EMBASSY OF THE UNITED STATES OF AMERICA

URIBE CUALLA TOXICOLOGY CLINIC

REPORTED HUMAN HEALTH EFFECTS FROM GLYPHOSATE

FINAL REPORT

Department of Putumayo

Bogota, D.C., Colombia
December, 2001

ACKNOWLEDGEMENTS

We wish to thank the Counter-Narcotics Police, the Putumayo Health Department (DASALUD) and Diva Reval, Chief of Epidemiology, the Governor of Putumayo, the public hospitals in Orito, La Hormiga and Puerto Asís, the National Police, Puerto Asís Police Commissioner Captain Alejandro Muriel, the Advisory Office of the Illicit Crop Eradication Program (PECI-/ Plan Colombia - PLANCO) and Mr. Luis Eduardo Parra for their cooperation in providing the information required for this report.

We look forward to working with these and other institutions and individuals who may wish to continue with projects of this type.

TECHNICAL TEAM

Camilo Uribe Granja, M.D.
Head Researcher and Director

Olga Lucía Melo, M.D.
Associate Researcher

Alejandra Salcedo M, M.D.
Associate Researcher

Juan Eduardo Céspedes, M.D., M.Sc., D.T.M. & H., P.D.F.
Associate Researcher

Tania Santodomingo, M.D.
Assistant Field Physician

Yesyd Gastelbondo
Logistics Manager

Boris Orlaff Hernández Chivata
Technician

CONTENTS

ATTACHMENTS AND APPENDICES

EXECUTIVE SUMMARY

For more than 30 years, Colombia has been fighting the problem of illicit drug crop cultivation, including coca, opium poppy and marijuana. Pursuant to its international agreements, the government of Colombia (GOC) started the Illicit Crop Eradication Program (PECI) to help control the production and supply of narcotics. The PECI includes several strategies, one of which is the aerial application of a mixture based on the herbicide glyphosate to eradicate coca, in accordance with criteria defined by the Drug Advisory Council (CNE) and the Counter-narcotics Department of the Colombian National Police (DIRAN).

In recent years, there has been a substantial increase in complaints from peasants living in areas where aerial spraying has occurred. Filed with local authorities, these complaints include the possible human health effects from exposure to glyphosate mixtures. Consequently, the GOC and the U.S. government (USG) believe it is critical to determine scientifically if these health effects could result from the aerial eradication program.

The Embassy of the United States of America, through its Narcotics Affairs Section (NAS), commissioned the Uribe Cualla Toxicology Clinic in Bogota to design and conduct a study in the municipalities in Putumayo where controlled spraying was carried out by DIRAN between December 2000 and February 2001. The project also included the presentation of two seminar-workshops on pesticide health and safety to local public authorities, departmental health workers and interested non-governmental organizations.

The study's objectives were to observe and measure, retrospectively, (1) the possible human health effects of glyphosate exposure associated with aerial eradication between December 2000 and February 2001 and (2) the possible effect of exposure to other pesticides used to cultivate coca in Putumayo.

Ideally, one should conduct a prospective epidemiological study to assess exposure to a chemical compound and possible health effects. Because the decision was made to conduct the current study five months after spraying occurred, it was not possible to conduct a prospective study. A retrospective study, the only kind that can be implemented after the fact, however, does not permit the investigator to establish or rule out a correlation between exposure to a given substance and specific health complaints. Furthermore, it does not allow the investigator to formulate a plausible hypothesis to explain morbidity attributable to the effect of low-level exposure to a chemical substance of low potential toxicity such as glyphosate. Despite these limitations, NAS decided to conduct the study in order to obtain objective field data that can help to determine if the alleged relationship between health complaints and the spray program has any validity.

Findings

Based on the data obtained and analyzed for this study, coupled with local and regional data on morbidity and existing toxicological and scientific information on glyphosate, the investigators could not determine that DIRAN aerial spraying with glyphosate between December 2000 and February 2001 was responsible for the complaints of illness and other health problems reported by inhabitants of Putumayo. In fact, the data show there are many other factors that contribute to health problems in this area.

Among the findings of this study are:

- First, the prevalence of health problems observed in the study population was similar to the prevalence found in epidemiological reports from years prior to the start of the PECI, both in towns targeted by the program (e.g. La Hormiga) and in towns in departments where illicit crops have yet to be sprayed for eradication, such as Puerto Wilches and San Vicente de Chucurí in the Department of Santander (See Table 5.1). The morbidity rates are consistent with poor health conditions, poverty, lack of potable water, inadequate personal hygiene, lack of adequate sewage facilities and solid waste disposal, and inadequate food handling in Putumayo. The rate of unsatisfied basic needs (UBN) was 78.7 percent in 2001. The poverty rate in the department was [1] 68.9 percent in 1998.

- Secondly, the diseases the study population attributed most often to glyphosate spraying - gastrointestinal symptoms (diarrhea, vomiting and nausea), skin problems (pruritus or itching, erythema or reddening, vesicles or blisters, burning sensation and pustules), eye problems (burning, reddening or conjunctival injection, pain and pruritus), respiratory symptoms (dyspnea or tiredness, coughing and a cold or rhinorrhea), cephalea and fever - can have a variety of causes. These include infection and allergies in addition to chemical exposure.

- Third, the health complaints are not related to the subjects' location at the time of spraying. According to the collected data, an important percentage of those who filed complaints were situated more than two kilometers from the field at the time of spraying (46 subjects, 11.4 percent). At this distance, it is virtually impossible to receive a sufficient dose of glyphosate to cause a clinically appreciable effect. The measured maximum drift of PECI aerial spraying is 5-10 meters. In contrast, the study found that most of the subjects who said they had not been ill were either in the field at the time of spraying or at a distance of less than one kilometer (75 subjects, 88.2 percent). If there were a relation between spraying and illness, we would expect the percentage of those unaffected to increase with distance, not decrease.

[1] National Department of Planning. www.dpn.gov.co

- The symptoms manifest by the population can be caused by chronic exposure to the wide variety of agricultural chemicals used to cultivate coca in Putumayo. For example, 382 (78.3 percent) of the 488 people studied claim to handle some type of agricultural chemical. Ten of the 26 pesticides used by the study population in the last six months belong to toxicity category I: "extremely toxic," with Gramoxone (paraquat) being the pesticide used by the highest percentage of individuals in the study population (20.9 percent). These substances are far more toxic than glyphosate and are known to cause the symptoms reported by inhabitants of the region. Moreover, the study found that 91.1 percent of the subjects who reported using pesticides (348 individuals) employ no means of personal protection. Pesticides are usually applied with a back pump or *cacorro.* Coca farmers also use inappropriate means such as static irrigation. The data shows that exposure to these chemicals can affect the entire family, because women and children (67.0 percent of the study population) help to mix and apply pesticides. These products are used frequently (weekly in some cases) and are commonly stored in the home, under beds and near food. Handling and storage of these products in such a manner significantly increases the likelihood of exposure.

Methodology

The field team collected complaints filed with municipal authorities to determine the number of people who complained, the principal symptoms reported and their frequency, and the number of people affected in each village. The team then designed a clinical research instrument (CRI) to obtain data from the study population. Questions addressed spraying dates, symptoms, their duration and evolution, the demand for and use of health care services, non-health-related problems attributed to spraying, exposure to other agricultural chemicals, the use of occupational protective measures, methods used to store, prepare and apply agricultural chemicals, and the handling of pesticide packages and containers. The clinical evaluation featured relevant questions on current illness and personal and family background, basic demographic data (identification, sex, schooling, etc.), a physical exam, a diagnosis and collection of blood and urine samples.

The field work for the study was conducted as part of a health brigade that offered free medical care, including general check-ups and distribution of medicines The brigade operated for 10 days, from June 10 to June 20, 2001. During that time, it visited nine of the 12 scheduled villages located in the municipal districts of San Miguel, Orito and Valle del Guamuez. The brigade served 1,244 outpatients and administered the CRI to 500 individuals. The investigators included subjects in the study based on two criteria:

1. Subjects who claimed to have experienced health problems or illness during the four weeks subsequent to the last spraying (designated as *case)*; and *.*

2. Subjects who claimed to have experienced no health problems or illness during the four weeks subsequent to the last spraying, in spite of living in the same village and being of the same sex and approximately the same age as the previous cases (designated as *control).*

The investigators also collected blood samples from 266 of the 500 subjects to determine cholinesterase activity and urine samples from 489 to determine levels of paraquat and glyphosate. The investigators invalidated 12 subjects because the CRI contained incomplete information, leaving 488 subjects in the study.

1. INTRODUCTION

1.1 BACKGROUND AND JUSTIFICATION

Most of the coca in Colombia is grown in the Department of Putumayo, which is located in the southern part of the country and has approximately 323,000 inhabitants in 13 municipalities (Arenas, Guerrero, Linero). It is an economically depressed and remote area with limited facilities, lacking adequate health care services. At least half the households have inadequate accommodations, mainly due to a shortage of public utilities. This has a negative effect on health. According to the National Department of Planning (DNP), the index of unsatisfied basic needs (UBN) in the Department of Putumayo was 78.7 percent in 2001 compared with 37.2 percent nationwide.

There are major health problems in Putumayo such as cardiocerebrovascular disease, cancer and violence and accidents related to alcohol abuse, drug addiction and unemployment. Putumayo has also become the largest single source of coca leaf, the raw material for cocaine, in Colombia. The GOC has implemented the Illicit Crop Eradication Program (PECI) as part of the fight against drugs.

Nearly 30,000 hectares of coca in Putumayo were sprayed for eradication between December 22, 2000 and February 6, 2001. At the same time, the number of complaints from peasants living in the areas where spraying has occurred has increased substantially. These complaints include the possible human health effects from exposure to glyphosate. Consequently, the GOC and the U.S. government (USG) believe it is critical to determine scientifically if these health effects could be due to the aerial eradication program.

The United States Embassy in Bogota, through the Narcotics Affairs Section, commissioned Uribe Cualla Toxicology Clinic to design and conduct a study to assess the actual human health effects from glyphosate exposure associated with aerial spraying and the possible effect of exposure to other pesticides used to grow coca in 12 villages in Putumayo. According to the complaints reviewed for the study, these are the areas where most of the supposedly affected individuals reside. The current study is retrospective, as it was designed and planned after aerial spraying. It is also descriptive and exploratory, since the only way to reach the population was through a health brigade for the general public (which generated a concentration of “supposed” cases).

1.2 OBJECTIVES

1.2.1 General Objective

The general objective was to determine and measure, retrospectively, the possible human health effects from glyphosate exposure associated with aerial eradication between December 2000 and February 2001 and the possible effects of exposure to other pesticides used to grow coca in Putumayo. The investigation team designed a clinical research instrument to obtain information from the study population. The team also collected blood and urine samples to determine current exposure to glyphosate and paraquat.

