs conducted in October and November 2009 demonstrate that the evidence of "fabricated or embellished" facts in the three subject plaintiffs' Questionnaire responses is illustrative of a widespread problem in most or all of the over 2,000 individual Plaintiffs' Questionnaire responses produced to the defendants.[1]

As the Court is aware, the individual plaintiffs were repeatedly ordered by the Court to "provide verified, factual and complete responses to the Plaintiffs' Questionnaire," Oct. 21, 2008 Order,[2] and the plaintiffs have already been sanctioned by the Court once for their failure to do

[1] Plaintiffs' Dec. 23 motion concedes the possibility that "the person completing each Questionnaire [may have] fabricated or embellished facts." Pls.' Mot. at 2 ¶ 7. Plaintiffs' counsel does not clarify whether the "persons" to whom they refer are plaintiffs or plaintiffs' counsel or their agents – either of which possibility raises serious questions about the accuracy of the Plaintiffs' Questionnaire responses and the *bona fides* of the plaintiffs' claims.

[2] *See* Oct. 21, 2008 Order ¶ 1. The plaintiffs' objections to the Oct. 21, 2008 Order were rejected by the District Judge at the Nov. 25, 2008 hearing, in the Minute Entries entered on Nov. 28, 2008 in the *Arias* and *Quinteros* dockets, and in the Court's Dec. 1, 2008 Order.

so.[3] In light of this history, plaintiffs' offer at this late date to "conduct an investigation into these inaccuracies" to now determine whether there are "similar issues in other responses" (Pls.' Mot. at 2 ¶ 7), is too little and too late. Prior to plaintiffs' present motion to dismiss, the DynCorp defendants had requested a meet-and-confer on the broader problem of false and inaccurate information in the Questionnaire responses of all of the test plaintiffs. Plaintiffs' counsel have indicated that they are not available for a meet-and-confer until January 26, 2010, and defendants accordingly are not yet in a position to fully address these concerns with the Court. However, the current motion does place at issue two problems that bear further discussion here: (1) the misrepresentation by all eight Mestanza family plaintiffs (four of whom are test plaintiffs) that they live on the border with Ecuador when in fact the principal residence of the Mestanza family has been in Guayaquil, Ecuador (275 miles from the border) for over 20 years, and (2) the testimony from numerous test plaintiffs that other family members for whom Questionnaire responses had been submitted were not plaintiffs and – with respect to their minor children – that they had not authorized their children to be designated as plaintiffs in this litigation.

I. <u>The Mestanza Family's Misrepresentations</u>

There are eight members of the Mestanza family who are individual plaintiffs in this litigation. Four are "test plaintiffs" and four are not.[4] All eight Mestanza family members

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[3] *See* Oct. 21, 2008 order and its subsequent approval as cited in n.2 *supra*. *See also* the Minute Orders entered on May 5, 2009 (sanctioning plaintiffs for violations of the Oct. 21, 2008 order). The District Judge rejected plaintiffs' objections to the May 5, 2009 sanctions order at the July 17, 2009 hearing and in the Minute Orders entered on July 22, 2009.

[4] The four Mestanza family members who are "test plaintiffs" (and their relationships with one another) are:

1. Victor Mestanza (59-year-old husband of Ercilia Bosquez, father of Edy, grandfather of Jennifer);

2. Ercilia Bosquez (57-year-old wife of Victor, mother of Edy, grandmother of Jennifer);

represented in their sworn responses to the Plaintiffs' Questionnaire that their "present home address" was "Puerto Mestanza," which is a small settlement near the border between Ecuador and Colombia in the Sucumbíos Province of Ecuador. (*See* Sec. II-H of each Plaintiffs' Questionnaire response.) All eight Mestanza plaintiffs also indicated in their Questionnaires that they were exposed to Plan Colombia herbicide while in Puerto Mestanza, and that they suffered various personal injuries.[5] (*See* Sec. V, VI, VII of each Plaintiffs' Questionnaire response.) In fact, the principal residence of the Mestanza family is in Guayaquil, Ecuador, some 275 miles from the border, where they own and operate a transport business. The family's farm in Puerto Mestanza is a second property that five of the Mestanza family members have only rarely visited

3. Edy Mestanza (41-year-old son of Victor and Ercilia, father of Jennifer); and

4. Jennifer Mestanza (14-year-old granddaughter of Victor and Ercilia, daughter of Edy).

The four other members of the Mestanza family who are plaintiffs but not test plaintiffs (and their relationships to the test plaintiffs) are as follows:

5. Cristina Josefina Mestanza (29-year-old daughter of Victor and Ercilia, sister of Edy);

6. Veronica Ercilia Mestanza (35-year-old daughter of Victor and Ercilia, sister of Edy);

7. Victor Manuel Mestanza Bosquez (9-year-old grandson of Victor and Ercilia, son of Edy, brother of Jennifer); and

8. David Mestanza Bosquez (5-year-old grandson of Victor and Ercilia, son of Edy, brother of Jennifer).

The plaintiffs' December 23 motion seeks to dismiss without prejudice the 6th, 7th, and 8th listed individuals, although plaintiffs' counsel refer to the 6th person as Ercilia Veronica Mestanza (which name also appears on her Plaintiffs' Questionnaire). This plaintiff's father, mother and brother all identified her as Veronica Ercilia Mestanza in their deposition testimony and in their own Questionnaire responses, so this response brief will likewise refer to her as Veronica Mestanza. The eighth plaintiff was identified as David by his father and in the plaintiffs' December 23 motion, even though his Questionnaire response and other family members said that his name was Edy David Mestanza. This response brief will refer to this 5-year-old plaintiff as David Mestanza.

[5] Some of the Mestanza family members also claim crop and animal damages, but the three plaintiffs addressed in the December 23 motion do not.

and did not visit at all during the years that Plan Colombia spraying allegedly occurred nearby in the Republic of Colombia.[6]

The Mestanza family's misrepresentations in their eight Questionnaires that they all lived in Puerto Mestanza (and that each of the adults had lived only in Puerto Mestanza for decades) set the stage for the numerous other misrepresentations that riddle their Questionnaire responses, only some of which are acknowledged in the plaintiffs' Dec. 23 motion. Defendants will reserve discussion of the misrepresentations in the Questionnaire responses of Victor Mestanza, Ercilia Bosquez, and Jennifer Mestanza until after the parties' meet-and-confer on January 26, 2010, as those three test plaintiffs at least allege being in Puerto Mestanza during the years of their alleged exposures. *See* n.6 below. However, plaintiffs' bare acknowledgement that four of the five other Mestanza family members were not exposed to herbicide spray fails to provide the Court with the full extent of the Mestanza family's misrepresentations to the defendants and the Court. These plaintiffs did not simply assert falsely that they had been in Puerto Mestanza at the time of the alleged spraying; they fabricated elaborate stories regarding the circumstances surrounding their fictitious exposures (*i.e.*, what they saw, felt and smelled) and their nonexistent alleged personal injuries.

For example, the sworn Questionnaire responses of both of the minor plaintiffs (Edy's sons, Victor Manuel and David) indicate that they saw small gray planes and green helicopters

[6] The combined deposition testimony of test plaintiffs Victor Mestanza, his wife Ercilia, his son Edy and his granddaughter Jennifer disclose that the family's principal residence has been in Guayaquil since 1985, but that Victor, Ercilia and their granddaughter Jennifer reportedly spent a majority of their time at the farm in Puerto Mestanza from 2000 to 2002 (and that Victor stayed longer for a majority of his time at the farm until 2004) – but that *no other members of the Mestanza family were at the farm during the dates of the alleged spraying in 2000 and 2002*. (*See* App. at 1-7, 11-14) (V. Mestanza Dep. 16-17, 41, 80, 133, 180-181, 185-186); (*see* App. at 15-26) (E. Bosquez Dep. 16-17, 24-25, 28, 42-43, 51, 74-77); (*see* App. at 27-28, 30-33, 35-38, 43, 45) (E.Mestanza Dep. 12-13, 19, 23-24, 53, 65-66, 89-90, 129, 131); (*see* App. at 58-61) (J. Mestanza Dep. 54-55, 93-94). All cited references to the test plaintiffs' and others' deposition testimony are included in the hand-paginated Appendix ("App.") filed as the last exhibit to this response brief.

along with a white cloud caused by the spraying. (*See* Ex. 1 at 14-15; Ex. 2 at 14-15.[7]) Both Questionnaire responses also claim that the boys saw plants turning yellow the day after the spraying, but they described what happened to nearby bodies of water differently: one said the water looked oily; the other said it turned yellow. (Ex. 1 at 15; Ex. 2 at 15.) One brother said he suffered itchiness, headaches, dizziness and fever immediately after the spraying, and was told by a doctor that his conditions were caused by the Plan Colombia spray (Ex. 1 at 16), whereas the other brother did not answer the same questions. (Ex. 2 at 16.) With respect to their medical backgrounds, both brothers' Questionnaire responses claimed that they had suffered from skin irritations and fainting or dizziness in the past, but the younger brother also claimed migraine headaches. (Ex. 1 at 21; Ex. 2 at 21.) One brother claimed "$500 U.S. dollars" in medical expenses paid related to the alleged exposures; the other claimed $700 U.S. dollars for medical expenses (consisting of $500 paid to a doctor and $200 in other out-of-pocket expenses or fees). (Ex. 1 at 26; Ex. 2 at 26.)[8]

The Questionnaire responses of both minor plaintiffs bear the signature of their father, Edy Mestanza. (Ex. 1 at 34; Ex. 2 at 34.) Edy Mestanza's signature also appears on the Plaintiffs' Questionnaire response of Veronica Mestanza, Edy's mentally retarded sister and the third plaintiff whose dismissal is sought in the plaintiffs' December 23 motion. (Ex. 3 at 36.)

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[7] Exhibits 1 through 5 are the English-translated Questionnaire responses for the five Mestanza family members identified therein. The "original" signature page of each Plaintiffs' Questionnaire response reflecting the plaintiff's photograph, thumb-print and signature appears only on the Spanish-text Questionnaires produced to the defendants. Accordingly, defendants' counsel have added a copy of the Spanish-text signature page from each person's Questionnaire at the end of his/her English-text Questionnaire response attached as Exhibits 1 through 5 to this Response. Moreover, because the English-translated Questionnaire responses produced by plaintiffs' counsel do not have page numbers, defendants have added handwritten page numbers to Exhibit 1 through 5 and will reference those handwritten page numbers throughout this response brief.

[8] In contrast, the boys' father Edy Mestanza testified that his sons did not see spray planes near Puerto Mestanza because they were at home in Guayaquil. (App. at 44, 53, 55.) (E. Mestanza Dep. 130, 143, 145.) And neither son suffered any personal injuries as a result of the alleged spraying. (App. at 45.) (E. Mestanza Dep. 131.)

Veronica's Questionnaire response falsely indicates that she was exposed to Plan Colombia spray and felt the spray on her skin, that she suffered from "bumps on her skin, like an allergy" as well as problems with her throat, that a health care provider at Red Cross in Lago Agrio (15 miles from Puerto Mestanza but 260 miles from her home in Guayaquil) told her that her injuries were caused by Plan Colombia, and that she paid $10,000 in cash for medical bills and expenses. (Ex. 3 at 14-17, 28.) All of these responses were fictional. (App. at 35, 42-43, 45-46) (E. Mestanza Dep. 65, 128-129, 131-132); (App. 16, 22) (E. Bosquez Dep. 17, 51.)

Test plaintiff Edy Mestanza's own Questionnaire response likewise provides specific details of a nonexistent alleged exposure in Puerto Mestanza (which was falsely identified as Edy's home for the past 28 years). (Ex. 4 at 4-5, 15.)[9] Edy's Questionnaire response states that Edy saw and heard two gray planes with white marking and one green helicopter conducting spraying operations at 10 a.m. one morning sometime in 2002, that he felt spray on his skin, smelled something "toxic," and saw an oily residue on the ground, that he witnessed plants turning yellow and wild animals dying, that he immediately suffered from headaches, dizziness, vomiting, skin irritation, and sore throat, that a health care provider at the Red Cross in Lago Agrio told him that Plan Colombia spray had caused his injuries, and that he was unable to work for 15 days as a result of his alleged injuries. (Ex. 4 at 14-17, 28.) At his deposition, Edy acknowledged that he has lived in Guayaquil since 1985 (App. at 27-28) (Dep. 12-13), that he did not visit the farm in Puerto Mestanza during the time of the alleged spraying and never saw a spray plane there (App. at 32, 40) (Dep. 24, 121), and that he did not suffer any of the personal

[9] Although Edy testified at his deposition that his correct signature does not appear on his own Questionnaire response (App. at 39) (Dep. 106), plaintiffs' counsel nonetheless refer to it as Edy's response (Pls.' Mot. at 2, n. 2) and much of the other information set out in the response is specific to Edy. As noted above, Edy's signature *does* appear on the Questionnaire responses of his two sons (Victor Manuel and David) and his sister Veronica, although Edy testified that he did not know that Questionnaire responses had been submitted for these individuals, and he

injuries listed in Section VI of his Plaintiffs' Questionnaire response. (App. at 40-41.) (Dep. 121-122.)

Although plaintiffs do not acknowledge the falsity of the exposure allegations of a fifth Mestanza family member (Cristina Mestanza), Edy Mestanza testified that Cristina (his second sister who is an attorney) likewise has always lived in Guayaquil. (App. at 29, 34.) (Dep. 18, 64.) Cristina's mother also testified that her daughter Cristina was *not* at the farm in Puerto Mestanza in either 2000 or 2002 when the mother claims to have seen spray planes. (App. at 19-22.) (E. Bosquez Dep. 28, 42-43, 51.) But Cristina's Questionnaire response falsely states that she has lived in Puerto Mestanza for her entire life and lays out an equally detailed (albeit different) story about her alleged exposure, which she claims occurred starting in 2000, when she saw and heard a helicopter or helicopters, saw a white cloud of spray and a residue on the ground that looked "like rain sprinkles" and smelled "something toxic" in the air. (Ex. 5 at 4-5, 14-16.) Cristina's Questionnaire response further states: that she saw plants and animals dying after the spraying, that she suffered a variety of subsequent personal injuries (itchiness, bumps, burning in the respiratory tract, headaches, dizziness), which a doctor at the Red Cross in Lago Agrio told her had been caused by the spraying, and that she was prescribed medications that she purchased at pharmacies in Lago Agrio. (Ex. 5 at 16-18.) Clearly, none of these statements is true.

The breadth and uniqueness of each of the Mestanza family members' misrepresentations in their Questionnaire responses cannot be attributed to "technological problems." To the contrary, the evidence now available to defendants indicates that the Mestanza family has been fabricating stories about certain family members being exposed and injured long before the Plaintiffs' Questionnaire responses were prepared in 2008. In particular, although Victor

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does not know how his signature came to be placed on any of the three responses. (App. at 49, 51-55, 57.) (E. Mestanza Dep. 135, 141-145, 149.)

Mestanza responded in Section V.H of his Plaintiffs' Questionnaire response that he had *not* previously complained to anyone or any organization about the alleged spraying of herbicide at his farm, Victor testified during his deposition in November 2009 that he had filed a suit against the Ecuadorian government in 2003 based on the same Plan Colombia spraying allegations being made in this case, and that, as part of the litigation against Ecuador, he had obtained "certifications" from a medical doctor about the illnesses suffered by himself and his family due to the spraying. (App. at 8-10.) (V. Mestanza Dep. 142-143, 146.) One of these certifications was for his grandson Victor Manuel Mestanza (copy attached as Exhibit 6 hereto, consisting of the original Spanish text of the certification and an English translation) – even though it is clear from the testimony of that boy's father and other family members (as cited above) that this boy was not in Puerto Mestanza and did not suffer any personal injuries as a result of the spraying that allegedly occurred there.

The doctor who signed these Mestanza family certifications in 2003 was Dr. Erwin Gonzabay, who was deposed in this case earlier this year. Dr. Gonzabay testified that he did not conduct any investigation to determine the cause of the Mestanza family's claimed ailments or to determine whether the family's allegations that their injuries were caused by Plan Colombia spraying were true. (App. at 64-70.) (E. Gonzabay Dep. 7-8, 59-63.) [10] Instead, Dr. Gonzabay simply related in the certifications what he had been told about each person's alleged illnesses or injuries. *Id.* During his deposition, Victor Mestanza acknowledged that he had obtained the certifications for his other lawsuit against the Ecuadorian governement back in 2003 and that the

[10] Dr. Gonzabay testified that he prepared the children's certifications at the request of "the father of the children," (App. at 69) (Dep. 62), which would have been Edy Mestanza. However, Victor Mestanza testified that he (Victor) asked Dr. Gonzabay to prepare the certifications. (App. at 9.) (V. Mestanza Dep. 143.) In either event, one of the Mestanza test plaintiffs procured a false certification in 2003 about the same son/grandson for whom a fraudulent Plaintiffs' Questionnaire response was submitted in this litigation in 2008.

certifications simply repeated the information that he had provided to Dr. Gonzabay. (App. at 8-10.) (V. Mestanza Dep. 142-143, 146.)

The Mestanza family's false claims of exposure and injury from Plan Colombia spraying amount to a fraud on the Court and the defendants and are a blatant violation of this Court's discovery orders.

II. The Unauthorized Designation of Minor Plaintiffs

During his deposition, Edy Mestanza testified that he had not authorized his minor sons (9-year-old Victor Manuel and 5-year-old David) to serve as plaintiffs in this litigation and that he did not believe that they were plaintiffs. (App. at 46, 49, 56.) (E. Mestanza Dep. 132, 135, 146.) Mr. Mestanza had no explanation for his signature on his sons' Questionnaire responses, nor could he explain when or how his sons' photographs and thumbprints had been placed on their Questionnaire responses. (App. at 49, 50-56.) (Dep. 135, 140-146.)[11] However, Edy Mestanza's assertion that two of his minor children had been improperly put forward as plaintiffs in this litigation is not unique. Among the six other families represented by the 20 test plaintiffs, the fathers in two other families likewise objected strongly when informed that certain of their minor children had been identified as plaintiffs in the litigation (including one child who has been designated as a test plaintiff). Test plaintiff Dociteo Sandoval made clear that his three minor children (Marcelo, Roque, and test plaintiff Wilber) should *not* be plaintiffs in this case:

> Q: I understand that you do not want Marcelo and Roque to be plaintiffs. Do you want Wilber to be a Plaintiff?

[11] Edy Mestanza's claimed surprise at seeing the photographs of his sons on the sworn Questionnaire responses raises a separate question about which other Mestanza family member(s) arranged to have these two young boys photographed and fingerprinted in order to submit what he or she must have (or should have) known would be fraudulent claims.

> A: . . . I don't want any of my children – I do not accept that they are plaintiffs. . . . I'm surprised. I'm very surprised for having signed that document with that explanation.

(App. at 62.) (D. Sandoval Dep. at 100) (referring to his surprise at seeing his son Roque's Questionnaire response). Test plaintiff Edgar Balcazar likewise testified that he did not "want [his] son Diego to be identified as a plaintiff in this litigation." (App. at 63.) (E. Balcazar Dep. at 106.)

By defendants' count, more than half of the individual plaintiffs not subject to a pending motion to dismiss are minor children. The testimony of the test plaintiffs raises serious questions whether these minors have been authorized by their parents to serve in that capacity or indeed about whether they or their parents even know that they have been identified as plaintiffs in this litigation.

III. <u>The Three Subject Plaintiffs Should Be Dismissed With Prejudice.</u>

The three subject plaintiffs, Veronica Ercilia Mestanza and the two minor boys (Victor Manuel Mestanza and David Mestanza), should be dismissed from this litigation with prejudice. Dismissal with prejudice is appropriate for three independent reasons. First, as generally conceded by plaintiffs and as explained in more detail herein, each of these plaintiffs provided false answers in their sworn Questionnaire responses, in violation of numerous Court orders.[12] Second, as to the two minor plaintiffs, their father Edy has not authorized them to be designated as plaintiffs and has expressly opposed their serving in that capacity.[13] Third, plaintiffs have

[12] The Court's October 21, 2008 Order, for example, expressly required the plaintiffs to provide "verified, factual, and complete responses" setting forth, *inter alia*, the date of "each alleged exposure to the 'Plan Colombia' herbicide, and then responding to all follow-up questions with respect to each alleged exposure event." *See also* n. 2 *supra*. In addition, because the parties agreed that the Questionnaire responses would also serve as answers to interrogatories under Fed. R. Civ. P. 33, the plaintiffs' false responses to the Questionnaire also violate Rule 33's requirement that each interrogatory "be answered separately and fully in writing under oath."

[13] It is not clear whether Veronica Mestanza, who is mentally retarded, is competent to appear on her own behalf as a plaintiff or if any other family member properly authorized her designation as a plaintiff.

acknowledged that none of the three plaintiffs was exposed to or injured by Plan Colombia spraying, so there is not even a theoretical possibility of a colorable claim in any event. A proposed order dismissing the three plaintiffs' claims *with prejudice* accordingly, is being filed with this Response for the Court's consideration.

While dismissal with prejudice is plainly warranted under applicable law,[14] defendants submit that it is not a sufficient or complete resolution of these matters. The DynCorp defendants believe that the false statements made by the Mestanza family plaintiffs are just the tip of the iceberg. Many other misrepresentations also appear to have been made in the sworn Questionnaire responses submitted by each of the 20 test plaintiffs, including the four Mestanza family test plaintiffs, as revealed by their recent deposition testimony. Because the parties have not yet had the opportunity to meet-and-confer on these problems, however, the DynCorp defendants will address these issues as necessary in (a) subsequent motion(s). Defendants also reserve the right to seek additional remedies and sanctions against the three plaintiffs here at issue for claims that should never have been filed under Rule 11 and/or for violations of Court orders and rules. Defendants will of course address such matters with the plaintiffs before filing such motions.

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[14] Plaintiffs admit that the exposure claimed by the two Mestanza grandsons and Veronica Mestanza "did not occur." (Pls.' Mot. at 2 ¶ 5.) "[A]dmissions can of course admit the admitter to the exit from the federal courthouse." *Jackson v. Marion County*, 66 F.3d 151, 153-54 (7th Cir. 1995). When a plaintiff's admission reveals that he has no basis for his claims, with prejudice dismissal of those claims is proper. *See, e.g., Riordan v. H.J. Heinz Co.*, No. 08-1122, 2009 WL 2485958, at *10 (W.D. Pa. Aug. 12, 2009) (after voluntarily withdrawing his patent infringement claim by "admit[ting] to having no claim," plaintiff's claim was dismissed *with* prejudice); *Legg v. Battle*, No. 06-CV-6583T, 2009 WL 691915, at *1 (W.D.N.Y. Mar. 12, 2009) (dismissing plaintiff's complaint *with* prejudice because plaintiff "failed to allege that the defendants engaged in any tortious conduct, or any conduct that would give rise to any civil liability" after plaintiff "admitted that she made no claim against the defendants personally, and stated that she did not believe that the defendants caused the [alleged damages]"); *Douet v. Diamond Offshore Co.*, No. 08-0267, 2008 WL 5395755, at *1 (W.D. La. Dec. 23, 2008) (denying plaintiffs' request for dismissal without prejudice where plaintiffs conceded that there was "no claim available" for them under current law); *Fayson v. Kaleida Health, Inc.*, No. 00-CV-0860E(SR), 2002 WL 31194559, at *3 (W.D.N.Y. Sept. 18, 2002) (after plaintiff conceded that "she can state no claim" with respect to several of her claims, including claims for negligence and intentional infliction of emotional distress, those claims were dismissed *with* prejudice).

Dated: January 6, 2010

Respectfully submitted:

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654918v4

EXHIBITS TO THE
DEFENDANTS' RESPONSE TO
PLAINTIFFS' MOTION TO DISMISS
<u>THREE INDIVIDUAL PLAINTIFFS</u>

<u>Document</u>	**<u>Exhibit No.</u>**
Plaintiffs' Questionnaire Response of Victor Manuel Mestanza Bosquez	1
Plaintiffs' Questionnaire Response of David Mestanza Bosquez	2
Plaintiffs' Questionnaire Response of Veronica Ercilia Mestanza	3
Plaintiffs' Questionnaire Response of Edy Geovanny Mestanza	4
Plaintiffs' Questionnaire Response of Cristina Josefina Mestanza	5
Certification dated August 19, 2003, by Dr. Erwin Gonzabay (original Spanish text and English Translation included here	6
Appendix containing all cited excerpts from the deposition testimony of test plaintiffs and others	App.

Annex 155

Arias v. Dyncorp, --- F. Supp. 2d ---, 2010 WL 94563 (DDC, 2010, Roberts J)

(United States District Court for the District of Columbia, Case No. 1:01-cv-01908-RWR-DAR, 2010 WL 94563)

HOnly the Westlaw citation is currently available.

United States District Court,
District of Columbia.
Venancio Aguasanta ARIAS, et al., Plaintiffs,
v.
DYNCORP AEROSPACE OPERATIONS, LLC, et al., Defendants.
Civil Action Nos. 01-1908 (RWR), 07-1042(RWR).

Jan. 12, 2010.

Natacha H. Thys, Terry Collingsworth, Eric J. Hager, Conrad & Scherer, LLP, Washington, DC, William R. Scherer, III, Conrad & Scherer LLP, Fort Lauderdale, FL, Brian J. Leinbach, Engstrom Lipscomb & Lack, Los Angeles, CA, for Plaintiffs.

Eric Gordon Lasker, Joe Gregory Hollingsworth, Katharine R. Latimer, Rosemary Stewart, Spriggs & Hollingsworth, Washington, DC, for Defendants.

MEMORANDUM OPINION

RICHARD W. ROBERTS, District Judge.

*1 Plaintiffs, citizens and domiciliaries of Ecuador, brought an action alleging physical harm and property damage stemming from the defendants' contract with the United States government to spray pesticides in order to eradicate Colombian cocaine and heroin farms. The parties moved jointly to dismiss two specific categories of plaintiffs who had failed to provide complete questionnaire responses to the defendants as a part of their discovery obligations, although the parties diverge on whether the dismissals should be with or without prejudice. The defendants later moved to add another 165 plaintiffs to those being dismissed. Because the plaintiffs in the two dismissal categories have failed repeatedly to comply with their discovery obligations and the failure prejudices the defendants, the plaintiffs identified in both motions will be dismissed from this action with prejudice.

BACKGROUND

The parties filed a joint status report and motion to dismiss a group of 425 plaintiffs who fall into two specific categories: (1) plaintiffs who have provided sufficient information about the alleged date(s) of their exposure to the defendants' spray but who did not disclose sufficient information about their location at the time of their exposure; and (2) plaintiffs who did not provide sufficient information about their alleged damages. (Joint Status Rep. and Mot. to Dismiss Without Prejudice the Pls. in Two Categories Specified by the Court on July 17, 2009 at 1.) The parties do not agree on whether these plaintiffs should be dismissed with or without prejudice. (*Id.* at 2 n. 2.)

The defendants then moved separately to dismiss with prejudice 165 additional plaintiffs who fall into the two named categories. (*See* Defs.' Mot. to Dismiss With Prejudice Add'l Pls. ("Defs.' Mot. to Dis.") at 1; Defs.' Reply at 1.) In support of their motion, the defendants argue that the plaintiffs in these two categories have been "given several chances to provide the information ordered by the Court but [have] failed to do so." (Defs.' Mot. to Dis. at 12.) The plaintiffs oppose additional dismissals and argue that no dismissal should be with prejudice because the plaintiffs have provided sufficient information regarding either exposure location or damages. (*See* Pls.' Opp'n to Defs.' Mot. to Dismiss With Prejudice Add'l Pls. ("Pls.' Opp'n") at 2.)

DISCUSSION

Federal Rules of Civil Procedure 37 and 41 govern dismissals. Under Rule 37(b), a court may dismiss an action or proceeding in whole or in part for a party's failure to comply with a court order. Fed.R.Civ.P. 37(b)(2)(A)(v). Under Rule 41(b), "[i]f the plaintiff fails to prosecute or to comply with ... a court order, a defendant may move to dismiss the action or any claim against it." Fed.R.Civ.P. 41(b). A dismissal under these provisions "operates as an adjudication on the merits" unless the order states otherwise. *Id.*

The central requirement of a Rule 37 sanction is that it be just. *Bonds v. District of Columbia,* 93 F.3d 801, 808 (D.C.Cir.1996). "In determining whether a severe sanction is justified, the district court may consider the resulting prejudice to the other party, any prejudice to the judicial system, and the need to deter similar misconduct in the future." *Id.* Furthermore, a district court must consider whether a lesser sanction "would be more appropriate for the particular violation." *Id.* Dismissal is appropriate as "a sanction of last resort ... after less dire alternatives have been explored without success." *Trakas v. Quality Brands, Inc.*, 759 F.2d 185, 186-87 (D.C.Cir.1985).

***2** While a Rule 37(b) dismissal usually follows some showing of willfulness, bad faith or fault, a plaintiff's persistent failure to comply with discovery and discovery-related orders can be viewed as willful where multiple warnings and second chances have been given to the plaintiff. *Handy v. Shaw, Bransford, Veilleux & Roth*, Civil Action No. 00-2336(CKK), 2006 WL 3791387, at *8 (D.D.C. Dec. 22, 2006) (noting that the plaintiff's failure to comply with the defendants' discovery requests prevented the defendants from defending against certain claims at trial). Also, less severe sanctions may be ineffective when despite ample opportunities to comply with a court order, a plaintiff produces discovery responses only selectively. *See Smith v. O'Neill*, Civil Action No. 99-00547 (ESH/DAR), 2001 WL 950219, at *6 (D.D.C. Aug. 3, 2001).