1.2.2 Specific Objectives

a) Collect complaints filed with municipal authorities to determine the number of people who complained, the principal symptoms reported and their frequency, and the number of people supposedly affected in each village.
b) Design a clinical research instrument (CRI) to obtain data from the study population about spraying dates, symptoms, their duration and evolution, exposure to other agricultural chemicals, the use of occupational protective measures, personal and family background relevant to the study, and basic demographic data (identification, sex, education, etc.). In addition to directed questioning, the procedure included a clinical evaluation, a physical examination and the collection of blood and urine samples.
c) Identify the villages with the highest number of people who complained or supposedly were affected and, depending on travel conditions, organize a tour of the three towns under study to acquire a representative sample from each, distributed according to the number of supposedly affected individuals.
d) Invite the community to take advantage of the health brigade as an opportunity to administer the CRI, to conduct clinical examinations and to collect blood and urine samples for the study.
e) Organize the field team and the equipment required for directed questioning, physical examinations and sample collection.
f) Compare the clinical findings of the health brigade with the supposed illnesses reported to local authorities.
g) Determine if there is a cause-effect relationship between the clinical findings and exposure to controlled aerial eradication with glyphosate.
h) Identify exposure to other pesticides, given the amount of agricultural chemicals used in Putumayo to grow both illicit and legal crops.
i) Evaluate hygiene and industrial safety measures applied by workers who are exposed to these chemicals.
j) Detect and measure the presence of glyphosate in urine sample collected from subjects who live in the sprayed areas.
k) Detect and measure levels of cholinesterase activity in blood samples from subjects exposed to PECI area spraying or to other agricultural chemicals.

l) Detect and measure the presence of paraquat in urine samples from subjects exposed to PECI aerial spraying or to other agricultural chemicals.

2. CONCEPTUAL FRAMEWORK

2.1 A BRIEF DESCRIPTION OF PUTUMAYO

2.1.1 Biogeographical Aspects

The Department of Putumayo is located in southern Colombia between 01º 26’ 18” and 00º 27’ 37” latitude north and 73º 50’ 39” and 77º 4’ 58” longitude west. It is part of the Amazon region and has 24,885 km^2 of territory. Putumayo is bordered on the north by the departments of Nariño and Cauca, and by the Caquetá River, which separates it from the Department of Caquetá; on the east by the Department of Caquetá; on the south by the Department of Amazonas and on the west by the Department of Nariño (a stretch of territory under dispute). The Putumayo and San Miguel rivers separate it from Perú and Ecuador. There were 3,997 registered urban properties on January 1, 1995 and 1,456 rural properties.

Putumayo has two distinguishing geographic features: the Llanura Amazónica (Amazon Plains) and the eastern flank of the Cordillera Oriental, which extends to the Amazon foothills. The western section is mountainous, with elevations up to 3,800 m above sea level. There are a number of rivers (the Putumayo, Caquetá, Mocoa, Mecaya, Caucaya, Sencella, Guamuez, San Miguel, Sabilla, Orito, Mulato and Rumiyaco) and many small streams. Concepción Creek is one example.

The plains region has temperatures above 27°C and 3,900 mm average annual precipitation. Most of the time, relative humidity is above 80 percent throughout the department. There are three climate zones: hot, temperate and cool highland or paramo.

2.1.2 Economic Aspects

Farming, cattle ranching and mining are the principal economic activities. Corn, potatoes, plantains, manioc, pineapple, palm peach and sugarcane are the most important crops. Rice, yams, sesame seed, vegetables and beans are also important, but to a lesser degree. Cattle ranching has resulted in a large surplus of dairy products, primarily in the Sibundoy Valley.

There is gold in the Colombian Massif, particularly the west central mountains. This mineral is also mined on the Caquetá River and two of its tributaries: the Curiaco and the Cascabel, and on the San Pedro River, a tributary of the Putumayo River in the Sibundoy Valley. Several oil deposits have been discovered at Orito and are being tapped.

The region has a wide variety of timber for construction, medicinal herbs, oleaginous and fibrous plants, and resins such as rubber. In 1994, the department's financial system reported 19,215 million pesos in deposits and 13,082 million pesos in loan placements.

Certain economic activities in Putumayo have caused deforestation in the upper areas. This, coupled with normal rainfall, has led to erosion. The threat to wildlife poses another environmental problem and is undermining the region's biodiversity. The Southern Amazon Sustainable Development Corporation (CORPOAMAZONIA) was created to develop environmental plans for Putumayo, Caquetá and Amazonas (Law 99/93).

Most of the villages and small settlements in Putumayo are situated along the rivers, which are the main transportation routes. There are two principal river ports. One is Puerto Asís. It served approximately 86,865 outgoing and 84,924 incoming passengers in 1994, along with 71 large and 600 small outgoing vessels, and 74 large and 458 small incoming vessels. The other is Puerto Leguízamo, which handled 21 large and 563 small outgoing vessels in 1994 and 22 large and 263 small incoming vessels.

Putumayo has only one highway; it connects Puerto Asís and Mocoa with the interior of the country. There is another small stretch of road in the middle of the jungle, between Taquía and Puerto Leguízamo on the Caquetá and Putumayo rivers. There are two airports: one at Puerto Asís and another at Orito.

2.1.3 Social Aspects

Preliminary figures from the 1993 census show Putumayo had 153,850 inhabitants, 31,398 households and 32,052 dwellings. There are a number of Indian tribes such as the Sibundoy, Inga, Huitoto, Siona, Cofan, Camsa, Coreguaje, Quechua and Paez. La Paya National Park and the Indian reservations of Afilador, Santa Rosa del Guamuez, Santa Rosa de Sucumbíos, Yarinal and San Marcelino are located in Putumayo.

The department currently has approximately 323,000 inhabitants, 13 towns, two judicial districts, 56 police districts and numerous villages and hamlets.

In the last eight years, the mortality rate has increased by 21.8 points from 722 deaths per 100,000 inhabitants in 1992 for a population of 221,580 to 1,198 in 1999 for a population of 323,549.

Male mortality accounted for 74 percent of the deaths in 1999. Average age at the time of these deaths was 24 years, for a mean of 30 years. Sixty percent of all mortality in Putumayo is due to accidents or violence, 18.7 percent to cardiovascular disease, 8.6 percent to transmittable disease, 7.4 percent to perinatal disease, 4.8 percent to tumors and 0.5 percent to other causes. Table 2.1 shows total mortality by external or violent cause.

TABLE 2.1. Death due to Accidents or Violence. Putumayo 1999.

Death by External Cause or Violence	No.	percent
Homicide*	575	80.2
Other accidents**	72	10.0
Suicide	51	7.1
Traffic accidents	19	2.7
TOTAL	**717**	**100.0**

* Ninety-three percent all homicide victims are male. Seventy-four percent are in the 15-to-34 age group, 20 percent in the 34-to-45 age group, 6.4 percent are over age 45, and one percent are under age 15. The highest homicide rates (74 percent) are found in the urban areas and the highest number of homicides in Valle del Guamuez and Puerto Asís.
** These include drowning, poisoning or intoxication, burns caused by explosive objects, and electrocution.

2.1.4 The Health Sector

For the most part, medical care and preventive health services in Putumayo are limited in coverage. The public health network has two second-tier hospitals, four first-tier hospitals, eight health centers, 24 health posts, six health management companies (EPS), four subsidized insurers (ARS) and 29 private institutions. There are physicians (80), nurses (22), bacteriologists (29), social workers (17), optometrists (3), assistant social workers (3), statisticians (4), assistant statisticians (12), nurse's aids (116), x-ray attendants (6) and rural health workers (114).

In short, Putumayo is a depressed and remote area with limited facilities, lacking adequate health care services. Housing for at least half the households is inadequate, mainly due to a lack of public utilities. Coverage in the urban area is 59 percent for water, 45 percent for sewage and 58 percent for electricity. According to the National Department of Planning (DNP), the index of unsatisfied basic needs (UBN) in the Department of Putumayo was 78.7 percent in 2001 compared with 37.2 percent nationwide. Lack of basic services has a negative effect on the population's health.

2.1.5 Use of Agricultural Chemicals

The Department of Putumayo has no record of occupational accidents involving intoxication with agricultural chemicals. This is contrary to Decree 1843 of 1991, which calls for all pesticide intoxication in Colombia to be reported to the authorities, regardless of where it occurs.

According to a 1999 report prepared by S. Uribe for the National Narcotics Agency and NAS, 98.7 percent of all farmers use insecticides and fungicides to control blight and disease; 92.5 percent use chemical fertilizers and 95.5 percent control weeds with herbicides. The same report identifies at least 75 commercial brands of agricultural chemicals in use. Regional differences in the type of substance used are determined by its availability on the market. Many of these substances are sold openly on the black market.

Tables 2.2. and 2.3 show the products used most often.

TABLE 2.2. Main Herbicides Used to Grow Coca

Trade Name	Active Ingredient	% of Use	Toxicity Category in Colombia*	Toxicity Category according to the EPA **	LD 50 Oral (Rats) (mg/k)	LD 50 Dermal (Rabbits) (mg/k)
Gramoxone	Paraquat	61.3	II	I	110-150	236-325
Faena	Glyphosate	10.7	IV	III	5.000	5.000
Round up	Glyphosate	8.4	IV	III	5.000	5.000
Anikilamina	2.4 D	9.7	II	II	375-666	1.500
Atrazina	Atrazine	4.8	III	III	672-3.000	7.500
Karmex	Diuron	2.6	III	III	>5.000	>1.000

*** Pursuant to Decree 1843 of 1991, pesticides in Colombia are classified into four toxicity categories: I - Extremely Toxic, II - Highly Toxic, III - Moderately Toxic and IV - Slightly Toxic.**
**** International classification by the United States Environmental Protection Agency (EPA).**

TABLE 2.3. Main Insecticides and Fungicides Used on Illicit Crops

Trade Name	Active Ingredient	Toxicity Category in Colombia	Toxicity Category according to the EPA	LD 50 Oral (Rats) (mg/k)	LD 50 Dermal (Rabbits) (mg/k)
INSECTICIDES					
Tamaron	**Metamidophos**	**I**	**I**	**21-16**	**118**
Sevin	**Carbaryl**	**II**	**I**	**250-850**	**>2.000**
Metavin	**Metomil**	**I**	**I**	**30**	**>2.000**
Furadan/Liquid/ granulated	**Carbofuran**	**I**	**I**	**5**	**885**
Curacrón	**Prophenophos**	**II**	**II**	**630**	**143.4**
Thionil	**Endosulfan**	**I**	**I**	**18-220**	**200-359**
Parathión	**Methyl parathion**	**I**	**I**	**4.5-24**	**6**
Matador	**Lambda-cyhalothrine**	**III**	**II**	**56-79**	**632**
Thiodan	**Endosulfan**	**I**	**I**	**18-220**	**200-359**
Malathión	**Malation**	**III**	**III or IV**	**480-10.700**	**>2.000**
Nuvacron	**Monocrotophos**	**I**	**I**	**17**	**354**
Lorsban Liquid/ Granulated	**Chlorpyriphos**	**II**	**II**	**82-270**	**1.000-2.000**
Convoy	**Cypermetrine and diazinon**	**III**	**III**	**2.75-450**	**-**
Politrin	**Cypermetrine**	**II**	**II**		**>2.000**
FUNGICIDE					
Manzate	**Mancozeb**	**III**	**III**	**4.500-11.200**	**5.000-15.000**
Copper Oxychloride	**Copper oxychloride**	**III**	**-**	**-**	**-**
Bavistin	**Carbendazim**	**III**	**-**	**-**	**-**

The study found no significant differences between large and small coca growers. Added to the high number of substances used is the fact that many growers still believe “more is better.” As a result, application rates typically exceed the manufacturer’s recommendation.