The plaintiffs here were first ordered to comply with the defendants' discovery requests in November 2007 by providing initial questionnaire responses to the defendants by April 25, 2008. (Scheduling Order, Docket # 63, at 1.) The parties modified this deadline, to require that initial questionnaire responses be due by June 25, 2008. (Consent Notice, Docket # 68 ¶ 3.) Then, on October 21, 2008, because the plaintiffs had provided incomplete initial questionnaires to the defendants, Magistrate Judge Deborah Robinson ordered the plaintiffs to provide to the defendants "verified, factual and complete" questionnaire responses no later than November 19, 2008. (Order, Docket # 76 ¶¶ 1-3.) Magistrate Judge Robinson further ordered the parties to discuss the "voluntary dismissal of plaintiffs who have failed to provide adequate responses to the [q]uestionnaire[,]" and "[a]ny resulting dismissals shall be with prejudice and the plaintiffs are not entitled to any further opportunity to supplement their [q]uestionnaire responses in support of their responses to the defendants' motions to dismiss." (*Id.* ¶ 6.) Notwithstanding this Order, on December 1, 2008, the final deadline for all questionnaire responses was yet again extended to January 21, 2009 (Order, Docket # 84) and, as of July 17, 2009, there were still outstanding incomplete questionnaires, belonging to plaintiffs who either (1) provided sufficient information about dates of exposure but who did not disclose their location, or (2) did not provide sufficient information about their alleged damages.

It has been over two years since the plaintiffs were first directed to complete the defendants' questionnaires. Multiple orders have directed the plaintiffs to respond in full to the questionnaires, and the plaintiffs received three extensions of time in which to do so. Despite these orders and extensions of time, however, the plaintiffs now argue that the defendants should draw their own conclusions from the incomplete information in the plaintiffs' questionnaires. For example, the plaintiffs state that some of the plaintiffs have "listed their address or community name and claimed damages to crops or animals," and "[t]he obvious conclusion drawn from these two pieces of information is that the crops or animals were exposed at the location identified." (Pls.' Opp'n at 3.) The plaintiffs further assert that if a questionnaire indicates that exposure occurred on "the farm" this should be read to mean "my farm" or at least a farm "within their communities." (*Id.* at 4.)

***3** The plaintiffs essentially are asking the defendants to draw conclusions based on incomplete information. If a plaintiff meant "my farm" rather than "the farm," that plaintiff simply should have stated so in his questionnaire. Despite the plaintiffs' ample opportunity to fill in the information gaps, they now turn to the defendants to do this work for them. This, however, is not the defendants' duty.

Moreover, the plaintiffs' failure to furnish the requested information impedes the defendants' ability to prepare their defense. Without the requested information, the defendants are hampered in knowing the full extent, nature and location of the plaintiffs' alleged damages. *See, e.g., In re Phenylpropanolamine (PPA) Prods. Liab. Litig.*, 460 F.3d 1217, 1234 (9th Cir.2006) (explaining that "the purpose of the Plaintiff's Fact Sheet was to give each defendant the specific information necessary to defend the case against it, and that without this device, [the] defendant was unable to mount its defense because it had no information about the plaintiff or the plaintiff's injuries outside the allegations of the complaint").

Contrary to the plaintiffs' claim that any "lingering doubts ... can be resolved through additional discovery" (Pls.' Opp'n at 4), plaintiffs have demonstrated no good cause entitling them to yet another extension of time to comply with discovery obligations with which they should have complied long ago. Nor have they shown that one more grant of additional time will succeed or that a lesser sanction would be effective here.

Furthermore, as the defendants note, the plaintiffs in the two dismissal categories are distinct from plaintiffs who have submitted no questionnaires altogether. The plaintiffs who have submitted incomplete questionnaires either are or have been available at some point during the course of this litigation. Yet, they continue to withhold essential information regarding their claims. Thus, unlike plaintiffs who have not participated in the litigation at all, these plaintiffs have repeatedly resisted prodding to plainly state data to which they have access.

By having failed to complete the defendants' questionnaires, the plaintiffs identified in the two dismissal categories disregarded multiple court orders and prevented the defendants from sufficiently defending their case. Thus, the parties' joint motion to dismiss will be granted in part and the defendants' motion to dismiss as revised will be granted. The claims of the plaintiffs to be dismissed will be dismissed with prejudice.

CONCLUSION

The plaintiffs in the two dismissal categories have been given repeated opportunities to provide the requested information about the location of their exposure and their alleged damages, but have failed to do so. Because this failure prejudices the defendants and violates multiple explicit court orders, and no lesser sanction is appropriate, the plaintiffs who fall within the two specified categories will be dismissed with prejudice in a separate Order signed today.

D.D.C.,2010.
Arias v. Dyncorp Aerospace Operations, LLC
--- F.Supp.2d ----, 2010 WL 94563 (D.D.C.)

END OF DOCUMENT

Annex 156

Arias v. Dyncorp, Defendants' Motion for Sanctions Against the Arias/Quinteros Plaintiffs for Violations of Discovery Orders, 26 January 2010

(United States District Court for the District of Columbia, Case No. 1:01-cv-01908-RWR-DAR, Document 176)

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

Venancio Aguasanta Arias, *et al*., Plaintiffs, v. DynCorp, *et al*. Defendants.	Case Number: 1:01cv01908 (RWR-DAR)
Nestor Ermogenes Arroyo Quinteros, *et al*., Plaintiffs, v. DynCorp, *et al*. Defendants.	Case Number: 1:07cv01042 (RWR-DAR) (Cases Consolidated for Case Management and Discovery)

DEFENDANTS' MOTION FOR SANCTIONS AGAINST THE *ARIAS/QUINTEROS* PLAINTIFFS FOR VIOLATIONS OF DISCOVERY ORDERS, WITH STATEMENT OF SUPPORTING POINTS AND AUTHORITIES INCLUDED HEREIN

Filed: January 26, 2010

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TABLE OF CONTENTS

In October and November 2009, the DynCorp defendants took the depositions of the 20 test plaintiffs (from seven plaintiff families) who were selected by the plaintiffs to serve as their first phase trial group. During these depositions, each of the test plaintiffs repeatedly departed from their earlier sworn Questionnaire responses regarding the purported factual bases for their claims (*i.e.*, the who, what, when, and where of their alleged exposures and injuries) and relied instead on *new* allegations of *different* purported exposures and damages. The test plaintiffs' disavowals of the most basic elements of their prior sworn disclosures – as detailed herein – makes clear that the test plaintiffs have willfully and repeatedly violated Court Orders over the past two years in which the Court required "verified, factual and complete" disclosures, with the explicit warning of dismissal for noncompliance.[1] Equally troubling, given that each of the 20 test plaintiffs disavowed a significant portion of the predicate facts that they had provided in response to the Plaintiffs' Questionnaire, neither the defendants nor the Court can have any confidence in the accuracy of the Questionnaire responses of the 2,001 *other* individual plaintiffs who remain as plaintiffs in these cases.[2] Indeed, some of the test plaintiffs' testimony makes clear that Questionnaire responses provided by other non-test-plaintiff family members are entirely fraudulent.

By Orders of the Magistrate Judge and the District Judge dated November 27, 2007, October 21, 2008, December 1, 2008, May 5, 2009, July 7, 2009, and July 17, 2009, the Court set forth clear directions to the individual plaintiffs requiring them to provide both (1) their best

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[1] Oct. 21, 2008 Order (Ex. A); *see also* the Nov. 27, 2007 Hr'g Tr. at 11-14 (Ex. B); the Nov. 25, 2008 Hr'g Tr. at 21-22, 52 (Ex. C); the Dec 1, 2008 Order; the May 5, 2009 Order; the July 17, 2009 Hr'g Tr. at 13-15, 50 (Ex. D); and the Sept. 19, 2009 order. (All discussed in detail below.)

[2] Following the Court's dismissal of 681 plaintiffs in its Order of September 16, 2009 and its dismissal of 590 plaintiffs in its Order of January 12, 2010, there are 2021 remaining individual plaintiffs in the *Arias* and *Quinteros* cases.

information as to the dates and circumstances of their alleged exposures to Plan Colombia spraying and the specific nature of their alleged personal injuries and property damages, and (2) individualized scientific causation statements by qualified experts linking each plaintiff's alleged exposures to his or her alleged personal injuries and property damages. Plaintiffs' repeated failures to provide the ordered information required defendants to engage in extensive motions practice and required the Court to conduct five separate motions hearings, each of which resulted in Court findings that plaintiffs had violated the Court's prior Orders. Despite this extraordinary expenditure of time and resources, defendants and the Court find themselves today in the same place now as they were when this case first began: with no credible information from any individual plaintiff setting forth a plausible factual basis for his or her claim.[3]

The question now before the Court is what – if anything – can be done to bring the individual plaintiffs into compliance with the Court's long-standing discovery Orders and move this case on to a meaningful path towards trial. The DynCorp defendants submit that the 20 test plaintiffs' unambiguous violations of the Court's Orders – and the resulting hopelessly-muddled nature of their factual allegations – require that each of the test plaintiffs' claims be dismissed with prejudice. In the alternative, defendants request that if the test plaintiffs are allowed to proceed to trial, they be precluded from offering any argument to explain away their misconduct and that the jury be instructed by the Court that the plaintiff provided false answers under oath in their 2008 Questionnaire responses.

The DynCorp defendants also submit that the claims of the remaining 2,001 individual plaintiffs should not be allowed to proceed until each of those plaintiffs have provided

[3] *See Ashcroft v. Iqbal*, 129 S. Ct. 1937, 1949 (2009) ("To survive a motion to dismiss, a complaint must contain sufficient factual matter, accepted as true, to 'state a claim to relief that is plausible on its face.'"), citing *Bell Atlantic Corp. v. Twombly*, 550 U.S. 544, 570 (2007).

meaningful assurance that they have provided accurate factual disclosures in their Questionnaire responses and that each plaintiff be required, as previously ordered, to provide individualized expert causation statements in support of their claims. Further, in light of numerous test plaintiffs' testimony that their children had been put forward as plaintiffs without their knowledge, approval or authorization, defendants request that plaintiffs be required to provide a parental authorization for each minor plaintiff within the group of remaining individual plaintiffs. Defendants also seek recovery of their reasonable attorneys' fees and costs in preparing this motion. A proposed Order including these requested remedies is being filed simultaneously with this motion.[4]

I. BACKGROUND FACTS

A. The Court's Prolonged Effort To Secure *Prima Facie* Disclosures from the Individual Plaintiffs.

This case involves 2,021 individual plaintiffs in Ecuador who – notwithstanding the repeated findings of the safety of the Plan Colombia spraying operations by the U.S. Department of State, the U.S. Environmental Protection Agency, the U.S. Department of Agriculture, and an expert panel assembled by the Organization of American States[5] – allege physical harm and property damage stemming from the defendants' contract with the United States government to spray herbicides in order to eradicate Colombian cocaine and heroin farms. At the initial

[4] The DynCorp defendants certify that before filing this motion, they conferred in good faith with the *Arias/Quinteros* plaintiffs about the relief to be sought in this motion but were not able to reach agreement (or to narrow the areas of disagreement) about the subjects and requests for relief set out herein. Plaintiffs' counsel have indicated that they will oppose this motion.

[5] *See*, *e.g.*, Keith R. Solomon, *et al.*, *Human Health and Environmental Risks from the Use of Glyphosate Formulations to Control the Production of Coca in Colombia: Overview and Conclusions*, 72 J. Toxicology and Envtl. Health, Part A, 914-920 (2009) (Ex. E); United States Department of State, *Memorandum of Justification Concerning the Secretary of State's 2007 Certification of Conditions Related to the Aerial Eradication of Illicit Coca in Colombia* (submitted to Congress on Aug. 10, 2007) (Ex. F).

scheduling conference on November 27, 2007, the Court recognized that the science behind plaintiffs' claims was "skimpy" and thus required each of the individual plaintiffs to provide the *prima facie* "who, what, when, and where" of their alleged individual exposures and injuries.[6] The Court explained:

> There ought to be the kind of detail that would be useful by way of identification of dates or times, if that's possible, airplanes, descriptions, what they saw, colors of fumes, any kind of details like that, and added into temporal connections. Plus, if they did have any doctors that they visited after the onset, assuming the onset was temporally connected in some way, what the doctors might have told them. . . . [T]o move the case forward to get some of these issues teed up, it would be *required* to put in some basis of that type.

(11/27/07 Hr'g. Tr. at 13:9-14:5 (emphasis added) (Ex. B)).[7] Plaintiffs' counsel agreed that these facts were of the type that should be gathered before the filing of a lawsuit and assured the Court that providing this information for each individual plaintiff "would be very doable." (*id*. at 12:10).

Over the next 18 months, however, it became increasingly clear that what counsel had represented was "very doable" was not, in fact, getting done. What followed instead was a series of delays, obfuscations, and violations of multiple Court Orders:

- Plaintiffs' first attempt to provide the ordered disclosures by the Court's January 28, 2008 deadline was so grossly deficient that plaintiffs did not even seek to defend it. Instead,

[6] *See* 11/25/08 Hr'g Tr. 60:1-4 (Court discussion of bases for its earlier November 2007 ruling) (Ex. C).

[7] At the same hearing, the Court clarified that the disclosures about when the alleged exposures occurred and what the plaintiffs saw would be required in addition to eight categories of information promised by the plaintiffs, including: "(1) name; (2) address; (3) exposure address (if different than current address … (6) claimed physical injuries (if any); (7) claimed property damages (if any) …" *Id.* at 11 (referencing plaintiffs' promise to produce all such data in the Joint Rule 16.3 Statement (ECF No. 62 in *Arias*, ECF No. 19 in *Quinteros*, Nov. 19, 2007) at 16).

following a meet-and-confer with defendants, the individual plaintiffs agreed to provide the ordered disclosures as part of their responses to the Plaintiffs' Questionnaire, the text of which had been negotiated and agreed to in advance by their counsel and would by agreement of the parties be treated as supplemental initial disclosures and interrogatory responses. Because the plaintiffs also represented that they would be unable to meet the Court's April 25, 2008 deadline to submit the first 800 Plaintiffs' Questionnaire responses, defendants agreed to extend this first Questionnaire "due-date" to June 25, 2008. (Consent Notice (ECF No. 68 in *Arias*; ECF No. 25 in *Quinteros*), April 17, 2008 at 1).

- Plaintiffs' initial responses to the Plaintiffs' Questionnaires, however, were equally deficient, requiring defendants to file a motion to compel with the Court. On October 21, 2008, the Magistrate Judge granted defendants' motion in full, and ordered each of the individual plaintiffs to "provide verified, factual and complete responses to the Plaintiffs' Questionnaire, using the previously agreed-upon text of that Questionnaire." Ex. A ¶1. The October 21, 2008 Order also listed specific requirements for completing the Questionnaire, including:

> 1. Providing the month, day and year of each alleged exposure to the "Plan Colombia" herbicide, and then responding to all follow-up questions with respect to each alleged exposure event;
>
> 2. The marking of the maps appended to the Questionnaire to show where the plaintiffs, their affected farms, and/or their affected farm animals were located when each alleged exposure event occurred;
>
> 3. The submission of medical records in accordance with the instructions in the Questionnaire by the plaintiffs who claim health injuries from their alleged exposure events …; and
>
> 4. Providing responses to Section VII.A of the Plaintiffs' Questionnaire to provide each individual plaintiff's

> monetary computation of each category of damages claimed.