Coca farmers throughout Colombia used an estimated 11.9 million kilograms of pesticides during the year 2000. This calculation is based on figures from detailed studies conducted for the National Drug Council by Sergio Uribe (1997) and SINCHI (1997), considering the average amount of pesticide used per harvest and assuming an average of six harvests per year for crops of more than one year. In Putumayo alone, it is estimated that nearly 4.14 million kilograms of pesticide were used during the same year on a maximum 60,000 hectares under cultivation. Accordingly, pesticide consumption in Putumayo accounted for nearly 34.7% of all pesticides used on coca crops nationwide

The average number of applications per harvest with coca is three. This is according to an estimate based on interviews and informal conversations with growers during more than 10 years of field work. The average quantity of active ingredient applied per hectare/harvest is 4.8 kilograms. This amounts to 12 liters of liquid pesticide per harvest (estimated according to the number of empty containers found in the field).

There is also the problem of pesticides smuggled into the country from Ecuador, with trade names different from those registered in Colombia. This makes prompt and proper diagnosis even more difficult in the event of eventual intoxication. An example is the product Killer, which is the trade name for paraquat in Ecuador.

2.2 GLYPHOSATE AND COMMERCIAL PREPARATIONS USED BY PECI

2.2.1 Definition

The herbicide glyphosate is a weak organic acid with a molecule formed by glycine and phosphonomethyl fractions (N-phosphonomethyl glycine). The empirical formula is $C_3H_8NO_5P$, with a molecular weight of 169.1 daltons. It is an odorless, clear white powder, melts at 200º C and as a vapor pressure of 2.59 x 10-5 Pa at 25° C, (13). Its solubility in water is 10.5 g/l at 20º C. It is soluble in organic solvents, susceptible to photodegradation, with an average disappearance time (TD50) of 30 days, and is not volatile. Its decomposition temperature is 199 ° C ±1 ° C.

In terms of ionic behavior, glyphosate is an amphoteric, and several ionic species can be found as a function of the pH in the medium. It is a herbicide used to control weeds [2] that compete with crops in the post-emergence phase. It acts systematically and non-selectively on plants and is a broad-spectrum product that works on both broad-leaf plants and grass.

2.2.2. Herbicide Action Mechanism

Glyphosate is a non-selective herbicide that blocks plant growth by interfering with essential aromatic amino acid synthesis. This inhibits enzyme enolpyruvylshikimate phosphate synthase, which is responsible for chorismate biosynthesis, a phenylalanine, tyrosine and tryptophan biosynthesis intermediary. As animals do not share this path of aromatic amino acid biosynthesis, it is blocked only in plants.

[2] Weed: a generic term applied to vegetation that competes with any crop.

2.2.3. Biochemical Effects on Laboratory Animals

Glyphosate increases oxygen consumption, ATP-asa activity and reduces the hepatic level of cytochrome P450. Using intact mitochondrions of rat liver, Olorunsaga y Bababunmi (1980) found that glyphosate acts as an oxidative phosphorylation uncoupler. This occurs as a result of two interactions with oxidative phosphorylation and with the energy-dependent transhydrogenase reaction.

In spite of being a phosphorus compound, it does not inhibit cholinesterases. Because of the reduction in $P\text{-}_{450}$, it may interfere with the metabolism of certain medicines and cause a predisposition to porphyria.

2.2.4 Toxicokinetics

To research glyphosate pharmacokinetics, several studies were done on rats with single oral and repeated doses of ^{14}C-glyphosate that varied between 10 mg/kg and 1000 mg/kg. The findings showed incomplete gastrointestinal tract absorption, which varied between 15 percent and 36 percent.

According to research with rhesus monkeys and *in vitro* studies on human skin samples, dermal penetration is low. With undiluted glyphosate applied to monkeys absorption was 0.4 percent at 24 hours and 1.8 percent at seven days. When diluted glyphosate (1:29) was applied to monkeys, absorption was 0.8 percent for a dose of 500 ug/cm2 and 2.2 percent for a dose of 5,400 ug/cm^2. Studies with human skin show less than two percent absorption with the concentrated and diluted product.

With a single dose of 10 mg/kg administered to rats, glyphosate tissual distribution determination showed levels above one percent in the small intestine, colon, kidney and bone. The maximum concentration observed in the large intestine was at two hours; peak concentration in other organs was at 6.3 hours. The levels declined quickly. The bone was the slowest to eliminate, apparently due to a reversible union of phosphonic acid with the bone matrix. The final measurement was taken 168 hours after administration and showed 100 percent elimination. Other studies done in 1973 with single doses of ^{14}C glyphosate showed 94-98 percent elimination in males and 82-84 percent in females at 48 hours and 99 percent elimination at 120 hours in both sexes. Studies with repeated doses show a trend similar to the single-dose study.

Glyphosate is metabolized to aminomethylphosphonic acid (AMPA). Administered orally, it biotransforms very little in animals. According to studies where ^{14}C glyphosate was administered to rats, only 0.2-0.3 percent of the administered dose metabolizes. After a single oral dose, it is excreted quickly in urine and feces, with no changes. Studies with rats report 90 percent eliminated in 72 hours. The fecal tract is the main elimination path, with a range of 62-69 percent. Less than 0.3 percent of the administered dose is recovered as CO_2 in exhaled air.

Subsequent to administration of repeated doses (1-100 mg/kg of body weight/day for 14 days), urinary elimination was less than 10 percent and fecal excretion 80-90 percent, mostly unmetabolized. The amount excreted daily declined quickly, reaching a plateau after four days. This is attributed to tissual residue movement and redistribution.

Studies done on non-rodents such as rabbits, chickens and goats show behavior similar to that described above.

2.2.5 Toxicity in Animals

Glyphosate shows low acute toxicity in animals. The World Health Organization (WHO) accepts the following toxicity values:

Oral:	LD_{50} 5,000 mg/kg in rats
Dermal:	LD_{50} 5,000 mg/kg in rabbits
Inhalation:	LC_{50} >12.2 mg/L of air for four hrs. exposure in rats

Consequently, the EPA classifies glyphosate in category III: “relatively low acute dermal and oral toxicity.” WHO classifies it in category IV: “not likely to pose acute danger with normal use.”

Subchronic toxicity in animals has been studied in rats, mice and dogs by administering high doses, as much as 20,000-50,000 mg/kg of body weight/day in rodents and 500 mg/kg of body weight/day in dogs, for period of 13 to 52 weeks. With doses above 25,000 mg/kg of body weight in rodents, weight loss was the principal finding. No other findings were reported and the conclusion was that glyphosate administered daily in doses of up to 20,000 ppm (1,445 mg/kg of body weight, NOAEL) is tolerated well.

Chronic toxicity with glyphosate has been studied in rodents exposed to diets with glyphosate levels that fluctuate between 0 and 30,000 ppm for periods of 24 months. As a result of the findings in three studies, 8,000 ppm (409 mg/kg of body weight/day) was established as the NOAEL level (no -observed - adverse - effect level) for chronic toxicity. With respect to its carcinogenic effect, the EPA classifies glyphosate in category E: “no evidence of carcinogenicity in humans.” This is based on the findings of experiments with rodents.

2.2.6 Toxicity in Humans

According to a number of studies, acute toxicity and the irritative potential of glyphosate in humans are low. Maibach (1986) studied 346 volunteers to determine irritation, sensitization, photoirritation and photsensitization, applying a formula with 41 percent glyphosate on intact and worn skin, compared with the effects of cleaning liquid, baby shampoo and dishwashing detergents. The effects of single and cumulative exposure for 21 days were evaluated. The findings showed the irritating effect of glyphosate on intact skin was equal to that of the other products. On worn skin, it showed a slightly higher incidence of erythema at 24 hours. However, at 48 hours, its irritative potential was similar to that of the cleaning products. At 21 days, the baby shampoo and glyphosate were less irritating than the cleaning products. No evidence of sensitivity was observed. The study demonstrated no potential photoirritation or photosensitivity.

Minor cases of reversible ocular irritation, with no permanent change in eye structure or function, have been found when evaluating occupational exposure. There are no reports of hospitalization related to its use.

Accidental exposure has been associated with ocular and cutaneous irritation, accompanied by tachycardia, high blood pressure, nausea and vomiting.

The lethal dose for humans has yet to be determined. Acute toxicity is accepted as low and correlates with acute toxicity in rats. In patients who ingested doses of 200 and 250 ml, there were no lethal effects. However there are reports of cases where doses of 184 ml have been fatal. The symptoms observed in suicide cases point to the cause of death as hypovolemic shock induced by the secondary cardiac depressor effect of high doses of surfactant.

There is no scientific evidence demonstrating the teratogenic or reproductive effects of glyphosate. Its reproductive toxicity has been studied in rats by administering doses of up to 30 mg/kg of body weight/day in three successive generations, with there being no effects on fertility or reproductive parameters. Wagner (1983) studied the reproductive effects in rabbits with a dose of 30 mg/kg/day and found no teratogenic effects. Toxicity in development has been evaluated with doses of up to 3,500 mg/kg of body weight /day in rats and up to 350 mg/kg of body weight/day in rabbits, with there being no sign of birth defects. In Colombia, the Huila Health Department found no variation in the incidence of abortion or premature birth during 1998-99 in the towns of Palestina, Iquira, Acevedo, Oporapa and Salado Blanco, where glyphosate was used in fumigation. This was based on an analysis of the epidemiological information found at these locations.

The potential genotoxicity of glyphosate has been researched through a wide variety of studies *in vitro* and *in vivo.* Research conducted pursuant to international guidelines and under conditions relevant for animals and humans shows no genotoxic activity.

2.2.7 Laboratory Analysis

2.2.7 Laboratory Analysis

As a rule, glyphosate determination is laborious, complex and costly. The most common method is transformation with fluorogenic substances in derivatives that are more easily detected and can be used before or after the column. Determination is usually done with high-performance liquid chromagraphy or gas-liquid chromagraphy. Glyphosate determination limits in water, plants, soil and human urine are 0.02-3.2 µg/liter, 0.01-0.3 mg/kg, 0.05-1 mg/kg and 0.1 mg/liter, respectively.

Table 2.4 outlines the methods used for glyphosate measurement, preparation and analysis in humans

TABLE 2.4. Specifications for Glyphosate Analysis in Human Biological Samples.

Sample Volume/Weight	Preparation	Derivation Reagent	Analytical Method	Determination Limit
Human urine	Absorption in anion exchange resins (SAX); elution resin with HCl; evaporation and drying	Triflouroacetic/trifl ouroethanol anhydride	GC-MS GC-EC	0.1 mg/lt
Human serum - 0.5 ml	Extraction with trichloroacetic acid; absorption or anion exchange resin; elution with HCl; evaporation and drying	ρ- chloride sulfonil tolune	HPLC with UV detection	Not reported

GC: Gas chromatography; MS: Mass spectrophotometry; EC Electron capture detector; HPLC: High-performance liquid chromatography

2.2.8. Treatment for Acute Intoxication

There is no specific antidote for glyphosate intoxication. Normal decontamination methods should used to reduce absorption. These include gastric wash and activated carbon if contact was outside the digestive tract, a thorough body wash with soap and water if exposure was dermal, and an eye wash if required by the type of contact. General measures to assess and maintain proper cardiovascular function and treatment, if required, depend on the symptoms reported by the patient.

2.2.9 History, Preparations, Commercial Use and PECI Use

Glyphosate was first introduced as a herbicide in 1971. It is a broad-spectrum herbicide, relatively non-selective, highly effective on deep-root annual, biennial and perennial species, broad-leaved grass and weeds. It is registered for use on edible and non-edible crops, and on non-crop areas where all vegetation is to be controlled. When applied in low concentrations, glyphosate is a plant growth regulator.

It is one of the largest selling pesticides in the United States. In 1997, glyphosate was fifth in pesticide sales, with 34-38 million pounds of active ingredient consumed. In recent years, approximately 13-20 million acres have been fumigated with glyphosate annually. It is used primarily on grass, hay, garden produce and cereals.

Three glyphosate salts are employed as active ingredients in registered pesticide products. Two of these active ingredients are found in 56 products. Isopropylamine, the largest selling glpyhosate salt, is the active ingredient in 53 products and is used as a herbicide to control broad-leaved weeds. It is used on edible and non-edible crops and on at a wide variety of sites, including lawns and meadows, residential areas, greenhouses, forest reserves and ornamental crops. Glyphosate is available in liquid, granulated or tablet form and is applied with aerial or land equipment.

Glyphosate sodium salt is the active ingredient in two (2) registered pesticides. It is used on peanuts and sugar cane to regulate growth and accelerate ripening. In peanut crops, it is applied to the ground. With sugar cane, it is applied by aerial spraying.

Glyphosate monoammonium salt is an additional active ingredient in seven (7) herbicide products and growth regulators. It was first registered in 1984. Popular with Colombian farmers, glyphosate accounted for 8.9 percent of all pesticides and 23.3 percent of all herbicides used in commercial agriculture nationwide, on average, during 1997 and 1998.

One of the eight components of the GOC counter-narcotics plan being implemented by the National Narcotics Council, through the Counter-narcotics Agency, calls for eradicating illicit crops (coca, opium poppy, marijuana, etc.) by different means. In this case, eradication includes:

⇒ Concerted action to substitute illicit crops, through a strategy for alternative development strategy.
⇒ Manual eradication, based on voluntary eradication agreements.
⇒ Aerial eradication with glyphosate in large areas (more than 2.0 - 6.0 and 10.0 hectares) using aircraft equipped for this purpose.

At different times since 1984, the GOC has relied on aerial spraying as a highly effective and productive way to eliminate illicit crops. In 1988, at the request of

INDERENA, the GOC expanded this method to include the environmental variable. This decision generated prior studies pursuant to Article 27 of Decree 2811/74, which is known as the National Resource and Environmental Protection Code. Based on studies done in 1988 and 1989, glyphosate was recommended following a systematic, scientific procedure that included environmental and toxicological risk variables such as LD_{50} above 3,000 ppm, residuality in the soil, volatility, selectivity, biodegradation, corrosiveness, water solubility, liquid formulation, hydric degradation and low cost.

This is why it has been used to eradicate marijuana, coca and opium poppy. Since 1997, PECI has used 13.2 percent of all glyphosate applied to agricultural crops in Colombia, particularly sugar cane, coffee, fruit trees, rice, African palm, etc. Table 2.5. compares the use of glyphosate in commercial agriculture with PECI use to eradicate illicit crops.

TABLE 2.5. Use of Glyphosate in Commercial Agriculture vs. Use to Eradicate Coca in Colombia
Period 1997 – 2000

Year	Glyphosate Sold for Agriculture + (Kg)	Glyphosate Used by PECI (Kg)	Percent
1997	1,540,960.23	156,726.09	10.7
1998	1,423,091.29	247,212.20	17.26
1999++	1,486,525.70	161,408.33	10.86
2000+++	1,486,525.70	217,428.68	14.63

\+ Source: Ministry of Agriculture and Rural Development - Colombian Agriculture and Livestock Institute (ICA). Pesticide Sales - 1998. Importation, Production, Sales and Exports
++ Crops such as rice, sugar cane, coffee, sorghum, cotton and African palm.
+++ The figures on glyphosate sales for commercial agriculture are approximate averages.

2.2.10 Risk Situation Posed by PECI Aerial Spraying

Considering the national scenario described earlier and the fact that PECI implementation is controlled from an operational and environmental standpoint to guard against any risk to human health and other elements in the environment, the risk from exposure to the mixture sprayed by PECI to eradicate coca is based on the figures noted below.

- Composition: The following mixture is used to spray one (1) hectare (ha) of coca by air.

  -Glyphosate: 10.4 L/ha
  (contains 360 g/L of glyphosate as acid and

	180 g/L of POEA[3])
-Cosmoflux 411F[4]	0.24L/ha
-Water	13.02 L/ha
Total Mixture:	23.66 L/ha

- Accordingly, each liter of the mixture contains:

Glyphosate as acid:	158.26 g/L
POEA:	79.13 g/L
Cosmoflux 411F:	0.00845 g/L (8.45 mg/L)

- The average corporal surface of a adult human weighing 70 kg. is 1.73 m^2.

Cutaneous and oral exposure to the PECI mixture (glyphosate+ POEA + Cosmoflux 411F) with ingestion of sprayed water is quantified in Appendix No. 1.

The results of this calculation are summarized below:

TABLE No. 2.6 Risk from Aerial Exposure to the PECI Mixture

Substance	Applied Dose (g/L)	DERMAL EXPOSURE			ORAL EXPOSURE			
		DL_{50} (mg/Kg)	DR[a] by organism (mg/Kg of live weight)	Comparison DR vs. DL_{50}	DL_{50} (mg/Kg)	CAA [b] (mg/L)	DR[a] by organism (mg/Kg of live weight)	Comparison DR vs. DL
Glyphosate acid	158.26	5,000	9.24	541 times less	5,000	3.74	0.05	100,000 times less
POEA	79.13	1,260	4.62	273 times less	1,200	1.87	0.03	40,000 times less
Cosmoflux 411F	0.00845	2,000	0.00049	4,048,583 times less	2,000	0.0002	2.8 E-6	714,285,714 times less

Notes:

a: DR: Dose received by a 70 kg individual who presumably has been impregnated completely with the sprayed mixture or consumed one (1) liter of sprayed water.

B. CAA: Concentration in sprayed water. It is assumed the dose is sprayed on a $1m^2$ sheet of water 10 cm deep, which is equivalent to 100 L of water.

2.3. HIGHLY TOXIC PESTICIDES USED TO GROW COCA

[3] POEA: ethoxylated tallowamine
[4] Surfactant

As indicated in the chapter entitled "A Description of Putumayo - Use of Agricultural Chemicals," 98.7 percent of the coca growers use insecticides and fungicides to control blight, 95.5 percent use chemical fertilizers, and 95.5 percent use herbicides to control competition from other plants. According to the report, at least 75 different brands of agricultural chemicals are used. The following are the toxicological characteristics of three pesticides mentioned in the report and used by coca growers. The EPA has classified them as "highly toxic" (Toxicity Category I).

2.3.1. Organophosphates

2.3.1.1. Definition

Organophosphates are esters, amides or thiols derived from phosphoric, phosphonic, thiophosphoric or thiophosphonic acid. They belong to the insecticide group. There are more than 100 known compounds. They have a common chemical nucleus and fall into four principal categories (I-IV), depending on the substitute radical. Some have different toxic properties, depending on the characteristics of the radical. They are considered highly sensitive to changes in pH and have a high water octanol partition coefficient and low vapor pressure. Their maximum hydrolysis occurs in a pH between seven and eight, and increases ten times for each unit of pH towards alkalinity. Their water solubility is limited, and organic solvents are used in their preparation. This can complicate intoxication due to the presence of chemical pneumonitis. They emulsify in water, changing their characteristic amber color for a milk white appearance. They have good resistance to a dry environment and hydrolyze easily in a moist environment. As a rule, they are biodegradable.

2.3.1.2 Toxicokinetics

Being highly liposoluble, organophosphates are absorbed by all tracts: oral, dermal, conjuntival, parenteral, rectal and inhalation. The airway provides for fast action; if the toxic is carried to the pulmonary alveolus with sufficient pressure and dispersion, fatal accidents can occur in a matter of minutes. Occupational exposure is mostly dermal and conjuntival. Oral exposure is found in suicide attempts and accidental ingestion.

Distribution is extensive in all tissue and organophosphates metabolize through a variety of chemical processes such as oxidation, hydrolysis, biotransformation and conjugation. The result can be more or less toxic than the precursor. For example, parathion oxidizes *in vivo* and forms paraoxon, a compound with more toxic force. It requires microsomal enzymes to metabolize, using $NADPH_2$ and oxygen and producing sulfur oxidation. Organophosphates that have paranitrophenil groups in their structure contain paranitrophenol in their metabolites. Excretion is primarily renal and very limited in feces. Some residue persists in exposed animals. The EPA classifies organophosphates as "highly toxic" (Toxicity Category I).

2.3.1.3 Toxic Action Mechanism in Insects and Humans

The toxicity of organophosphate compounds is due to inactivation of the carboxyestearases. Because of its quantity and physiological activity, the most important of these enzymes is acetylcholinesterase (its function is to hydrolyze acetylcholine as a neurotransmitter in the synapse of postganglion and preganglion parasympatic and sympatic fibers and in somatic fibers for striated and skeletal muscles and the central nervous system). Acetyl acid and choline result from this mechanism. Separately, they are inert compounds. When the enzyme is inactivated, the acetylcholine persists. This produces a heightened cholinergic effect in the nerve endings.

The toxic action of organophosphates is characterized by often irreversible unions of phosphate radicals with the enzyme's active sites, creating phosphorilate and inactive enzymes.

2.3.1.4. Clinical Manifestations of Acute Intoxication

By inhibiting cholinesterases, organophosphates produce an agglomeration of acetylcholine that initially stimulates, then paralyzes cholinergic transmission of the synapse. Traditionally, acute intoxication symptoms correspond to three major syndromes. However, the intermediate syndrome should be added as well.

a) Muscarinic syndrome: This is the most striking manifestation of serious intoxication. Blurred vision, paralytic punctiform myosis, lacrimation, sialorrhea, bronchorrhea, bronchospasm, dyspnea, vomiting, diarrhea, abdominal cramps, urine emission, vesicle tenesmus, respiratory failure and bradycardia are the principal symptoms.

b) Nicotinic syndrome: The signs include mydriasis, temporary arterial hypertension, reflex hypotension, weakness, cramps, myalgias and muscular fasciculations.

c) CNS syndrome: anxiety, mental confusion, behavioral changes, convulsions, coma, ataxia, delayed response to stimuli, collapse and respiratory depression.

d) Intermediate syndrome: respiratory muscle paralysis, weakness of the tongue muscles and pharynx, and effect on the skull wall. Occurs 24 to 96 hours after exposure, and is produced by a combination of nicotinic and muscarinic effects.

Death is generally due to hemodynamic compromise within the first 24 hours. Neurological complications can occur after the first 24 hours, as a secondary effect and associated primarily with the intermediate syndrome.

In frequent occupational exposure among farmers and ranchers, the pathway is mostly dermal and respiratory, resulting in subtle symptoms of chronic intoxication with neuropsychological and behavioral changes.

The patient who overcomes an episode of acute intoxication may experience neurological aftereffects such as acute or retarded polyneuropathy, leukoencephalopathy induced by organophosphates, persistent electroencephalographic changes, and chronic dermatitis.