Id. The same Order required the parties to discuss the "voluntary dismissal of plaintiffs who have failed to provide adequate responses to the Questionnaire" and stated that "[a]ny resulting dismissals shall be with prejudice and the plaintiffs are not entitled to any further opportunity to supplement their Questionnaire responses in support of their responses to the defendants' motion to dismiss." *Id.* ¶ 6. Moreover, in light of plaintiffs' inability (or unwillingness) to provide the *prima facie* disclosures that had been ordered nearly a year earlier in November 2007, the Magistrate Judge further required that "[i]n addition, the Questionnaire responses provided by the individual plaintiff shall be accompanied by sworn statements by qualified medical or scientific witnesses that specifically link each plaintiff's alleged personal injuries or property damages to the effects of the 'Plan Colombia' spraying." *Id.* ¶ 5.

The plaintiffs filed Objections to the October 21, 2008 Order, accusing the Magistrate Judge of "cultural bias and lack of complete sensitivity to the reality of these Plaintiffs' lives."[8] Plaintiffs acknowledged their obligation "to provide information within their knowledge to the best of their recollection" but represented that "[t]hey have done this, and this is all they can do." *Id.* at 6. The District Judge rejected plaintiffs' objections and affirmed the October 21, 2008 Order in full. The Court did provide plaintiffs a further extension of time to produce "all of the completed questionnaires and supplements to make them complete" until January 21, 2009 and an extension of time until March 23, 2009 to submit the individualized causation statements by qualified medical or scientific witnesses. *See* 11/25/08 Hr'g Tr. (Ex. C) at 24; Minute Entry entered on Nov. 28, 2008 in the *Arias* and *Quinteros* dockets; and the Court's Dec. 1, 2008 Order

[8] Plaintiffs Objections to Magistrate Judge's Oct. 21, 2008 Order on Defs.' Mot. to Compel Disc., ECF No. 77 in *Arias*; ECF No. 40 in *Quinteros*, Nov. 3, 2008, at 2.

(ECF No. 84 in *Arias*; ECF No. 47 in *Quinteros*).

In response to plaintiffs' counsel's claimed confusion as to the causation statement requirement, the Court explained that plaintiffs were required to produce for each individual plaintiff an expert causation statement that "at minimum, … mak[es] some connection based upon some scientific assessment between the allegation that spraying happened and that spraying caused these symptoms." 11/25/08 Hr'g. Tr. (Ex. C) at 60; *see also id.* at 53 ("each one of the 2500 or so questionnaires that's returned will have to have appended to it a separate sworn statement from some expert opining about causation with regard to that individual").

- Despite being provided yet another opportunity to make sure that they had really done their best to truthfully answer the Questionnaire, plaintiffs again failed to provide defendants with the "verified, factual and complete responses" explicitly required by the Court's Orders. To the contrary, the individual plaintiffs made no changes whatsoever to their previous Questionnaire responses.[9] When confronted with this fact in defendants' subsequent motion to dismiss, plaintiffs' counsel again assured the Court that "all 2,463 Plaintiffs who submitted a completed Questionnaire responded as fully as they could based on personal knowledge," and argued that the plaintiffs could not be required to produce information that they did not have. Joint Mot. to Dismiss Nonresponsive Plts. and Plts. Without Claims, ECF No. 86 in *Arias*, ECF No. 48 in *Quinteros*, Feb. 19, 2009, at 10. Based upon this representation, the District Court granted in part and denied in part the defendants' motion to dismiss but allowed the majority of individual plaintiffs who had completed the Questionnaire to proceed with their claims. 7/17/09

[9] This is precisely what the Court lamented in its January 12, 2010 Memorandum Opinion dismissing 590 plaintiffs with prejudice: "Multiple orders have directed the plaintiffs to respond in full to the questionnaires, and the plaintiffs received three extensions of time in which to do so," and yet, "[d]espite the plaintiffs' ample opportunity to fill in the information gaps," they did not do so. 1/12/10 Mem. Op., at 5-6.

Hr'g Tr. (Ex. D) at 13-15 . In a subsequent dismissal order addressing two categories of disclosure failures, however, the Court made clear that individual plaintiffs who failed "to plainly state data to which they have access" or who had "produce[d] discovery responses only selectively" would be dismissed with prejudice. 1/12/10 Mem. Op., ECF No. 173 in *Arias* , ECF No. 133 in *Quinteros*, at 4, 7; *see also* 7/17/09 Hr'g Tr. (Ex. D) at 15 (explaining reasoning for dismissal categories).

In response to a separate defendants' motion relating to the causation statements, the Court held that the plaintiffs' submission of aggregate general causation statements (one for personal injuries and one for property damages) violated the Court's order that they submit individualized causation assessments. In granting the defendants' request for sanctions, the Magistrate Judge explained:

> The Court finds that there is nothing in this Court's order, or in the order of the assigned District Judge, which permits the plaintiffs to substitute "an aggregate review" for the paragraph 5 requirement . . . of this Court's October 21, 2008 order, . . . that the plaintiffs provide a sworn statement of a qualified medical or scientific witness regarding "each plaintiff's alleged personal injuries or property damages." The plaintiffs simply have not done so. The plaintiffs concede they haven't done so, and there's nothing ambiguous about the order directing that they do so.

5/5/09 Hr'g Tr. (Ex. G) at 43:16-44:5; *see also* the Court's May 5, 2009 Minute Order. After rejecting plaintiffs' subsequent objections to the Magistrate Judge's ruling, the District Court ordered plaintiffs to produce the "individualized assessments with regard to each individual plaintiff and each individual plaintiff's complaints about harm or damage" by October 2, 2009. 7/17/09 Hr'g Tr. (Ex. D) at 39; *see also id*. at 50 ("the [submitted] reports . . . that had been provided did not comply with what I had asked for from the beginning. The Magistrate Judge was quite right that they didn't and that the reports did not comply, and I find no error in their conclusion that the individualized expert assessments are required."); *see also* 7/22/09 Minute

Order entered in the *Arias* and *Quinteros* without ECF numbers and the Court's amended scheduling Order (ECF No. 147 in *Arias*; ECF No. 109 in *Quinteros*, Sept. 17, 2009).

B. Plaintiffs' Most Recent Violation of the Court's Order to Provide Individualized Causation Statements.

Despite the explicit and repeated direction from both the Magistrate Judge and the District Judge, the individual plaintiffs on October 2, 2009, again failed to provide individualized expert assessments supporting their claims. Instead, plaintiffs simply repackaged the general causation statements previously rejected by the Court by merging them into a single causation statement that they then produced to defendants over 2,000 times (one for each individual plaintiff). The only change in the language of the previous aggregate causation statements was the addition of a single paragraph in each statement that summarizes each individual plaintiff's alleged personal injuries and property damages (taken directly from his/her Plaintiffs' Questionnaire response), followed by an identical statement, repeated for each of the 2,000-plus plaintiffs that the injuries "could have been caused by Plan Colombia spraying." *See* the sample Campaña causation statement attached at Ex. H ¶ 16.

This boilerplate paragraph does not make the required connection "based upon some scientific assessment between the allegation that spraying happened and that spraying caused these symptoms" in any of the plaintiffs. 11/25/08 Hr'g Tr. (Ex. C) at 60:18-21 (the District Judge's description of what was expected). Campaña's paragraph 16 provides no information whatsoever as to the dates, times and frequencies of the individual plaintiffs' alleged exposures, the location of each plaintiff in proximity to contemporaneous Plan Colombia spraying, or the amount of the herbicide as to which each plaintiff purportedly could have been exposed. The paragraph also provides no scientific data linking the Plan Colombia herbicide spray to the specific types of illnesses alleged, no test data showing even the presence of the herbicide in any of the plaintiffs' blood, and no explanation why the symptoms alleged by the plaintiffs should be linked to Plan Colombia spraying as opposed to the widespread health problems endemic to the impoverished communities in which the plaintiffs live.[10] Instead, paragraph 16, like the rest of the aggregate causation statement, makes clear that plaintiffs' expert simply assumed that any and all ailments in the region – as asserted in any one of the plaintiffs' Questionnaire responses – might be attributed to the spraying, no matter how outlandish the claim might be. See, *e.g.*, Campaña Decl. (Ex. H) ¶19 (recounting a Sucumbios resident's claim that "since the fumigations [my son] no longer gets good grades in school"); *id.* ¶20(b) (stating that the affected population generally attribute infectious diseases like influenza, bronchitis, and pneumonia to Plan Colombia spraying); *id.* ¶20(d) (stating that "women think" that the number of miscarriages in the region must be associated with the spraying despite admission from the Provincial health authorities that they cannot make such a link); *id.* ¶¶ 29-34 (identifying mosquito-borne diseases like malaria and dengue fever as possible results of the spraying).

Moreover, Campaña's paragraph 16 largely ignores the separate requirement in the Court's Order that the individual plaintiffs provide "sworn statements by qualified … scientific witnesses that specifically link each plaintiff's alleged … *property damages* to the effects of the

[10] For example, published epidemiologic studies in communities in Northern Ecuador identified alarmingly high rates of bacterial and insect-born diseases of the eyes, skin, and gastrointestinal tract. *See*, *e.g.*, Simonetta Gatti., *et al.*, *Amebic Infections Due To The Entamoeba Histolytica-Entmoeba Dispar Complex: A Study of the Incidence in a Remote Rural Area of Ecuador*, 67(1) Am. J. Trop. Med. Hyg. 123, 125-26 (2002) (176 of 178 individuals in study population (98.9%) tested positive for intestinal parasites; "This high detection rate is clearly related to poor sanitation, nutrition [and] use of contaminated water …"); Rodrigo X. Armijos, *et al.*, *The Epidemiology of Cutaneous Leishmaniasis in Subtropical Ecuador*, 2(2) Tropical Med. and Int'l Health 140-152 (1997) (14% of study population tested positive for active parasitic skin disease, leishmaniasis, and 33% had evidence of prior disease); P.J. Cooper, *et al.*, *Onchocerciasis in Ecuador: Ocular Findings in Onchocerca Volvulus Infected Individuals*, 79 Brit. J. of Opthalmology 157-162 (1995) (insect-born disease; Onchocercal ocular lesions identified in over 33% of the study population). Copies of these studies were attached as Exhibit H to the defendants' April 3, 2009 motion for sanctions at ECF No. 91 in *Arias*; ECF No. 53 in *Quinteros*, April 3, 2009.

Plan Colombia spraying." 10/21/08 Order (Ex. A) ¶ 5 (emphasis added). Other than passing parenthetical references to the alleged impacts of the spraying on each plaintiff's crops and animals – also taken directly from each Plaintiffs' Questionnaire response – plaintiffs' expert simply combines these allegations with the plaintiffs' alleged personal injuries and concludes – for all plaintiffs – that the alleged property damages "could have been caused by Plan Colombia spraying." Ex. H ¶ 16. Again, the statements contain nothing in the way of an individualized scientific assessment: no scientific studies linking the alleged exposure scenarios to the types of crop and animal losses alleged; no soil, air, or water testing detecting even the presence of the herbicide on the plaintiffs' farms; and no discussion of potential alternative causes. Plaintiffs' expert's scant references to property damages are not surprising because the expert, as a medical doctor with purported specialties in the areas of mental health and public health, does not even claim to have the expertise or experience in animal toxicology or agricultural science that he would need to address causation for the plaintiffs' property damage claims.[11]

C. The Deposition Testimony of the 20 Test Plaintiffs Establishes Numerous Further Violations of The Court's Orders.

In its July 17, 2009 ruling, the Court granted plaintiffs' request that they be allowed to select 20 test plaintiffs who plaintiffs believed could best advance their claims as a first phase trial group. Plaintiffs had previously represented to the Court that they would be selecting in this initial group, "people who had the most information [about the alleged facts of their claims] so that we could in the first trial be in a position to really prove what happened in detail." 11/25/08

[11] At the November 25, 2008 hearing, the Court specifically addressed the fact that plaintiffs would need to have an expert who could address each individual plaintiff's claims of crop or animal damage. *See* 11/25/08 Hr'g Tr. (Ex. C) at 20:13-17 ("Do you at this point … have any expert or experts lined up, scientific or medical, who have either examined the plaintiffs or examined their medical records *or evidence of crop or animal damage so far*?"). (Emphasis added.)

Hr'g Tr. (Ex. C) at 11:14-12:1.[12] During the depositions of these test plaintiffs in October and November 2009, however, these self-selected test plaintiffs repeatedly demonstrated that they had not or could not provide any accurate account of the basic facts underlying their legal claims. To the contrary, all of the test plaintiffs repeatedly changed their stories as to their previously-disclosed dates and circumstances of alleged exposures and as to the personal injuries and property damages purportedly arising therefrom. Thus, either the sworn Questionnaire responses – and expert causation statements derived solely from those responses – or the deposition testimony provided by each of the test plaintiffs, or both, are materially false with respect to the basic factual underpinnings of the test plaintiffs' claims. Because the test plaintiffs have not produced any independent documentary evidence supporting their claims (*e.g.*, medical records relating to the injuries allegedly caused by the Plan Colombia spraying, business or tax records relating to the alleged property losses), the defendants have no meaningful way to choose among the plaintiffs' varying representations and can only guess at what story these same plaintiffs will present at trial. Further, with this clear showing of the meaningless of the Plaintiffs' Questionnaire responses and causation statements of the plaintiffs' "best" individual cases, the defendants and the Court can have no confidence whatsoever in the information provided to date by the remaining 2,001 individual plaintiffs.

The changing stories of each of the 20 test plaintiffs, as grouped by plaintiff family,[13] are discussed below:

[12] In their written proposal about how to select the test plaintiffs, plaintiffs' counsel likewise promised that they would "select plaintiff cases that provide the parties with the most useful information." Pls.' Proposal for Selection of 20 Sample Test Plaintiffs, ECF No. 88 in *Arias*, ECF No. 50 in *Quinteros*, March 23, 2009, at 8.

[13] Each test plaintiff family has multiple other family members who are also plaintiffs in the litigation but who are not serving as test plaintiffs.