2.3.1.5.1. Laboratory Analysis

Organophosphate exposure and its effects can be measured in several ways to diagnose intoxication. These include measuring dermal exposure and determining metabolites in the urine. As a rule, there is no correlation between the concentration of urinary metabolites and the degree of intoxication.

Plasmatic or erythrocytic acetylcholinesterase (AChE) levels are an acceptable guide to the degree of acute intoxication. Pseudocholinesterase levels in serum or plasma are only considered indicators of exposure. A decline in acetylcholinesterase or pseudocholinesterase activity below 75 percent of the level prior to exposure is considered dangerous and the worker should avoid all contact with the insecticide until he has recovered. Signs of intoxication usually do not appear until AChE levels fall below 50 percent. Severe symptoms are associated with levels below 30 percent. Analytical methods, such as the modified Michel Electrometer, are used to measure levels of erythrocytic cholinesterase activity in blood or plasma.

2.3.1.6. Treatment for Acute Intoxication

Organophsophate intoxication can be treated gradually, depending on how severe it is. Therapy for most of the compounds is based on the administration of atropine, diphenhydramine, sodium bicarbonate and “cholinesterase reactivating agent” oximes, besides the general measures required to handle the symptoms of a patient suffering from acute intoxication, such as decontamination, elimination, maintaining electrolyte equilibrium and basic acid.

There is no specific therapy for severe neuropathic damage. Moderate neuropathies tend to reverse, apparently due to regeneration or adaptation of the peripheral nerve.

2.3.2. Endosulfan

2.3.2.1. Definition

Technically speaking, endosulfan (6,7,8,9,10, 10-hexachloro-1,5,5a,6,9,9a, hexahedron 6,9-methane-2,4,3-benzodioxatyepine, 3-oxide) is a clear brown substance formed by two alpha and beta isomers. It is used as a broad-spectrum insecticide, primarily in agriculture. In some countries, it is applied as a public health measure.

Both isomers are clearly resistant to photodegradation, but their endosulfan-sulfate and endosulfan-thiol metabolites are susceptible to photolysis. Their estimated average life in water is four days, but anaerobic conditions or low pH can increase this span. In water, endosulfan degrades primarily to endosulfan-diol. Fish are extremely sensitive to this compound. In the field, the alpha isomer disappears faster than the beta isomer and edosulfan-sulfate is the principal product of degradation.

2.3.2.2. Toxic Action Mechanism

The toxic action mechanism consists of inhibiting the influx of chlorine induced by gamma aminobutryric acid (GABA).

2.3.2.3. Toxicokinetics

Endosulfan can be absorbed by ingestion, inhalation or contact with the skin. Subsequent to ingestion, it is absorbed quickly and excreted in feces and urine. After acute exposure, high concentrations of endosulfan are found temporarily in the liver. Concentrations in plasma decline quickly. Its principal matabolites are endosulfan-sulfate and endosulfan-diol.

2.3.2.4. Toxicity in Animals

Endosulfan is regarded as moderately or severely toxic. The LD_{50} in rats fluctuates between 18-355 mg/kg of body weight. It is classified by the EPA as "highly toxic" (Toxicity Category I).

In rats, a dose of 2.5 mg/kg of body weight per day, administered for seven days, induced hepatic oxidase activity. A dose of 100 mg/kg in the diet for 104 weeks produced testicular atrophy and renal tubular damage with interstitial nephritis. No adverse long-term effects were observed with the administration of 1.5 mg/kg of body weight in rats and 0.75 mg/kg of body weight in dogs.

There is no adequate information concerning the impact of endosulfan on reproduction, teratogenicity and carcinogenicity, nor its embryotoxic effects.

2.3.2.5. Toxicity in Humans

There are many reported cases of suicidal or accidental intoxication. In fatal cases, death occurs a few hours after ingestion. The symptoms of intoxication include vomiting, restlessness, irritability, muscle spasms, hyperactivity, convulsions, pulmonary edema and cianosis.

2.3.2.6. Laboratory Analysis

Endosulfan and indosulfan-sulfate isomers are determined with gas chromatography and electron capture detection.

2.3.2.7. Treatment for Acute Intoxication

Decontamination measures, anti-seizure drugs and calcium gluconate. Oily cathartics, epinefrin and other adrenergic drugs or central nervous system stimulants should not to be taken.

2.3.3 Paraquat

2.3.3.1. Definition

Paraquat is 1-1'dimetyl-4,4'-bipyridium. Its chemical formula is $C_{12}H_{14}N_2$. Paraquat is comprised of two identical pyridine rings (bipyridyls). The two rings are quaternized with the addition of a methyl group to each nitrogen atom. It forms colorless or bromine yellow chlorine salts. These are highly soluble in water (70 gr/100 ml of water), insoluble in organic solvents, and of very limited solubility in alcohol. Paraquat has a slightly ammoniacal smell and decomposes in ultraviolet light. It is stable in acid or neutral solutions, and unstable in alkaline solutions where biperidyl cations have the facility to oxidate and reduce themselves by breaking the pyridine ring. The products formed are dark red. It is a non-selective, contact herbicide that destroys the green parts of the plant in the presence of sunlight.

2.3.3.2. Herbicide Action Mechanism

It affects the plant's surface organelles, moving in some quantity to the xylem and interrupting the ferredoxin reduction processes and the reactions conducive to NADPH formation, which is indispensable for energy production.

2.3.3.3 Toxic Action Mechanism in Humans

It is toxic because of a process known as lipidic peroxidation, which involves several chemical reactions:

- Inhibition of the flow of NADP to NADPH, which depletes at pulmonary level and interferes with electron transport
- Generation of superoxide radicals (O_2-), hydroperoxides (HO_2-) and hydrogen peroxide ($H_2 O_2$), which attack cell membranes.
- Paraquat is reduced by NADPH - cytochrome- c - reductase in the presence of NADPH and is reoxidated by O_2-. It reoxidates after two cycles, producing a superoxide radical directly responsible for cell damage. The PQ^+ ion, as such, has no direct toxic effect other than being irritative.
- The superoxide radicals that are produced deplete the organism's detoxification system; the dismutase and catalase superoxide, which transforms them into water, becomes activated oxygen. It joins the unsaturated lipids of the membranes, generating lipidic hydroperoxides.

2.3.3.4 Toxicokinetics

Absorption in the intestine is only five to 10 percent of what is consumed. Even so, most fatal intoxication with paraquat occurs by this tract. Theoretically, paraquat is not absorbed through dermal contact because of its low liposolubility. Studies show that 0.3 percent is absorbed because the causticity of the product alters the cutaneous barrier. If there is extensive damage, there may be absorption and systemic toxicity. As to inhalation, drops deposited in the nose and throat can produce local symptoms such as irritation and epstaxis,[5] but no symptoms of systemic intoxication via this tract have been found, since the droplets that reach the lower respiratory tract are larger than five micras and do not pass through the alveolus membrane. Most paraquat is eliminated by the kidneys, with no changes.

2.3.3.5. Clinical Manifestations of Acute Intoxication

These are associated with ingestion of 20-40 mg/kg. Death can occur up to 70 days after acute contact. The symptoms can occur in three phases:

- Gastrointestinal phase: Given the caustic effect of paraquat, this phase is characterized by nausea, vomiting, retrosternal pain, epigastralgy, abdominal pain, dysphonia and dysphagia. It can be complicated with esophageal, gastric perforation and mediastinitis.
- Hepatorrhenal phase: Usually begins between the second and fifth day and is characterized by hepatic centrolobulillar necrosis and renal tubular necrosis.
- Pulmonary fibrosis phase: The lungs are usually the target organ. This phase generally sets in after a week and is responsible for death.

Ocular contact with paraquat can result in severe irritation, which peaks at 12-24 hours corneal postexposure. With chronic poisoning, one sees lesions, primarily on the skin and nails, dermatitis and ulcerations.

[5] Epistaxis: nasal bleeding

2.3.3.6 Laboratory Analysis

Qualitative urine tests are used to detect paraquat in samples for laboratory analysis. Quantitative tests are based on a variety of methods, such as radioimmunoassay (with maximum levels of 30 mg/ml in urine), fluoroimmunoassay, ultraviolet-visible spectrometry and gas-liquid chromatography (maximum level of 0.01 ppm in plasma).

A qualitative determination in urine is possible by alkalinizing the sample with sodium bicarbonate and adding sodium dithionite. When the product is present, an intense greenish blue color is produced.

2.3.3.7 Treatment for Acute Intoxication

Treatment essentially involves trying to prevent the toxic from being absorbed. This is done by administering Fuller's earth in repeated doses, accelerating its excretion with cathartics, and performing hemodialysis within the first ten hours, if possible. Pharmacological interventions have been proposed to interrupt the toxic biochemical cascade. Drugs such as b-blockers, n-acetylcysteine, vitamin C, vitamin E and colchicine are also part of the treatment.

Oxygen is not to be administered, as it increases the substrate for the formation of free radicals.

3. MATERIALS AND METHODS

Although existing scientific information points to low toxicity and irritative potential in humans, aerial fumigation with glyphosate in the Department of Putumayo between December 2000 and February 2001 sparked considerable protest over its reported impact on the local environment and the population. This controversy poses two questions:

1. *Did health problems or illness increase after aerial spraying, compared with the baseline defined by the regional epidemiological profile prior to application?*

2. *If so, has the population been exposed to glyphosate from aerial spraying in a way that might explain the increase in health problems or illness?*

Theoretically, these questions could have been answered through prospective epidemiological-environmental research. However, because this study was conducted after spraying, a **retrospective design** was the only option. The possibility of an analytical observational study (cases-controls) was considered initially, but ruled out in favor of a **descriptive observational study**, because the only way to reach the population was through a health brigade for the general public and not necessarily for those potentially affected by spraying. This posed certain limitations. *"Descriptive observational studies do not allow the investigator to establish a cause-effect relationship. They do not indicate if the cause appeared before the effect and pose problems with bias in collecting cases. It is possible to determine the frequency with which a case occurs, but not how representative it is of the population. So, frequencies cannot be calculated. These studies are, however, useful in forming a hypothesis. By offering a complete description, they give a better idea of the mechanism of an illness or its evolution. From a clinical standpoint, descriptive observational studies require a cautious and critical approach. By generating questions or a hypothesis, they can be of interest and can encourage other studies as well."*[6]

The study population included the inhabitants of three municipalities in Putumayo where coca crops were sprayed between December 22/2000 and February 6/2001. The villages with the highest number of reported complaints were selected in each municipality, and twelve were targeted for study. The procedure used to collect complaints and select the villages is described in Appendix 2: Preoperative Phase. The municipalities and selected villages are listed as follows.

TABLE 3.1. Villages Selected for Field Work.

MUNICIPALITY	VILLAGES
Orito	El Empalme Jardín de Sucumbíos Siberia
San Miguel	San Marcelino Chiguaco Yarinal El Aguila Bajo Amarón
Valle del Guamuez (La Hormiga)	La Esmeralda Los Angeles Las Vegas El Placer

Due to travel problems, field work was conducted in only nine of the 12 selected villages. The population was invited to take advantage of a 10-day health brigade (June 10-20, 2001). The invitation was extended by radio and through community health workers. (Attachment 2: Invitation Broadcast by Radio). The HEALTH BRIGADE offered general medical check-ups and distributed medicines at no cost. Samples for the toxicology tests were collected by the health brigade. In all 1,244 people responded spontaneously to the invitation. There was no restriction as to occupation, age or sex. The activities and movements of the HEALTH BRIGADE are described in Appendix 3 - Operative Phase.

[6] Ruiz, A., Gómez, C., Londoño, D. "Investigación clínica: Epidemiología clínica aplicada." P.117-119.

The CRI was administered to 500 people in this group. It is divided into nine sections and contains 38 pages (Attachment 1: CRI). The subjects were selected on the basis of two criteria.

1. Subjects who claimed to have experienced health problems or illness during the four weeks subsequent to the last spraying (designated as *case*); and

2. Subjects who claimed to have experience no health problems or illness during the four weeks subsequent to the last spraying, in spite of living in the same village and being of the same sex and approximately the same age as the foregoing cases (designated as *control*).

Initially, the idea was to conduct a paired, analytical observational study of cases and controls, based on these criteria. However, in practice, most of the people served by the HEALTH BRIGADE were evaluated as cases. Therefore, this is a **descriptive operational study.**

Variables explored with the CRI:

1. Demographic characteristics such as sex, age, marital status, SGSSS[7] affiliation, educational level and occupation.
2. Glyphosate exposure through PECI aerial spraying: contact with the substance, exposure pathway, and distance from the sprayed field.
3. Health problems or illness reported by the subjects during the four weeks subsequent to the last spraying: occurrence, affected organ (skin, eyes, digestive tract, etc.) and primary symptoms.
4. Demand for and use of health services: type of service, diagnosis, treatment, evolution and subsequent check-ups.
5. Non-health-related problems attributed to spraying: type of problem and complaints filed with local authorities
6. Other occupational risks: exposure to other agricultural chemicals, how they are prepared and applied, means of protection, pesticide storage and disposal of packages and containers.
7. Clinical evaluation: pathological background, current illness, physical examination, diagnosis.
8. Laboratory results: cholinesterase activity levels in the blood, presence of paraquat in urine and determination of glyphosate in urine

The CRI was administered to 500 of the 1,244 people served by the health brigade. The directed questioning was done by two members of the team, after which peripheral venous blood samples were taken from the forearm, using a tourniquet and venoyet. The samples were collected in heparinized tubes and kept in portable coolers at a temperature of 5.0°C. The urine samples were taken

[7] General Social Security System for Health

under the supervision of one of the interviewers. The plastic containers with the samples were stored in portable coolers at a temperature of 2.0°C. Their transportation and handling are described in Appendix No. 3

Two other members of the team performed a clinical evaluation and produced a diagnostic printout for each subject.

The samples were sent immediately to Bogota for toxicological analysis pursuant to the following methods.

- High-performance liquid chromatography was used to analyze glyphosate in urine. The minimum detection limit with this method is 0.1 mg/l.)
- The modified Michel potentiometric colorimetric test was used to measure cholinesterase activity. It measures pH change, expressed as pH delta units/hour. Acetyl-cholinesterase enzyme activity is measured by the pH change produced in the substrate. Heparin (neutral sodium salt) was the anticoagulant used. The anticoagulant EDTA was not used, as it would affect the pH in the sample and produce abnormal results.
- A qualitative test to detect paraquat in urine was done by reducing the paraquat cation to a blue ion radical in the presence of an alkaline reactive and sodium dithionite.

The information and findings obtained with both procedures (directed questioning and laboratory analysis) were noted in the CRI then consolidated in a database, using the ACCESS program. The database was exported to the SPSS program to analyze the results (See Appendix 3).

4. FINDINGS

4.1 STUDY POPULATION

The health brigade from the Uribe Cualla Toxicology Clinic examined 1,244 outpatients between June 10 and 20 and administered the CRI to 500 of them. The investigators invalidated 12 subjects because the CRI contained incomplete information, leaving 488 subjects in the study. Most of the subjects were females (58.4 percent) (males, 41.6 percent). The majority of the study population was single (59.6 percent or 291 subjects) and most had not completed their primary education (269 subjects); 135 said they had no schooling. In terms of age, 44.1 percent belong to the 15-44 age group, 29.1 percent to the 5-14 age group, 21.5 percent to the 0-4 age group, 3.7 percent to the 60 age group, and 1.6 percent to the 45-59 age group.

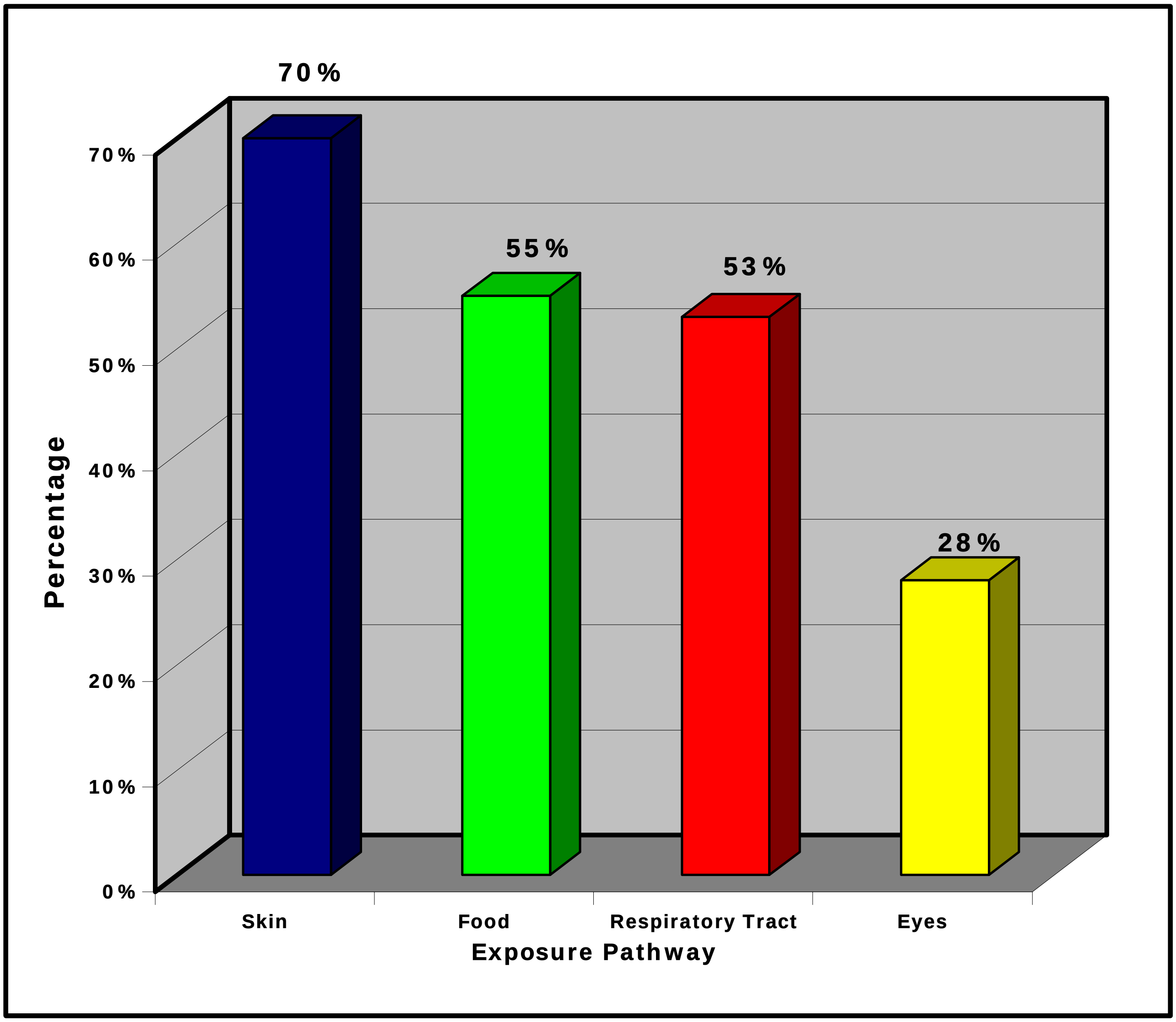
As to place of residence, 53.7 percent of the subjects live in Valle del Guamuez, 33.2 percent in Orito, and 12.9 percent in San Miguel.

The majority were minors or students (211 subjects, 43.2 percent). The others included housewives (116 subjects, 23.8 percent), farmers (55 subjects, 11.3 percent) and day laborers (35 subjects, 7.2 percent). Less than one percent were involved in other occupations (mechanic, shopkeeper, teacher) (See Appendix 4).

4.2. GLYPHOSATE EXPOSURE THROUGH AERIAL SPRAYING

All the subjects claimed direct or indirect glyphosate exposure from aerial spraying between December 2000 and February 2001, although in different degrees. Indirect exposure refers to having consumed food or water sprayed with glyphosate. However, 87 percent said they had direct contact with the mixture sprayed by DIRAN. As indicated in Graph 4.1, the skin was considered the most important exposure pathway, followed by food, the respiratory tract and the eyes.

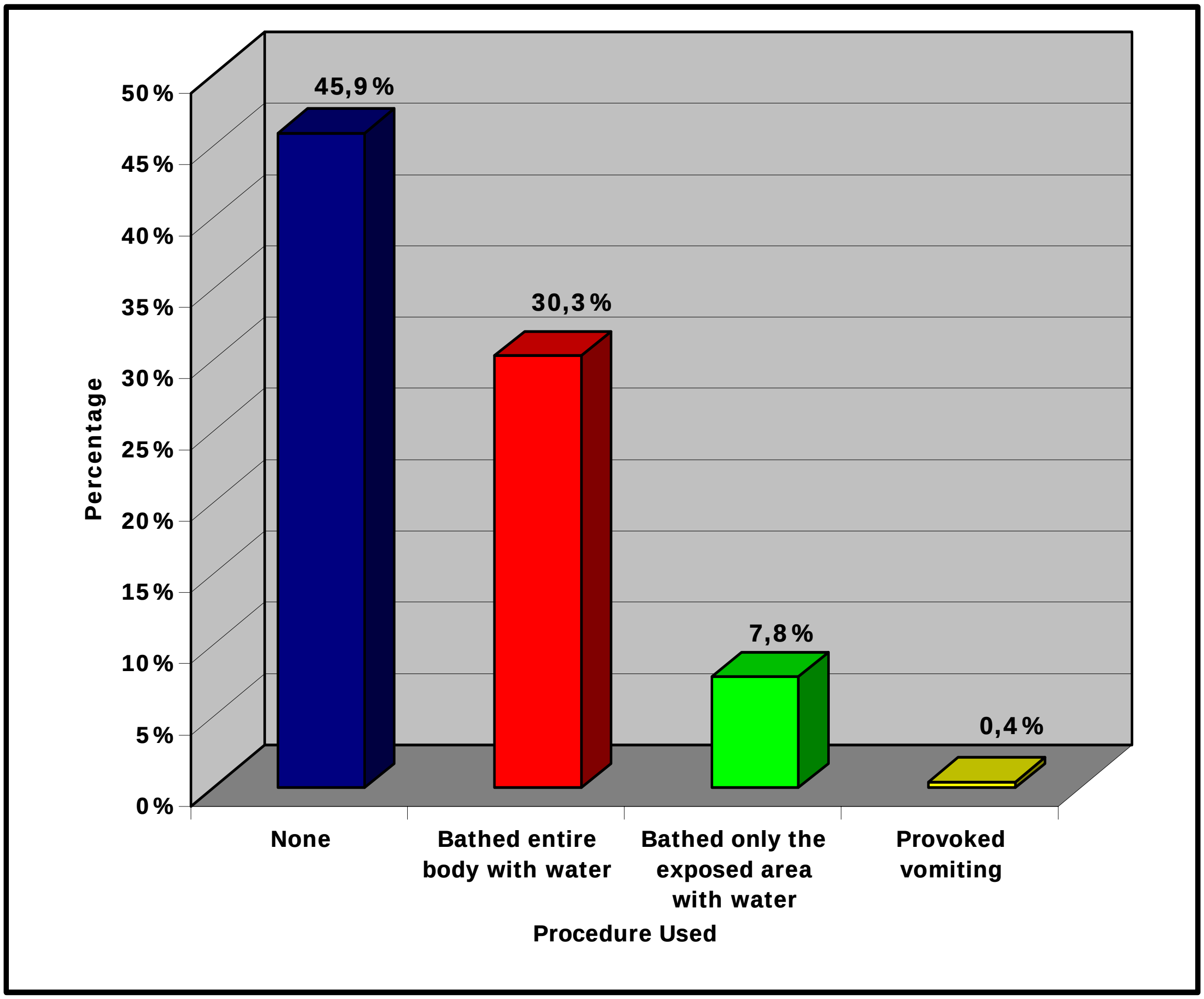
GRAPH No. 4.1
Exposure Pathways to the PECI Mixture*



Note: : The percentages are not exclusive. A single individual could have reported exposure by more than one pathway.