1. The Calero Family

Four of the test plaintiffs are members of the Calero family, as follows:

- Santos Calero (husband of Calixta; father of Betty; grandfather of Yuli)
- Calixta Pineda (wife of Santos; mother of Betty; grandmother of Yuli)
- Betty Calero Pineda (daughter of Santos and Calixta; mother of Yuli)
- Yuli Calero Pineda (11-year-old daughter of Betty; granddaughter of Santos and Calixta)

In their Questionnaire responses, the Calero plaintiffs provided general and inconsistent representations that their alleged exposures to Plan Colombia herbicide occurred sometime in 2001 (Yuli), sometime in 2002 (Betty), sometime in 2002 or 2003 (Calixta), or sometime in 2001, 2002, 2003, 2004, 2005, and/or 2006 (Santos). (App. 1, 5, 24, 37, 55.)[14] At their depositions, however, each of the Calero plaintiffs told a different story. The adult Caleros (Santos, Calixta, and Betty) now each testified that they were exposed only on a single occasion in August 2003, and while Santos and Calixta did not identify the number of helicopters they saw in their Questionnaire responses, and Betty said that she saw 3 helicopters in her Questionnaire response, at deposition they each testified to having seen 2 helicopters at the time of the alleged exposure. (App. 2, 11-13, 24, 32, 39-40, 45-47.) On the other hand, Yuli Calero, who in her Questionnaire response provided specific details of her recollection of an alleged spraying event in 2001 (*e.g.*, that she saw two white spray planes and a green helicopter on a clear morning at 9 am, that she saw a white cloud sprayed from the plane and both smelled the herbicide and felt it on her body) (App. 56-57), admitted in her deposition that she had no recollection of seeing (or smelling) any spraying event whatsoever. (App. 61, 62-63.)

[14] In response to the Questionnaire inquiry: "When were you or your property exposed to herbicide?" Santos Calero responded: "2001." However, in response to the question: "What was the date and time of the day that your crops were exposed to the Plan Colombia herbicide? Santos Calero responded: "2001, 2002, 2003, 2004, 2005, 2006." (App. 1, 5.) All of the citations to the test plaintiffs' sworn Questionnaire responses and deposition transcripts have been compiled in an Appendix filed as the last exhibit to this motion.

Defendants also learned that the maps provided by the Caleros with their Questionnaire responses were wildly inaccurate in identifying the alleged location of their exposures. (App. 10, 30, 44-B, 60.)

Further, the Caleros presented a notably different account at deposition of their alleged personal injuries from the purported spraying event. In their Questionnaire responses, both Calixta and Betty Calero alleged that they had incurred medical expenses of $5,000 in connection with their alleged exposures, which they had paid in cash. (App. 28-29, 44-45.) At their depositions, however, both women admitted that they had incurred no such expenses: Calixta acknowledged that she did not even have access to that amount of money (App. 35-36), and Betty testified that her medical expenses were in fact only 5,000 sucres or less than $20 (a sucre is an Ecuadorian currency that was discontinued in 1999 – four years before Betty's alleged exposure – when Ecuador adopted the U.S. dollar as its currency). (App. 53.) The Caleros also changed their stories as to the nature of their alleged personal injuries: Santos Calero testified about bone and kidney pains that were nowhere mentioned in his Questionnaire response (App. 3-4, 5, 17), and Betty Calero testified about previously-unmentioned mental problems, stroke, pain in the kidneys, and pain in the legs (App. 39, 41-43, 48, 49, 51).[15] Not surprisingly, because they were prepared solely from the Questionnaire responses, the causation statements submitted for these two plaintiffs say nothing about these newly alleged health claims. (App. 23, 54.) Moreover, Betty Calero's claim of medical injuries arising from Plan Colombia spraying completely fell apart when it was pointed out at deposition that the medical

[15] While Calixta Pineda's testimony as to her alleged personal injuries from the spraying was generally consistent with her Questionnaire response, she separately admitted that the medical history in her Questionnaire – in which she represented that she had suffered from chagas, respiratory illness, migraine headaches, bacterial and fungal infections, and anemia or other blood disorders – was entirely incorrect because she suffered from none of these ailments. (App. 25-27, 33, 34.)

record she had produced only days earlier as evidence of her injuries was dated March 2003, some seven months prior to her alleged exposure. (App. 50, 51.) Betty Calero's only explanation for this obvious and fatal inconsistency was that the medical record must have been inaccurately dated. (App. 52.)

While Santos Calero claimed in his Questionnaire response that the family had crop losses of nearly $15,000 (App. 8-9), at his deposition, he admitted that he had not in fact calculated any monetary losses for his purportedly damaged crops and did not know most of his crops' market value because he used them only for personal consumption. (App.18-20, 21-22.) Mr. Calero also repeatedly reversed himself during his deposition on the question whether he had planted crops in the years following the alleged crop damage from Plan Colombia spraying, initially testifying that he did not plant crops for the following four years, then (after being shown his Questionnaire response claiming damage to crops planted in 2004) testifying that he could not remember whether he had planted any crops between 2003 and 2007, and then testifying that "of course we planted because with the crops we continued to live. That's what we live off of." (App. 5, 14-16.)

2. <u>The Salas Family</u>

Three of the test plaintiffs are members of the Salas family:

- Jorge Salas (husband of Laura; father of John)
- Laura Sanchez (wife of Jorge; mother of John)
- John Salas (15-year-old son of Jorge and Laura)

In contrast to the Calero family, Jorge Salas provided very specific information in his Questionnaire response as to the date of his alleged exposure: October 4, 2002. (App. 67.) His wife, Laura Sanchez gave a consistent, though more general date of exposure of "since 2002" in her Questionnaire Response. (App. 101.)[16] At deposition, however, the Salas's abandoned those dates and testified to a hodgepodge of exposure dates that do not match up with either their Questionnaire responses or with the testimony of the other family members who were purporting to describe the same alleged exposures. Jorge testified that the exposures occurred in December 2000, May 2001, and October 2003 (App. 76, 80-81, 85-86); Laura testified that the exposures occurred in June 2002, January 2003, and October 2003 (App. 105, 106, 109); and their son John admitted that he cannot remember when the exposures occurred, but that he believed he was exposed on two occasions. (App. 118-120.) Defendants can only guess what dates of exposure the Salas family might allege at trial.

The Salas family's testimony as to what they saw during the alleged spraying events also changed significantly, with the number of spray planes decreasing (from multiple planes to 1-2 planes for Jorge and from 5 planes to 2-3 planes for John) (App. 67, 77, 81, 86, 114, 118) and the number of helicopters increasing (with Jorge and Laura now claiming to have seen a helicopter after having not so claimed in their Questionnaire responses). (App. 67, 77, 81, 86, 101, 105, 107, 110.) The Salas family also changed their statements as to *where* they were allegedly exposed, with John testifying that the exposure took place 2 kilometers from the border (rather than the 300 meters from the border stated in his and his mother's Questionnaire responses and causation statements (App. 101, 113, 114, 119, 123)), and Jorge testifying that the exposure was 3 kilometers from the border (up from the 2 kilometers response in his Questionnaire and in his causation statement). (App. 67, 75, 77, 82, 87, 98.) As with the Caleros, the marked maps of the location of the alleged exposures provided with the Salas family's Questionnaire responses were inaccurate and thus do not provide any clarification. (App. 74, 104, 117.)

[16] John Salas stated in his Questionnaire response that the exposure occurred in 2000 (App. 114), but he would have only been six years old at the time.

The Salas family plaintiffs also testified to a whole host of alleged personal injuries that are at odds with the personal injuries identified in their Questionnaire responses. Jorge Salas testified that the herbicide spray caused inflammation of the eyes and caused him to lose his vision whereas he had not mentioned any problems with his eyes in his Questionnaire response. (App. 68, 70-71, 97.) Laura Sanchez, on the other hand, abandoned the claims of respiratory disease and stomach burning set forth in her Questionnaire response. (App. 102, 108, 111.)[17] John Salas likewise abandoned his Questionnaire response alleging respiratory problems; at his deposition, John testified instead that the herbicide exposure caused previously-unidentified body pain, bone pain, sore throat and a strong headache. (App. 115, 121.) Thus, once again, the causation statements submitted for the Salas family test plaintiffs do not even correctly identify the personal injuries alleged by the plaintiffs at deposition. (App. 98, 113, 123.)

The Salas family also changed their claims of injuries to farm animals. In his Questionnaire response, Jorge Salas claimed monetary damages for the death of 40 chickens, 2 cows, and 2 pigs. (App. 72, 73.) At his deposition, however, Mr. Salas testified that the cows were not his, but he added new damages claims for 2 horses, 2 dogs, and an additional 2 pigs. (App. 87-A to 92.) He produced no documentation whatsoever to support either set of numbers. Jorge Salas also testified at deposition that the Salas family members are plaintiffs in a separate lawsuit alleging contamination by waste from an oil well 500 meters from their home. (App. 93-96.) In his Questionnaire response, Jorge had specifically denied being exposed to oil pollution and denied being involved in such litigation. (App. 64-66.)[18]

[17] When confronted with this fact at her deposition, Laura responded that she had testified about her sore throat, which she considered to be a respiratory disease. (App. at 112 to 112-A.)

[18] Test plaintiff John Salas testified that an oil spill near the family's home "is like black crude that comes down … and it flows along the edge of the road like water, and the spill reached the river … where we used to wash." (App. 122.)

3. **The Quevedo Family**

There are four test plaintiffs from the Quevedo family:

- Luciano Quevedo (husband of Rosa; father of Edith and Robinson)
- Rosa Altamirano Miranda (wife of Luciano; mother of Edith and Robinson)
- Edith Quevedo Altamirano (14-year-old daughter of Luciano and Rosa)
- Robinson Quevedo Altamirano (9-year-old son of Luciano and Rosa)

The deposition testimony of the Quevedos follows the same winding course as that of the other test plaintiffs. Although Luciano Quevedo stated in his Questionnaire response that he was exposed to Plan Colombia herbicide "from 2002 til 2006," he testified during his deposition that he could only recall seeing a single spray plane on one occasion flying close to the San Miguel River (which is 3 km from his farm), and that he could not recall the date. (App. 124, 129, 131-133.) Luciano's wife Rosa had claimed exposure "from October 2002 on" in her Questionnaire response and stated further that she had seen 2 lead-colored planes and a green helicopter in 2002 (App. 157-158); at her deposition, however, Rosa testified that she had not seen a helicopter and had only had heard what she believed to be a spray plane. (App. 162-163, 164-165, 166-167.) Luciano and Rosa's daughter Edith claimed exposure in her Questionnaire response "since April 10, 2002" and claimed in the same response that she saw 2 spray planes, but Edith admitted during her deposition that she could not provide any date for the one time she allegedly saw a single spray plane. (App. 173-174, 177, 178.) The Quevedos did provide testimony consistent with their Questionnaire responses that their home was 4 km from the border, but at deposition, Edith testified that she was exposed at school, not at home as stated in her Questionnaire response. (App. 173, 178.)

As to personal injuries, in his Questionnaire responses, Luciano Quevedo alleged that the spraying had caused him to suffer itchiness, headaches, aching bones and fever. (App. 125.) The individual causation statement submitted on his behalf listed these same alleged injuries (as well as another ailment listed in the medical history section of Luciano's Questionnaire). (App. 126-A, 154.) At his deposition, however, Luciano initially abandoned his claims of headaches, aching bones, and fever and substituted in their place only a claim of vision problems.[19] He then revised his testimony (after being shown a copy of his Questionnaire response) to once again allege that he had suffered all of the injuries. (App. 139, 140.) Finally, Luciano abandoned all of his personal injury claims, testifying that he was not seeking any damages at all in connection with any alleged personal injuries. (App. 149.) Meanwhile, Luciano's wife, Rosa, who had alleged "headache, fever, diarrhea, and spots" in her sworn Questionnaire response, came to deposition with different complaints of a rash, headaches, and kidney and bone pains. (App. 159, 168-169.)

The Quevedos' claims of property damages likewise changed. In his Questionnaire response, Luciano had alleged damage to 1 hectare of plantains, 5 hectares of coffee, and 5 hectares pasture. (App. 127, 128.) At deposition he bumped those numbers up, adding another 5 hectares of pasture and 1 hectare of cacao beans. (App. 130.) Further despite having provided a dollar value for his lost crops in his Questionnaire response, Luciano initially testified at deposition that he had never placed a monetary value on his allegedly lost crops. (App. 134.) When confronted with his Questionnaire response, Luciano (again) changed his testimony and stated that he had calculated the stated dollar amounts for his crops. (App. 145-148.) But then, when the written response was taken away, Luciano conceded once more that he had not – and

[19] *See* App. 137-138 (Q: Other than the itchiness on your skin and the eyesight problems, do you believe you have suffered any additional personal injuries from the spray? A: No, just that).

could not – quantify the value of his allegedly lost crops (App. 150-151), and he produced no farming records to assist in making such calculations.[20]

4. The Mestanza Family

The Mestanza family provides 4 of the test plaintiffs in the first phase trial group:

- Victor Mestanza (husband of Ercilia; father of Edy; grandfather of Jennifer)
- Ercilia Bosquez (wife of Victor; mother of Edy; grandmother of Jennifer)
- Edy Mestanza (son of Victor and Ercilia; father of Jennifer)
- Jennifer Mestanza (14-year-old daughter of Edy; granddaughter of Victor and Ercilia)

Although the Mestanza family demonstrated problems with changing testimony similar to the other test plaintiffs, the misstatements in their Questionnaire responses raise even more serious concerns. The four Mestanza test plaintiffs family all stated in their Questionnaire responses that they were exposed to Plan Colombia herbicide at their "current home address" in Puerto Mestanza, a small community in the Sucumbíos province of Ecuador, right beside the river border with Colombia. Each plaintiff likewise submitted an individual causation statement asserting that he or she had lived in Puerto Mestanza for most of their lives (App. 179-180, 221, 225-226, 241, 242-243, 273, 275, 301.) At deposition, however, all four of the test plaintiffs admitted that their principal place of residence both now and on the date of their alleged exposures was not in Puerto Mestanza but in Guayaquil, which is 275 miles from the Ecuador-Colombia border (App. 189, 229-230, 247-248, 282-283). While Victor and Ercilia testified that they had spent the majority of their time at the family farm in Puerto Mestanza during 2000-2004 and that their granddaughter Jennifer had been with them at the farm when spraying allegedly

[20] Luciano likewise reversed course with regard to his alleged animal losses, first testifying that he did not know the value of the animals, then testifying that he had calculated the values in his Questionnaire response, and then, after the response was taken away, admitting again that he could not state how much the animals were worth. (App. 135-136, 141-144, 152-153.)

occurred between 2000 and 2002, no other members of their family were at the farm during the times that Victor and Ercilia allegedly saw spray planes. (App. 190-191, 231 to 231-A, 236-A, 293-295, 283-A to 283-B.) Victor's grown son Edy acknowledged in direct contravention to his Questionnaire response that he was rarely in Puerto Mestanza and that he had never been exposed to any Plan Colombia spraying. (App. 250-252, 256-257.) In his Questionnaire response, Edy had falsely alleged exposure in 2002 and claimed personal injuries including headaches, dizziness, vomiting, skin irritation, and sore throat, all of which were likewise falsely attributed to Plan Colombia spraying in his individual causation statement. (App. 244-245, 273-274.)[21] Moreover, as addressed more fully in Defendants' Response to Plaintiffs Motion to Dismiss Three Individual Plaintiffs, ECF No. 172 in *Arias*, ECF No. 132 in *Quinteros* (Jan. 6, 2009) at 3-10, the deposition testimony of the Mestanza test plaintiffs made clear that Questionnaire responses of four other Mestanza family members in the larger individual plaintiff group of non-test-plaintiffs were completely fictitious. Each of these plaintiffs (two of Victor's other grown children and two of Edy's minor children) live full time in Guayaquil and were not in Puerto Mestanza during any of the alleged spraying events. (App. 190, 193, 236-236-A, 253-255, 262-264, 267, 269.) Nonetheless, as set out in the defendants' Jan. 6th response brief at 3-10, each of these four Mestanza family members submitted sworn Questionnaire responses containing numerous false representations about, *e.g.*, having seen spray planes and helicopters overhead and having suffered a wide variety of personal injuries. Moreover, this apparent fraud

[21] Edy Mestanza claimed at his deposition that his correct signature did not appear on the Questionnaire response provided for him, although he acknowledged that certain portions of the response were specific to him. (App. 258.) Edy also identified his own signature on other Questionnaire responses submitted for his two minor sons and for his daughter (test plaintiff Jennifer). (App. 265, 266, 268-269, 270-272.) Edy insisted, however, that he had not authorized his minor sons (9-year-old Victor Manuel and 5-year-old David) to serve as plaintiffs in this litigation and that he did not believe that they were plaintiffs. (App. 264, 269 to 269-A.)

cannot be attributed solely (or even at all) to these other (non-test-plaintiff) Mestanza family members, as two of them are minors and one is mentally retarded.[22]

The testimony of the Mestanza test plaintiffs also includes the same changing stories that characterize the testimony of the other test plaintiffs. For example, in their Questionnaire responses, the four Mestanza test plaintiffs provide only broad and conflicting statements as to the dates of their alleged exposures to Plan Colombia herbicide, with Victor alleging exposure in 2002, Ercilia alleging exposure from 2000 until October 2002, Edy alleging exposure in 2002, and Jennifer alleging exposure in 2002-2006. (App. 181-182, 227, 244, 276.) At deposition, Edy admitted that he had not been exposed at all, as noted above. (App. 255-256, 257.) Victor and Ercilia, on the other hand, were now in agreement as to five specific dates of alleged exposure (December 2000, January 2002, September 2002, and October 7 and 10, 2002). (App. 192, 196, 201-203, 205, 232, 233, 235, 237-240.) Ercilia also changed her Questionnaire response stating that she had seen 3 planes and 1 helicopter during the alleged spraying events, testifying at deposition -- again now consistent with her husband Victor – that she in fact had seen 5 spray planes and 5 helicopters. (App. 227, 233-234.) Jennifer, meanwhile, changed her prior five-year potential exposure period to just two years, 2000 and 2002, and further admitted that she doesn't recall anything from 2000 and is relying solely on her grandfather Victor Mestanza's say-so as to her alleged exposure during that year. (App. 284, 285, 286, 288, 297.) After having provided a detailed Questionnaire response stating that she had seen 5 spray planes, multiple helicopters marked with the Colombian flag, a white cloud in the air and residue on the

[22] On December 23, 2009, without offering any explanation for the fraudulent Questionnaire responses, plaintiffs counsel moved to dismiss the claims of Victor Mestanza's two minor grandsons and the claim of his mentally-challenged daughter. The DynCorp defendants' January 6, 2009, response addresses in detail the misrepresentations made by each Mestanza non-test-plaintiff and by test plaintiff Edy Mestanza (ECF No. 172 in *Arias*, ECF No. 132 in *Quinteros*), to which plaintiffs' January 13, 2010 reply brief did not respond in any detail.

ground, Jennifer acknowledged at deposition that (other than claiming that she once saw a plane spraying in 2002), she could not recall anything else she had seen at the times of the alleged spraying events. (App. 276-277, 284-285, 286-290.)

The Mestanza test plaintiffs also changed course repeatedly on their claims of personal injuries and property damages. Edy Mestanza, whose Questionnaire response had alleged that exposures to Plan Colombia spraying had caused him to suffer from headaches, dizziness, vomiting, skin irritation, and a throat infection, conceded at deposition that he had not suffered any of these injuries (App. 245, 256-257), although he raised an entirely new claim that he had suffered emotional and psychological damages due to his alleged property losses and the alleged personal injuries of family members. (App. 256-257.) Edy's father, Victor Mestanza, backed away from the claims made in his Questionnaire response that his exposures had caused headaches, stomach aches, gastric problems and vomiting, stating at deposition that he wasn't sure what was causing those and other new medical problems he was experiencing. (App. 183, 195, 197, 204, 206, 209-210.) Jennifer Mestanza abandoned claims of headaches and stomach aches in her Questionnaire response and causation statement and further admitted that she had no basis for the $20,000 in paid medical expenses she had claimed in her Questionnaire response. (App. 278, 281, 290-291, 296, 301.) On the flip side, however, Victor Mestanza expanded at deposition the already expansive claims of property damage set out in his Questionnaire response and causation statement, adding new allegations of damages to 10 hectares of sugar cane, tomatoes, green peppers, cassava and grasslands, and the alleged deaths of large numbers of sheep, ducks, pigs and chickens. (App. 184, 187-188, 194, 198-200, 207, 208, 218, 221-222.)[23]

[23] Mr. Mestanza's allegation that all of his animals were dead as of the date of his last alleged exposure to Plan Colombia spraying in October 2002 (App. 214-215), is belied by a video he produced to defendants before his deposition, which Victor confirmed was taken at his property

Remarkably, despite contending in his Questionnaire response that his property damages exceeded $600,000, Victor Mestanza could produce no business or farming records to support his claims. (App.186, 187, 188, 213-214, 217, 211-212, 214-216, 220.) Edy Mestanza testified consistently with his Questionnaire response as to the hectares of crops and numbers of animals allegedly killed by the Plan Colombia spraying, but testified that he was relying solely on his father Victor for these numbers because he (Edy) had never even seen the crops or animals allegedly at issue, and Edy further completely disavowed the monetary values set forth in his Questionnaire response for the alleged losses. (App. 252, 259-261.)

5. **The Sandoval Family**[24]

Three members of the Sandoval family are serving as test plaintiffs:

- Dociteo Sandoval (father of Edgar and Wilber)
- Edgar Sandoval (25-year-old son of Dociteo; brother of Wilber)
- Wilber Sandoval (14-year-old son of Dociteo; brother of Edgar)

The Sandoval test plaintiffs present the same pattern of changing alleged dates of exposure, changing alleged personal injuries, and changing alleged property damages. In their Questionnaire responses, the three Sandoval test plaintiffs disagreed as to the date of their

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in Nov. 2002 (App. 207-208) and which is replete with pictures of lush green plants and apparently healthy farm animals. Excerpted photos from that video are attached hereto as Ex. I.

[24] Other children of Dociteo Sandoval are also named plaintiffs in this litigation, despite Mr. Sandoval's testimony that he did not want any of his children (except 25 year old Edgar) to be plaintiffs:

> Q: I understand that you do not want Marcelo and Roque to be plaintiffs. Do you want Wilber to be a Plaintiff?
>
> A: . . . I don't want any of my children – I do not accept that they are plaintiffs. . . . I'm surprised. I'm very surprised for having signed that document with that explanation.

(App. 322) (referring to his surprise at seeing his son Roque's Questionnaire response).

alleged exposure to Plan Colombia spraying, with Dociteo claiming that the exposure occurred at the end of 2003, Edgar claiming that the exposure occurred in 2006, and Wilber claiming that the exposure took place in 2004. (App. 304-305, 325-326, 341-342.) At deposition, however, Dociteo and Edgar were now in agreement that the exposure took place during three days at the end of 2003; Wilber also testified that the exposure took place on three separate days, but he could not recall the year in which this occurred. (App. 313, 319-320, 321, 330-331, 334, 338, 351-352.) Wilber's memory was far more detailed at deposition, however, as to what he saw during these purported spraying events: while his Questionnaire response states that he didn't see anything (App. 326), at deposition, Wilber testified that he saw 5 spray planes and 2 helicopters on 3 separate occasions, all flying in a specific formation. (App. 331-333, 335-339.) Dociteo and Edgar also provided new answers to these questions at deposition, with Dociteo and Edgar for the first time specifying that they had seen 2 helicopters and Edgar increasing the number of planes he had seen from 3 to 5. (App. 305, 314, 342, 348.) As a result, at deposition, the three Sandoval test plaintiffs were all suddenly testifying to the same story. Moreover, whereas Edgar's Questionnaire response had claimed exposure 4 kms from the border, at deposition, Edgar testified (now consistent with his father) that he was exposed on the family farm adjacent to the river border. (App. 312, 313, 342, 347.) Wilber, meanwhile, who stated in his Questionnaire response that he was exposed at his home, testified at deposition that two of his alleged exposures occurred while he was at school. (App. 326, 332, 336.)

As to personal injuries, Edgar and Wilber both abandoned in their depositions the claims in their Questionnaire responses that they had incurred specified out-of-pocket expenses for medical treatment ($20 and $300, respectively) (App. 329, 340, 346, 350), but Edgar and Dociteo added new personal injury allegations to those claimed in their Questionnaire responses and causation statements, with Dociteo adding a new claim of vision loss (App. 306-307, 323, 324), and Edgar newly contending that his alleged exposure had caused him to suffer vomiting and diarrhea. (App. 343-344, 349, 353-354.) Dociteo likewise added to the family's claims for crop damage, testifying that in addition to the alleged crop damages set forth in his Questionnaire response and causation statement, the herbicide spray also had killed 10 coconut trees, as well as cassava, bananas and oritos. (App. 308, 310-311, 315-318, 324.)

6. <u>Elvia Alvarez</u>

Ms. Alvarez is the only member of her family who has been proffered as a test plaintiff. Her testimony is typical of the other test plaintiffs. In her Questionnaire response, Ms. Alvarez stated that she was exposed to Plan Colombia spraying several times between 2002 and 2006. (App. 355-356.) In her deposition, however, she testified that she witnessed only two spray events, in April 2001 and sometime around October 2001. (App. 366, 378-379.) Whereas her Questionnaire response did not answer the question about the number of helicopters that she had seen, Elvia testified at deposition that she saw 6 helicopters. (App. 356, 366-367.) The location of the alleged exposures also changed, from 3 km from the border in her Questionnaire response and causation statement, to 7 km from the border at her deposition. (App. 356, 365, 396.) Ms. Alvarez's testimony regarding her alleged exposure in April 2001 became particularly convoluted when she was confronted with the fact that her son Byron – who Ms. Alvarez had alleged was with her during the April 2001 exposure – had stated in his Questionnaire response (App. 401, 402) that he had *not* seen any spray planes. Ms. Alvarez responded that Byron had not seen the planes because he was working on another part of the farm that was more mountainous, a fact she claimed to recall because she had recorded that information in a notebook along with the April 2001 date. (App. 372-373, 402.) When asked if she could produce the notebook, however, Ms. Alvarez claimed to have thrown it away three years ago. (App. 373-374, 375-377.)

Ms. Alvarez also used her deposition testimony as an opportunity to expand upon the broad allegations of personal injury and property damage set forth in her Questionnaire response. As compared to her Questionnaire response and causation statement, Ms. Alvarez testified to new personal injuries (headache, dizziness, stomach ache, diarrhea), new alleged crop damages (2 additional hectares of pasture, 1 additional hectare of plantains, 1 hectare of peanuts and 30 assorted plants of guava, grape, and avocado), and new alleged animal deaths (2 additional cows, 1 additional horse, 1 additional dog, and 40 guinea pigs). (App. 357-359, 361-364, 368-371, 386-387, 388.) Like other test plaintiffs, Ms. Alvarez first tried to justify in her deposition the high values placed on her crops in her Questionniare response, *see e.g.*, App. 389-390, but her calculations quickly fell apart upon questioning. (App. 390-393.)

7. <u>Edgar Balcazar</u>

Mr. Balcazar is the only test plaintiff from his family.[25] Like the other test plaintiffs, his deposition was replete with new and different claims as to his alleged exposures and damages. In his Questionnaire response, Mr. Balcazar alleged that he had been exposed to Plan Colombia spray "in the year 2001 and 2002 until the year 2007," while at his deposition, Mr. Balcazar was unwilling even to guess at the years of his alleged exposure. (App. 403, 413, 414, 415.) Whereas his Questionnaire stated that he had not seen a spray plane, at deposition he testified that he had, albeit at a distance. (App. 403, 412, 413.) While Mr. Balcazar repeated at deposition his claim in his Questionnaire responses to a variety of non-specific personal injuries, he admitted that he

[25] Like test plaintiffs Edy Mestanza and Dociteo Sandoval, Edgar Balcazar was surprised to learn at his deposition that his son is also a plaintiff, testifying that he did not "want [his] son Diego to be identified as a plaintiff in this litigation." (App. 424.)

has no basis for and cannot confirm the representation in his Questionnaire response that he spent $3,000 out-of-pocket for medical expenses. (App. 406, 416-417.) Moreover, Mr. Balcazar's testimony in explaining why he initially forgot during his deposition to mention his claimed respiratory symptoms (symptoms for which, as with all of the medical symptoms claimed by all the test plaintiffs, there is no documentary evidence) raises obvious red flags as to the reliability of his testimony: "You cannot be after every detail for what happened to you because time goes by and, but that's something we can recognize if it comes into your eyes and your nose why shouldn't your respiratory ways be affected as well?" (App. 422-423.)

Finally, Mr. Balcazar's testimony as to his alleged crop damages bears virtually no resemblance to his identification of crop damages in his Questionnaire responses: Some of the alleged crop damages decreased (6 hectares of cacao in his Questionnaire dropped to 2 hectares at deposition, 5 hectares of coffee dropped to 2-3 hectares, 35 hectares of pasture dropped to 20 hectares, and ½ hectare of allegedly damaged coconuts disappeared altogether), while others increased (1 hectare of rice became 3 hectares at deposition, ½ hectare of yucca increased to 1-1½ hectares, and 2 hectares of lost plantains and a variety of lost fruit trees, including avocado, lime, orange, and grapefruit were identified at deposition whereas such crops had not been identified in his Questionnaire). (App. 407, 418-420.) Further, at his deposition, Mr. Balcazar conceded that he did not even own the two farms at which he alleged that these damages occurred, as the title to one farm is held solely by his mother and title to the other is held by his wife, neither of whom are plaintiffs in this litigation. (App. 408-409.)

D. The Test Plaintiffs' History of Changing Stories Regarding Their Alleged Exposures Began Long Before This Litigation.

In Section V.H. of the agreed-upon Plaintiffs' Questionnaire, each of the test plaintiffs was asked whether they had made any previous complaints about their alleged exposures to Plan

Colombia spraying to any other party. In their responses, 19 of the 20 test plaintiffs either denied having made any such complaints or failed to respond to this question,[26] and the one plaintiff who answered "yes" failed to provide the requested information as to whom he had complained and what had been communicated. (App. 246.) These representations were not true. Rather, as evidenced by documents produced by the test plaintiffs on the eve of their depositions, as well as an Ecuadorian judicial complaint located by the DynCorp defendants through their own investigation, at least six of the seven test plaintiff families had raised claims of alleged exposures and damages from Plan Colombia spraying in other forums. While the test plaintiffs' failure to disclose these complaints in their Questionnaire responses is improper in its own right (and impeded the DynCorp defendants in their ability to effectively prepare for the test plaintiffs' depositions), the documents now available to defendants are particularly telling in that they demonstrate that the test plaintiffs' history of false and changing stories regarding alleged exposures to and injuries from Plan Colombia spraying began long before this litigation.