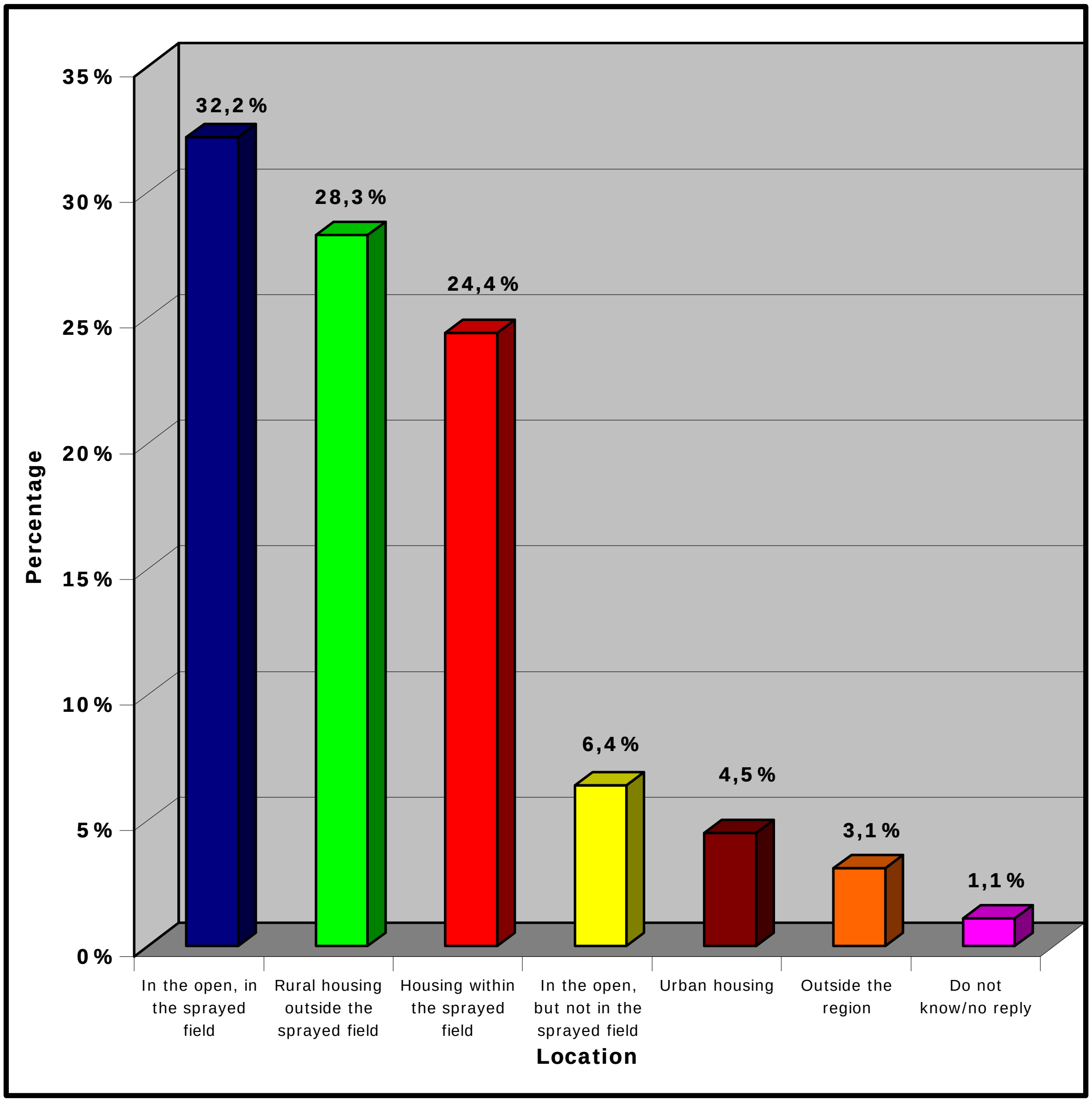
When asked about their behavior after "reported contact" with the PECI mixture, 45.9 percent (224 subjects) indicated they took no measures in this respect; 30.3 percent, (148 subjects) washed their entire body with water and only two (0.4 percent) induced vomiting. Thirty-eight subjects (7.8 percent) washed part of their body with water, while 76 (15.6 percent) did not recall or did not respond to the question (See Graph No. 4.2).

GRAPH No. 4.2
Behavior After "Reported Contact" with the PECI Mixture



When asked about their exact location at the time of spraying, most of the subjects said they were out in the open, in the field being sprayed, or inside a dwelling in or outside the field (See Graph 4.3).

GRAPH No. 4.3
Location at the Time of the Last Spraying



As to place of residence, 95 percent of the subjects said they live in the village where they work. Half of these individuals live on the lot that was sprayed.

4.3. HUMAN HEALTH EFFECTS FROM GLYPHOSATE EXPOSURE

The following question was asked to assess the supposed human health effects from aerial spraying with glyphosate: *Did you experience health problems or illness during the four weeks after the last time the aircraft sprayed near where you live or* *usually work?* In response, 82.6 percent (403 subjects) said they experienced some type of health problem or illness.

The subjects indicated the following when asked about the most frequent symptoms or the organs or tracts most affected.

TABLE 4.1. Most Affected Organs or Tracts

Most Affected Organs or Tracts	No. of subjects	Percent[8]
Gastrointestinal - digestive tract	256	63.5 percent
Skin	235	58.3 percent
Eyes	105	26.1 percent
Cephalea	187	46.4 percent
Dyspnea or fatigue[9]	66	16.4 percent

Also mentioned were symptoms such as fever (139 subjects, 34.5 percent), coughing (36 individuals, 8.9 percent), colds or flu (57 subjects, 14.1 percent) and muscle pain (15 subjects, 3.7 percent). [7]

- The following digestive or gastrointestinal disorders were mentioned most often:

TABLE 4.2. Gastrointestinal Disorders

Disorder	No. of subjects	Percent[7]
Diarrhea	199	49.4 percent
Vomiting	170	42.2 percent
Nausea	96	23.8 percent
Abdominal pain	17	4.2 percent

- The dermal symptoms mentioned most often:

[8] These percentages are not exclusive. In other words, an individual could have reported more than one symptom or illness. The percentage is calculated according to the total number of subjects who reported a symptom or illness (403 subjects).
[9] Breathlessness or difficulty breathing

TABLE 4.3. Dermal Symptoms

Symptom	No. of subjects	Percent[7]
Pruritus or itching	221	52.4 percent
Erythema or reddening	206	51.1 percent
Vesicles or blisters	58	14.4 percent
Burning sensation	29	7.2 percent
Pustules	24	6.0 percent

- The eye problems mentioned most often:

TABLE 4.4. Eye Problems

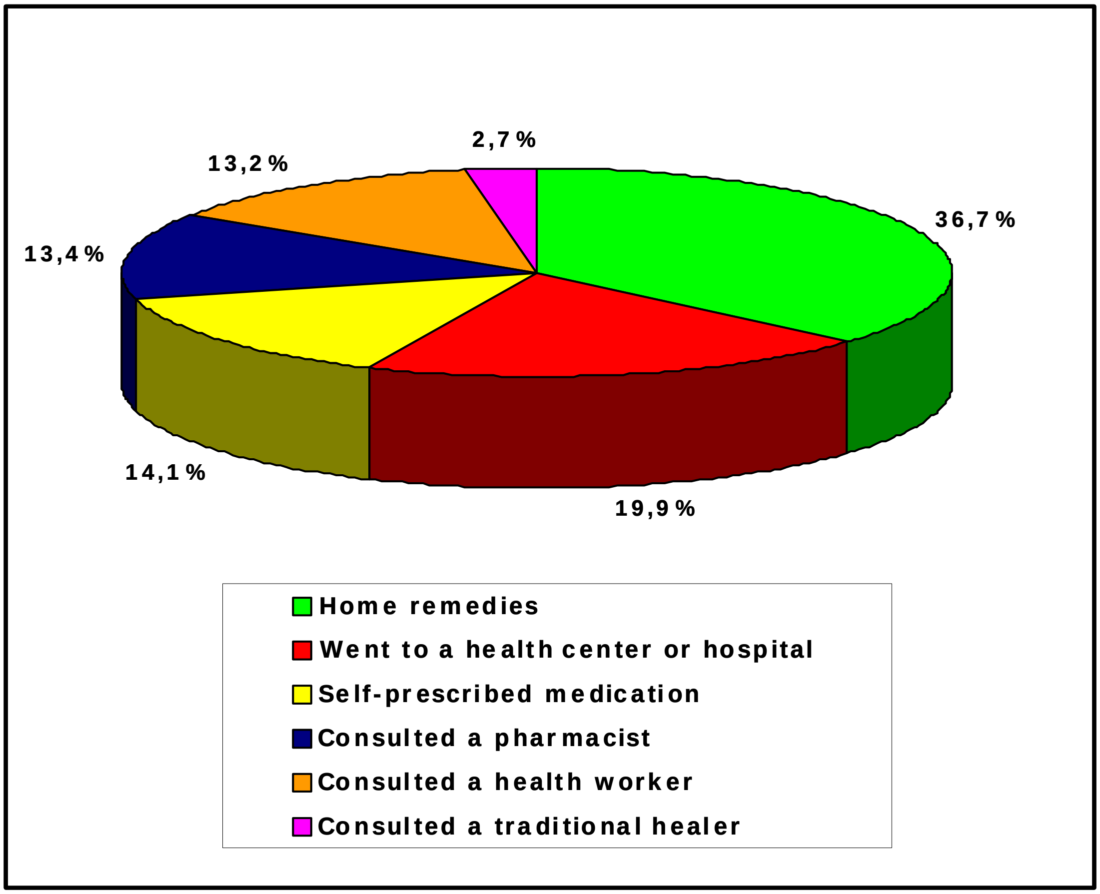
Symptom	No. of subjects	Percent[7]
Burning sensation	85	21.1 percent
Reddening or conjuntival injection	59	14.6 percent
Pain	19	4.7 percent
Pruritus	5	1.2 percent

The subjects indicated the following when asked about therapeutic measures taken in response to the problems described. (See Graph No. 4.4)

TABLE 4.5. Therapeutic Measures

Therapeutic Measure	No. of subjects	Percent
Home remedy	148	36.7 percent
Went to a health center or hospital	80	19.9 percent
Self-prescribed medication	57	14.1 percent
Consulted a druggist or pharmacist	54	13.4 percent
Consulted a health worker	53	13.2 percent
Consulted a traditional healer	11	2.7 percent
TOTAL	403	100.0 percent

GRAPH No. 4.4
Therapeutic Measures in Response to the Reported Illness



When asked about the course of their symptoms, 60 percent of those who went to a hospital or health center said the symptoms evolved satisfactorily. Only 20 percent of those who consulted a health professional (16 subjects) went for subsequent check-ups to monitor the symptom. These findings seem to indicate the illnesses reported by the study group were slight, improved with analgesics or home remedies, did not require medical care, and evolved satisfactorily within a short period of time.