For example, in December 2002, various Ecuadorian plaintiffs sued the President of Ecuador and other government officials in an Ecuadorian court for failing to protect them from alleged personal injuries and property damages purportedly arising from exposure to the Republic of Colombia's spraying of herbicide during the period December 2000 through July 2002. (App. 427 *et seq*.) Test plaintiff Santos Calero signed this complaint despite his acknowledgment in this litigation that he was not exposed (even allegedly) to Plan Colombia spraying until August 2003, eight months after the Ecuadorian complaint was filed. (App. 11,

[26] App. 6-7, 25, 41, 59, 69, 103, 116, 126, 160-161, 172, 175-176, 185, 228, 279-280, 309, 328, 345, 360, 405.

15, 443.)[27] Similarly, in March 2002, test plaintiff Elvia Alvarez signed the same complaint (App. 448) and also prepared two certifications with her brother, the President of her residential commune Rivera Del Oriente, in support of her complaint that Plan Colombia spraying in December 2000 and January 2001 had, *inter alia*, caused the death of her husband in February 2001. (App. 380-385, 397-398, 399-400) But in this litigation, Ms. Alvarez testified that she was not exposed to Plan Colombia spraying until April 2001, two months after her husband's death, and conceded that her husband's illness began in early 2000, well before even the dates of alleged exposure asserted in the prior certification she prepared with her President-brother. (App. 366, 382-383, 394-395A.) (Ms. Alvarez is not claiming damages for the death of her husband in this litigation.)

Further, the third party complaints by other test plaintiffs set forth litanies of alleged personal injuries and property damages that are far different from those they claim in this case – either in their 2008 sworn Questionnaire responses or in their 2009 deposition testimony. In the DynCorp defendants' prior briefing in response to plaintiffs' motion to dismiss three non-test plaintiff Mestanza family members, defendants demonstrated that test plaintiff Victor Mestanza had secured, for purposes of a separate litigation in Ecuador, a fraudulent medical certification identifying alleged personal injuries to his grandson Victor Manuel, despite the now-acknowledged fact that his grandson was not exposed to any spraying operations and was living 275 miles away in Guayaquil at the time of the alleged spraying events. *See* Defendants' Response to Plaintiffs' Motion to Dismiss Three Plaintiffs, ECF No. 172 in *Arias*, ECF No. 132 in *Quinteros*, at 9-10. In addition to this, however, Victor Mestanza also secured medical

[27] A second test plaintiff, Rosa Altamirano, also signed on to the Ecuadorian complaint (App. 481), despite stating in her Questionnaire that her first exposure was not until October 2002, three months after the end of the exposure period alleged in that complaint. (App. 163.) She also failed to answer the Questionnaire section asking about other complaints. (App. 166-167.)

certifications on his own behalf and on behalf of his granddaughter, test plaintiff Jennifer Mestanza, in which he claimed personal injuries that his and Jennifer's deposition testimony now indicates did not occur. (App. 223, 302.) In particular, while the 2003 medical certification Victor secured for his granddaughter Jennifer states that Plan Colombia spraying had caused her to suffer both a 35% vision loss requiring eyeglasses and chronic gastritis, Jennifer testified at her deposition in this case that she has never worn eyeglasses or had vision problems, and she could not recall ever suffering from any stomach problems. (App. 292, 298-300.) The 2003 medical certification for Victor Mestanza is virtually identical to that prepared for his granddaughter (and indeed virtually identical to the admittedly-fraudulent certification prepared for his young grandson, Victor Manuel), similarly claiming that Plan Colombia spraying had caused him to lose 35% of his vision and caused chronic gastritis. Victor Mestanza notably backed away from those claims at his deposition in November 2009. (App. 209-210.)

Test plaintiff Jorge Salas signed a December 2002 certification in which he alleged that exposure to Plan Colombia spraying caused skin infections, acute sores, inflammation of the throat and dry cough, fungus in the intestines, dizziness, and fevers – a laundry list of alleged maladies that only marginally intersects with his claims of nose and eye irritation, throat inflammation, and skin itching and infection at his deposition in this case. (App. 78-79, 83-84, 99-100.) Test plaintiff Rosa Altamirano assisted in preparing a March 2002 certification signed by the president of her cooperative setting out Rosa's complaint that the Plan Colombia spraying had caused her family (the Quevedos) to suffer respiratory problems – an allegation not made in any of the Quevedo test plaintiffs' Questionnaire responses, causation statements, or deposition testimony – as well as Rosa's complaints of crop damage to rice and cassava that likewise are nowhere alleged in this litigation. (App. 155-156, 170-171.) Finally, test plaintiff Edgar

Balcazar prepared an alleged "report of damages and harms from Plan Colombia" in May 2002 in which he made no mention of the now-alleged loss of cacao, coffee, coconuts, sugarcane, rice and yucca, did not claim of the now alleged death of 2 or 3 horses and 30-50 hens, and alleged only 4 pigs dying as compared to the 10 now alleged in this case. (App. 407, 421, 425-426.)

The only consistent message that emerges from the test plaintiffs' third party complaints, the test plaintiffs' Questionnaire responses, and the test plaintiffs' deposition testimony, is that every time these test plaintiffs are asked about their alleged exposures to Plan Colombia spraying, they come forward with a different story – a pattern that defendants can only assume will continue if these cases ever get to trial. While this record would surely provide defendants with a wealth of material for cross-examination, the test plaintiffs' repeated changes in their allegations dating back before this litigation was filed significantly prejudices defendants in their ability to prepare their defense (to exposures allegedly occurring when? occuring where? causing what alleged personal injuries and property damages?), and they demonstrate that the problems in the plaintiffs' Questionnaire responses and their violations of repeated Court orders cannot be blamed on technical glitches or misunderstandings. The inherent unreliability of the test plaintiffs' factual claims cannot support the continued prosecution of their claims.

II. THE TEST PLAINTIFFS SHOULD BE SANCTIONED FOR THEIR FALSE AND FRAUDULENT DISCOVERY RESPONSES AND REPEATED VIOLATIONS OF COURT ORDERS

A. Dismissal Is Warranted As Sanction For The Test Plaintiffs' Submission Of False and/or Fraudulent Discovery Responses.

Although dismissal is "a severe sanction, and should be resorted to only to the extent necessary to induce future compliance and preserve the integrity of the system . . . the most severe in the spectrum of sanctions provided by statute or rule must be available to the district court in appropriate cases." *Weisberg v. Webster*, 749 F.2d 864, 869-870 (D.C. Cir. 1984). As the Supreme Court has explained, the Rule 37 sanction of dismissal "must be available . . . not merely to penalize those whose conduct may be deemed to warrant such a sanction, but to deter those who might be tempted to such conduct in the absence of such a deterrent." *Nat'l Hockey League v. Metro. Hockey Club, Inc.*, 427 U.S. 639, 643 (1976). The availability of dismissal is essential for effective case management. "[I]f district court judges are to discharge their heavy case processing responsibilities effectively, their power to dismiss . . . must be more than theoretical." *Bristol Petroleum Corp. v. Harris*, 901 F.2d 165, 167 (D.C. Cir. 1990) (internal citations and quotation marks omitted). As this Court noted in its January 12, 2010 Opinion dismissing the claims of 590 other plaintiffs in this litigation with prejudice for failure to submit accurate Questionnaire responses, dismissal is particularly appropriate here, because lesser sanctions have been imposed previously but without success. *See* 1/12/10 Mem. Op., at 3-4.

The test plaintiffs' misconduct in this case in providing false evidence under oath strikes at the core of the judicial process and cannot be countenanced. As the United States Supreme Court has explained, "[f]alse testimony in a formal proceeding is intolerable. We must neither reward nor condone such a 'flagrant affront' to the truth-seeking function of adversary proceedings." *ABF Freight Sys., Inc. v. N.L.R.B.*, 510 U.S. 317, 323 (1994) (citations omitted). Accordingly, numerous courts faced with discovery abuses of the type here at issue have concluded that dismissal is the appropriate sanction. *See Chavez v. City of Albuquerque*, 402 F.3d 1039, 1046 (10th Cir. 2005) (affirming district court's dismissal of plaintiff's jury verdict where plaintiff perjured himself during discovery); *Archibeque v. Atchison, Topeka and Santa Fe Ry. Co.*, 70 F.3d 1172, 1175 (10th Cir. 1995) (affirming dismissal of case for plaintiff's submission of false and misleading discovery responses); *Dotson v. Bravo*, 202 F.R.D. 559, 574 (N.D. Ill. 2001) ("Dismissal is an appropriate sanction for giving false interrogatory responses.")

(bold and italic typeface omitted); *In re Amtrak "Sunset Limited" Train Crash*, 136 F. Supp. 2d 1251, 1257, 1271 (S.D. Ala. 2001) (dismissing plaintiff's claim with prejudice for providing knowing false interrogatory answers).

The D.C. Circuit has set forth three basic justifications that support the use of dismissal as a sanction for misconduct:

- "First, the court may decide that the errant party's behavior has severely hampered the other party's ability to present his case – in other words, that the other party has been so prejudiced by the misconduct that it would be unfair to require him to proceed further in the case." *Webb v. District of Columbia*, 146 F.3d 964, 971 (D.C. Cir. 1998) (internal quotations and citations omitted).
- "Second, the court may take account of the prejudice caused to the judicial system when the party's misconduct has put an intolerable burden on a district court by requiring the court to modify its own docket and operations in order to accommodate the delay." *Id.* (internal quotations and citations omitted).
- "And finally, the court may consider the need to sanction conduct that is disrespectful of the court and to deter similar misconduct in the future." *Id.* (internal quotations and citations omitted).

Any one of these justifications alone is sufficient grounds for dismissal. *Id.* In this case, all three justifications are present.

1. **The Test Plaintiffs' Failure to Provide Accurate Information Regarding The Alleged Factual Bases Of Their Claims Has Significantly Prejudiced Defendants.**

The test plaintiffs' submission under oath of the factual bases of their claims, which they have now acknowledged are false, has significantly prejudiced defendants at every stage of the pretrial process. As this Court noted in its January 12, 2010 Opinion, plaintiffs' failure to provide accurate and complete Questionnaire responses, "impedes the defendants' ability to prepare their defense." 1/12/10 Mem. Op., at 6 ("Without the requested information, the defendants are hampered in knowing the full extent, nature and location of the plaintiffs' alleged damages.") (citing *In re Phenylpropanolamine (PPA) Prods. Liab. Litig.*, 460 F.3d 1217, 1234 (9th Cir. 2006). This prejudice began with defendants' enormous expenditure of time and resources in repeatedly seeking judicial assistance over the course of five separate motions hearings in 2008 and 2009 in an (apparently futile) effort to secure accurate Plaintiff Questionnaire responses and with defendants' prodigious but wasted efforts in analyzing Questionnaire responses that have now been shown to be wholly unreliable.

The prejudice continued with the defendants' frustrated efforts to meaningfully prepare for the 20 test plaintiff depositions, conducted over a four-week period in Quito, Ecuador. While defendants were able to expose during these depositions at least some of the falsehoods in the test plaintiffs' Questionnaire responses, defendants did not and could not question the test plaintiffs as to every response set forth in their Questionnaires and have no way to determine whether the other Questionnaire responses are equally false. *See In re Amtrak*, 136 F. Supp. 2d at 1260 ("A party is entitled to rely on an opposing party's written responses to interrogatory questions; he/she/it is not required to ask a party deponent every question in his/her deposition that the party previously answered in the set of interrogatories. Indeed, such a practice would render the interrogatories superfluous and unnecessarily increase the expense of a deposition."). Moreover, because of the false information in the Questionnaire responses, defendants prepared their deposition questions to address now-abandoned factual allegations, and defendants were unable to adequately prepare question regarding the *new* factual allegations the test plaintiffs made for the first time at the depositions themselves. In addition, as noted above with respect to the test plaintiffs' false Questionnaire responses as to complaints to third parties, the test plaintiffs' misconduct also prevented defendants from pursuing potential fruitful areas of investigation in preparation for the depositions.

Looking forward, defendants will be significantly prejudiced in their ability to meaningfully prepare for trial. Defendants plainly cannot rely on any of the information set forth in the test plaintiffs' Questionnaire responses. Nor, given the ever changing nature of the plaintiffs' allegations, can defendants have any confidence that the test plaintiffs will stick to the stories told at deposition. The prejudice to defendants is particularly significant given the central importance of the information at issue in the test plaintiffs' false Questionnaire responses. For example, in preparing their expert case, it is essential that defendants have accurate information about, *e.g.*, the times and locations of the alleged exposures (to rebut plaintiffs' necessary showing that any herbicide spray in the vicinity could have reached the individual plaintiff or reached them at a sufficient dose to cause injury), the types of personal injuries allegedly caused by the spraying (as well as an accurate history of other medical or environmental conditions that might present alternative causes), and the types of crops and livestock allegedly impacted by the spray and the nature of these alleged impacts. As it is, however, defendants can only proceed based upon guesswork and speculation, must sift through plaintiffs' varying and often mutually exclusive discovery responses, and must prepare for any variety of different allegations that might be made by the test plaintiffs at trial. As this Court explained in its January 12, 2010 Opinion, "draw[ing] conclusions based on incomplete information … is not the defendant's duty." 1/12/10 Mem. Op. at 6.

More fundamentally, of course, defendants are prejudiced in having to respond at all to inherently unreliable and demonstrably false factual allegations. The test plaintiffs have been provided numerous opportunities to present a reliable factual predicate for their claims, and they have failed to do so. They should not be allowed to continue to impose upon defendants the significant costs of litigating their nebulous and shifting claims.

2. The Test Plaintiffs' Failure to Provide Accurate Information Regarding The Alleged Factual Bases Of Their Claims Has Significantly Prejudiced The Judicial Process.

The Court has since November 2007 devoted considerable time and resources in an effort to secure accurate factual disclosures from the individual plaintiffs. At each turn, when defendants were forced to file motions to compel, to seek sanctions for plaintiffs' noncompliance with prior orders, or to defend against plaintiffs' objections to the Magistrate Judge's orders, the Court has ruled in favor of the defendants. In so doing, the Court was required to wade through a total of 435 pages of briefing (plus over 1,150 pages of exhibits) and to partake in motions hearings totaling some 278 transcript pages. In an effort to resolve the Court's concerns, plaintiffs' counsel provides specific assurances that each of the individual plaintiffs had answered the Questionnaire "as fully as they could based upon personal knowledge." Jt. Mot. to Dismiss, ECF No. 86 in *Arias*, ECF No. 48 in *Quinteros*, Feb. 19, 2009, at 10. The Court accepted these assurances absent evidence to the contrary, but the Court made clear through its dismissal with prejudice of two categories of plaintiffs who failed to provide information that they clearly should have known that a plaintiff's knowing failure to provide accurate information in his or her Questionnaire response would not be tolerated. *See* 1/12/10 Mem. Op.

The testimony of the test plaintiffs demonstrates that the plaintiffs' counsel's representation that plaintiffs had provided full and accurate Questionnaire responses to the best of their knowledge was false and that all of the Court's efforts over the past two years have been for naught. Moreover, if the test plaintiffs are allowed to continue with their claims, the Court undoubtedly will be required to intervene again and again in the day-to-day pretrial process in an effort to somehow mitigate the prejudice caused to the defendants by the test plaintiffs' misconduct. The Court will also be required to preside over a trial where it will be "virtually impossible for the jury to determine the truth" behind the test plaintiffs' allegations. *In re Amtrak*, 136 F. Supp. 2d at 1268.

As the D.C. Circuit explained in affirming a dismissal sanction in *Weisberg*, 749 F.2d at 193 (citation omitted), "if parties are allowed to flout their obligations [to respond to interrogatories], choosing to wait to make a response until a trial court has lost patience with them, the effect will be to embroil trial judges in day-to-day supervision of discovery, a result directly contrary to the overall scheme of the federal discovery rules." The test plaintiffs have failed to abide by the Court's orders, they have repeatedly embroiled the Court in futile efforts to compel compliance, and they have through their false discovery responses subverted the judicial process. Their claims should be dismissed.

3. The Test Plaintiffs Have Shown Disrespect to the Court and Dismissal Is Necessary to Deter Such Misconduct By These and Other Litigants.

The history of the test plaintiffs' repeated violations of the Court's discovery orders leaves no question that the test plaintiffs have failed to provide the Court with the proper respect. Dismissal is necessary to sanction the test plaintiffs' disrespectful behavior and to deter other litigants from engaging in similar misconduct. The need for a clear sanction in this case is particularly compelling because the Court's response to the test plaintiffs' misconduct likely will determine whether the Court will be able to maintain any control whatsoever with respect to the remaining 2,001 individual plaintiffs in this case, whose Questionnaire responses must be assumed to contain the same glaring problems as those of the 20 test plaintiffs. Moreover, litigants in other proceedings may be tempted to resort to similar misconduct if they believe that the Court is unwilling to impose appropriate and meaningful sanctions to ensure compliance with its orders. *See Nat'l Hockey League*, 427 U.S. at 643 (stating that if the court of appeals' reversal of the sanction of dismissal were to remain undisturbed, "other parties to other lawsuits would feel freer than we think Rule 37 contemplates they should feel to flout other discovery orders of other district courts").

The Court has shown ample patience in its dealings with the plaintiffs. The Court has repeatedly given the plaintiffs additional time to provide factual information they should have had in hand before they even filed their claims, and it has repeatedly indulged plaintiff counsel's now-disproved assurances that the information had been accurately provided. The time for patience is over. If the Court's orders are to have any meaning, the 20 test plaintiffs' claims must be dismissed. Moreover, because the test plaintiffs' misconduct was willful and because the test plaintiffs have now, in any event, conclusively demonstrated their inability to present any reliable, consistent evidence that would state a cause of action for alleged harms from purported Plan Colombia spray exposures, their dismissals should be with prejudice. *See* 1/12/10 Mem. Op.; *see also Norman v. United* States, 467 F.3d 773 (D.C. Cir. 2006) (affirming dismissal with prejudice where evidence demonstrated that refiling of claim would be futile); *Handy v. Shaw, Bransford, Veilleux & Roth*, No. 00-2336, 2006 WL 3791387, at *7 (D.D.C. Dec. 22, 2006) (dismissal with prejudice appropriate as sanction for willful misconduct).

B. <u>In the Alternative, Defendants Request That The Test Plaintiffs Be Precluded From Defending Their False Questionnaire Responses and That The Jury Be Instructed Regarding the Test Plaintiffs' Misconduct.</u>

If the Court elects to allow the test plaintiffs to proceed with their claims, defendants request that the Court issue an alternative sanctions order that provides defendants with at least some measure of relief from the prejudice imposed upon them by the test plaintiffs' misconduct. <u>First</u>, defendants request that the test plaintiffs be precluded from presenting any evidence or argument at trial to defend, explain, or mitigate the fact that they provided false statements under oath in their Questionnaire responses. As this Court has noted, such a preclusion order is an "unexceptional remedy that is contemplated in the federal rules" and it is plainly warranted here. *See Moore v. Napolitano*, No. 00-953 (RWR-DAR), 2009 WL 2450280, at *1-2, 9 (D.D.C. Aug. 7, 2009) (precluding defendant from introducing as evidence any information responsive to an interrogatory that was not produced in a timely manner); *see also Jung v. Neschis*, No. 01 Civ. 6993, 2009 WL 762835, at *24 (S.D.N.Y. Mar. 23, 2009) (adopting report and recommendation precluding the plaintiffs from using fraudulent evidence or amending reports to take it into account). Second, defendants request that the Court instruct the jury at any future trials that the test plaintiffs provided false information under oath regarding the basic factual foundations of their alleged claims and that this conduct may be considered by the jury in assessing the test plaintiffs' credibility. *See, e.g., Jung*, 2009 WL 762835, at *24 (adopting report recommending jury instruction that jurors should consider fabricated evidence and false statements in assessing the plaintiff's credibility on other matters); *Bernal v. All Am. Investment Realty, Inc.*, 479 F. Supp. 2d 1291, 1301 (S.D. Fla. 2007) (ordering jury instruction that jurors may take into account the defendant's false statements and conduct when considering his credibility); *Rybner v. Cannon Design, Inc.*, No. 95 Civ. 0279 (SS), 1996 WL 470668, at *6 (S.D.N.Y. Aug. 20, 1996) ("[D]efendants will be permitted to inform the jury of [plaintiff's] dishonesty and a jury charge will be given that any falsehood under oath should be considered seriously by jurors in assessing [plaintiff's] credibility.").

III. THE REMAINING 2,001 INDIVIDUAL PLAINTIFFS SHOULD BE BROUGHT INTO COMPLIANCE WITH THE COURT'S PRIOR DISCOVERY ORDERS.

In addition to establishing their own inexcusable misconduct, the test plaintiffs' depositions demonstrated without question: (1) that defendants (and the Court) can have no confidence in the factual information provided to date by the remaining 2,001 individual plaintiffs in this litigation and (2) that without further order from the Court to finally secure accurate and meaningful information from these plaintiffs, this litigation cannot meaningfully proceed. Defendants accordingly request the Court to issue a detailed order providing the 2,001 individual plaintiffs with one last opportunity to provide what the Court has long required: verified, factual and complete responses to the Plaintiffs' Questionnaire and individualized expert causation statements based upon a meaningful scientific assessment that links each individual plaintiff's alleged exposure to his or her alleged personal injuries and/or property damages. The Court's order should further provide that if plaintiffs fail to provide the ordered information and causation statements, their claims will be dismissed with prejudice.

With respect to the Plaintiffs' Questionnaire, defendants submit that the Court need not order the individual plaintiffs to prepare completely new Questionnaire responses. Indeed, absent some showing that the individual plaintiffs would approach the Questionnaires differently, such an order would not provide any meaningful assurance that the plaintiffs' new responses would be any more accurate than their old ones. Instead, defendants request that each individual plaintiff be required to provide a sworn certification that confirms the accuracy of his or her prior Questionnaire responses and/or provides corrected information to those questions that were answered inaccurately. To ensure that the individual plaintiffs are providing accurate information, the proposed certification should contain a number of additional safeguards:

First, the certification should state that plaintiffs are being required to prepare the certificate because of the Court's concerns about the reliability of the previous Questionnaire responses. Second, the certification should state that if the certification is shown to be knowingly inaccurate in any respect, the plaintiffs' claims will be dismissed and that the plaintiff (or his or her counsel) will be required to pay defendants' costs in seeking such dismissal. Third, plaintiffs should be required to certify that he or she has read both the certification and his or her prior Questionnaire responses in full (or, if the plaintiff is unable to do so, that the documents have been read to him or her). Fourth, the plaintiffs should be required to physically sign the certificate (as opposed to providing an electronic signature), have it witnessed, and have the original copy of the signed certificate maintained by plaintiffs' counsel in the United States and available for inspection by defendants upon reasonable demand. A proposed certification providing such assurances is attached to the proposed order being filed with this motion.

With respect to the previously-ordered causation statements, the DynCorp defendants submit that the only possible course of action is an order requiring plaintiffs to provide new statements. As set forth above, the aggregate causation statements provided by plaintiffs to date (with only a one-paragraph boilerplate recitation of the individual plaintiff's allegations) are directly contrary to the Court's repeated Orders that plaintiffs provide *individualized* causation statements that make "some connection based upon some scientific assessment between the allegation that spraying happened and that spraying caused these symptoms." 11/25/08 Hr'g Tr. (Ex. C) at 60:19-21; *see also* 7/17/09 Hr'g Tr. (Ex. D) at 39 ("I have made it clear that there's got to be some individualized assessments with regard to each individual plaintiff and each individual plaintiff's complaints about harm or damage.").

Moreover, because the prior causation statements are based solely on Questionnaire responses that have now been shown unreliable, the boilerplate paragraph 16 in each causation statement likely does not even address the individual plaintiffs' actual alleged exposures or harms. Further, the failure of the test plaintiffs after three years of litigation – and after defendants' production of hundreds of thousands of pages of Plan Colombia documents and nine years of electronic "spray line" data covering the entire Colombia-Ecuador border – to provide any reliable and consistent information as to the factual predicates of their claims makes the need for meaningful causation statements all the more evident. *See In re Vioxx Products Liability Litigation*, 557 F. Supp. 2d 741, 744 (E.D. La. 2008) (noting that while individual causation statements "may not have been appropriate at an earlier stage before any discovery had taken place … this case is no longer in its embryonic stage").

In light of plaintiffs' repeated – albeit baseless – claims that the Court's prior orders requiring causation statements were ambiguous, defendants request that the Court issue a detailed order that clearly specifies what the Court is requiring by way of a scientific assessment of each individual plaintiff's claims: First, the causation statement must specifically address the individual plaintiff's allegations of exposure, including some scientific assessment of the proximity of the plaintiff to any alleged spraying events on the dates of alleged exposure and some scientific basis for a conclusion that the spray could have reached the plaintiff or their property at a dose level sufficient to cause injury or damage. Second, the causation statement must specifically address the individual plaintiff's claims of personal injury and provide some scientific basis for a conclusion that his or her alleged exposure to Plan Colombia spray could have caused each of the specific types of injury alleged. Third, the causation statement must specifically address the individual plaintiff's claims of property damage and provide some scientific basis for a conclusion that the alleged exposure to Plan Colombia spray could have caused each of the specific property damages alleged.

In addition, each of the foregoing assessments in the causation statements must be proffered by an expert who is specifically qualified to speak to the issue at question. *See Acuna v. Brown & Root, Inc.*, No. SA-96-CA-543-OG, 1998 WL 35283824, at *5 (W.D. Tex. Sept. 30, 1998) (That the court's orders requiring "affidavits from qualified experts" did not "specif[y] the particular type of expert required . . . does not excuse Plaintiffs from the requirement that the experts they offer actually be qualified in the subject matter area in which [they] testif[y]."), *aff'd*, 200 F.3d 335 (5th Cir. 2000). Thus, for example, plaintiffs may not rely, as they have to date, solely on Dr. Campaña to prepare the causation statements because Dr. Campaña does not even purport to have the requisite expertise in exposure assessment, animal toxicology, or agronomy to speak to the plaintiff's exposure and property damage allegations.

Finally, in light of the testimony from three of the test plaintiff families that minor children have been put forward as plaintiffs in this litigation without their parents' knowledge, approval, or authorization, *see supra* nn. 21, 24, and 25, defendants request that the Court require signed parental authorizations on behalf of each of the minor plaintiffs in the remaining individual plaintiff group. *See* Fed. R. Civ. P. 17(c) (addressing capacity of minors to bring suit); *Weinbaum v. City of Las Cruces, New Mexico*, 465 F. Supp. 2d 1164, 1166 n.1 (dismissing claim of minor plaintiff because she "lacks the legal capacity to sue on her own behalf"); *Woods v. Wills*, 400 F. Supp. 2d 1145, 1181 (E.D. Mo. 2005) ("To maintain a suit in federal court, a minor must be represented by a competent adult").

IV. THE COURT SHOULD ORDER PLAINTIFFS' COUNSEL TO PAY THE DEFENDANTS THEIR EXPENSES AND FEES IN BRINGING THIS MOTION.

Finally, the defendants request their reasonable expenses, including attorney's fees, in bringing this motion. Rule 37 provides that when granting a motion for sanctions for failure to comply with a court order, "the court must order the disobedient party, the attorney advising that party, or both to pay the reasonable expenses, including attorney's fees, caused by the failure, unless the failure was substantially justified or other circumstances make an award of expenses unjust." Fed. R. Civ. P. 37(b)(2)(C); *see also Kornagay v. AT&T*, No. 05-0001, 2008 WL 4482970, at *1 (D.D.C. Sept. 29, 2008) ("This section of Rule 37 is mandatory unless 'the disobedient party' meets its burden to avoid expenses"). Plaintiffs' failures here are not justified and no known circumstances make an award of fees unjust. In light of defendants' understanding that plaintiffs' counsel have agreed to cover all of plaintiffs' costs in this litigation, defendants request that the Court specify in its order that the payment of defendants' expenses be made by plaintiffs' counsel, as the Court did in its previous order sanctioning plaintiffs in this case. *See* 7/17/09 Hr'g Tr. at 50:12-51:1 (Ex. D).

CONCLUSION

For the foregoing reasons, defendants respectfully request that their motion for sanctions be granted.

Dated: January 26, 2010

Respectfully submitted:

/s/ Eric Lasker

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EXHIBITS TO DEFENDANTS'
MOTION FOR SANCTIONS

Document	Exhibit No.
October 21, 2008 Order	A
Excerpts of Nov. 27, 2007 Hearing Transcript	B
Excerpts of Nov. 25, 2008 Hearing Transcript	C
Excerpts of July 17, 2009 Hearing Transcript	D
Soloman, K.R., Marshall E.I.P., Carrasquilla, G, *Human Health and Environmental Risks from the Use of the Glyphosate Formulations to Control the Production of Coca in Colombia: Overview and Conclusions,* 72 Journal Toxicology and Environmental Health, Part A, 914-920 (2009)	E
U.S. Dept. of State, Memorandum of Justification Concerning the *Secretary of State's 2007 Certification of Conditions Related to the Aerial Eradication of Illicit Coca Colombia* (submitted to Congress on Aug. 10, 2007)	F
Excerpts of May 5, 2009 Hearing Transcript	G
Sample of Dr. Campana Causation Statement	H
Photographs from 2002 Video produced by Test Plaintiff Victor Mestanza	I
Appendix Containing the Excerpts of All Cited References to the Test Plaintiffs' Questionnaire Responses, Deposition Transcripts, and Other Documents	"App."