The following table compares the location of the 403 subjects who said they experienced some type of illness during the four weeks subsequent to PECI aerial spraying with the location of the 85 subjects who said they experienced no illness during this period.

TABLE 4.6. Distance from the Sprayed Field

Reference to some illness		Distance from the field at the time of PECI aerial spraying			Total
		1 km (0-14' by foot)	1.1-2 km (15-29' by foot)	More than 2 km. (More than 30' by foot)	
YES	# of subjects	342	15	46	403
	Percentage (percent)	84.9	3.7	11.4	100.0
NO	# of subjects	75	5	5	85
	Percentage (percent)	88.2	5.9	5.9	100.0

A high percentage of the complaints originated with subjects who were more than two kilometers from the field (46 subjects, 11.4 percent). This is surprising, since the measured maximum drift of PECI aerial spraying is five meters. It is, therefore, unlikely that someone located at such a distance could receive enough of a dose to cause appreciable clinical symptoms.

Furthermore, most of the subjects who experienced no illness were located in the field at the time of spraying or less than one kilometer away. This distribution is contrary to what one would expect if the glyphosate sprayed by PECI were the cause of the symptoms reported by the population.

Cutaneous problems (pruritus and erythema), digestive disorders (diarrhea, vomiting and nausea), cephalea and eye problems (burning and reddening) were the illnesses mentioned most by those who were in the field at the time of spraying or in a dwelling less than one kilometer away.

The following were the conditions reported by subjects who were more than two kilometers from the sprayed field (46 subjects):

TABLE 4.7. Illnesses Reported by Subjects Located More than Two Kilometers from the Sprayed Field

Reported Condition	No. of Subjects	Percent[10]
Gastrointestinal symptoms (diarrhea, nausea, vomiting	37	80.4
Cutaneous disorders (erythema, pruritus and vesicles)	25	54.3
Fever	19	41.3
Cephalea	16	34.8
Eye problems (reddening and burning)	11	23.9
Respiratory problems (coughing, rhinorrhea and nasal pruritus)	8	17.4
Myalgia and bone pain	3	6.5
Gingivorragy (bleeding gums)	1	2.1

Fever, vesicles, blisters and cutaneous pustules cannot be attributed to glyphosate exposure through PECI spraying. Toxicology research on glyphosate and its formulation aids indicates they have no properties that irritate the skin. Nor can diarrhea, vomiting and nausea be attributed to exposure from aerial spraying of the PECI mixture. Clinical research shows these symptoms appear only in cases where a relatively high volume of the concentrated commercial preparation is ingested. Cephalea is an unspecified symptom. Like the others, it is associated with infections that are prevalent in the region, such as intestinal polyparasitism, scabiosis, pyodermitis and acute respiratory infections. Eye problems such as burning, pruritus and reddening, and respiratory symptoms such as coughing and rhinorrhea correspond to the clinical manifestations described in literature as secondary to acute accidental exposure to undiluted glyphosate and are due to respiratory and ocular mucus irritation. However, with minimal exposure to the PECI mixture through aerial spraying, the dose that could come in contact with ocular, pharyngeal and respiratory mucus is insufficient to have an appreciable clinical effect.

4.4 OCCUPATIONAL RISKS

4.4.1 Commonly Used Agricultural Chemicals

When questioned about agricultural chemicals, 382 subjects (78.3 percent) said they use some type of chemical substance on legal and illicit crops. Gramoxone (paraquat) is the pesticide used most often (20.9 percent, 80 subjects). The following are figures on exposure to these products.

TABLE No. 4.8 Agricultural Chemicals Used by the Study Population During the Six Months Subsequent to the Last Aerial Spraying

[10] These percentages are not exclusive. In other words, an individual could have reported more than one symptom or illness. The percentage is calculated according to the total number of subjects who reported some type of symptom or illness and were located more than two kilometers from the sprayed field.

Agricultural Chemical (trade name)	Active Ingredient	TC Ms[a]	TC EPA[b]	No. of subjects	Percentage (%)	FREQUENCY			
						Only once during the entire period	At least once a month	At least once a week	NK/NR
Roundup[11]	Glyphosate	IV	III	38	9.95	1.04 %	5.76 %	2.62%	0.53 %
Faena	Glyphosate	IV	III	5	1.31	0.00 %	1.31 %	0.00 %	0.00 %
Gramoxone	Paraquat	I	I	80	20.94	3.19 %	12.98 %	3.70 %	1/07 %
Furadan	Carbofuran	I	I	32	8.38	1.35 %	4.32 %	2.43 %	0.28 %
Carboter	Carbofuran	I	I	1	0.26	0.26 %	0.00 %	0.00 %	0.00 %
Thiodan	Edosulfan	I	I	31	8.12	0.26 %	5.49 %	1.84 %	0.53 %
Curacrón	Prophenophos	II	II	30	7.85	0.79 %	5.24 %	1.57 %	0.25 %
Metilparatión	Methylparation	I	I	29	7.59	0.95 %	4.43 %	1.89 %	0.32 %
Tamaron	Methamidophos	I	I	53	13.87	1.98 %	8.21 %	3.11 %	0.57 %
Dithane	Mancozeb	III	III	7	1.83	0.00 %	1.31 %	0.52 %	0.00 %
Manzate	Mancozeb	III	III	8	2.09	0.26 %	1.31 %	0.26 %	0.26 %
Bavistín	Carbenzadim	III	-	5	1.31	0.22 %	0.65 %	0.44 %	0.00 %
Methavin	Methomyl	I	I	14	3.66	0.00 %	2.09 %	1.05 %	0.52 %
Lannate	Methomyl	I	I	1	0.26	0.00 %	0.26 %	0.00 %	0.00 %
Matancha	2.4 D Amine	II	II	2	0.52	0.52 %	0.00 %	0.00 %	0.00 %
Amina SL	2.4 D Amine	II	II	1	0.26	0.00 %	0.26 %	0.00 %	0.00 %
Anikil	2.4 D Ester	III	II	5	1.31	0.00 %	1.31 %	0.00 %	0.00 %
Monitor	Monocrotophos	I	I	6	1.57	0.00 %	0.31 %	1.26 %	0.00 %
Malathión	Malathion	IV	III	1	0.26	0.00 %	0.26 %	0.00 %	0.00 %
Karate	λ Cyhalothrin	IV	II	4	1.05	0.00 %	1.05 %	0.00 %	0.00 %
Canidia	BeauveriaBassiana	IV	IV	1	0.26	0.00 %	0.00 %	0.26 %	0.00 %
Sirus	Pyrazosulfuron	IV	III	1	0.26	0.00 %	0.00 %	0.26 %	0.00 %
Busan	Metansodium	I	ND	1	0.26	0.00 %	0.26 %	0.00 %	0.00 %
Terranius	NI	-	-	1	0.26	0.00 %	0.26 %	0.00 %	0.00 %
Sistemin	Dimethoate	II	II	1	0.26	0.00 %	0.00 %	0.26 %	0.00 %
Lorsban	Chlorpiriphos	II	II	1	0.26	0.26 %	0.00 %	0.00 %	0.00 %
Klip boro	Boric acid	NA	NA	2	0.52	0.00 %	0.00 %	0.00 %	0.52 %
Todo en Uno	Fertilizer	NA		1	0.26	0.00 %	0.26 %	0.00	0.00 %
Unspecified product				20	5.24	-	-	-	-
TOTAL				382	100.0	-	-	-	-

Abbreviations:

TC: Toxicity Category.

a. MS: According to the Ministry of Health in Colombia
I: Extremely Toxic. II: Highly Toxic. III: Moderately Toxic. IV: Slightly Toxic.

b. EPA: As classified by the United States Environmental Protection Agency

NI: Not identified as a commercial product in Colombia.

NA: Not applicable, because it is a fertilizer.

ND: Registration canceled and no data found.

[11] Refers to glyphosate sold commercially, not that used by PECI for aerial fumigation.

4.4.2 Methods Used to Prepare and Apply Agricultural Chemicals

Only 28.2 percent of those who handle agricultural chemicals (107 subjects) are involved in their preparation. The majority (95.3 percent, 102 subjects) prepare the product by hand, without gloves. The others (4.7 percent, 5 subjects) use gloves.

As to the application, 24.4 percent (93 subjects) use a back pump or *cacorro,* 6.3 percent (24 subjects) use a stationary pump and 69.3 percent said they have no direct role in application (e.g., women and minors).

4.4.3 Hygiene and Industrial Safety

Only 8.9 percent of those who handle agricultural chemicals (34 subjects) use some type of hygiene or industrial safety equipment. In other words, 91.1 percent of those exposed to pesticides (348 subjects) use no means of personal protection. Boots are the most common element, but are used only occasionally (See Table 4.9).

TABLE 4.9 Use of Hygiene and Industrial Safety Equipment

Hygiene & Industrial Safety Equipment	No. of subjects	Percent
Boots	**17**	**4.4 percent**
Overalls	**9**	**2.3 percent**
Gloves	**5**	**1.3 percent**
Helmet	**1**	**0.3 percent**
Surgical mask	**1**	**0.3 percent**
Protective mask	**1**	**0.3 percent**
TOTAL	**34**	**8.9 percent**

Similarly, 17.8 percent of those who handle agricultural chemicals (68 subjects) had some type of accidental contact with these substances during the last six months. The highest number of accidents involved Gramoxone (paraquat), with 46 cases, followed by thiodan (endosulfan), with 18 incidents.

As to what was done in the event of accidental exposure, only 22 subjects (32.4 percent) employed some type of decontamination procedure.

TABLE 4.10 Decontamination Procedures

Decontamination After Accidental Contact	No. of subjects	Percent

None	46	67.7 percent
Washed entire body with water	12	17.6 percent
Removed and changed clothes immediately	6	8.8 percent
Washed the affected area with water	2	2.9 percent
Induced vomiting	1	1.5 percent
Applied a specific antidote (atropine)	1	1.5 percent
TOTAL	68	100.0 percent

4.4.4 Pesticide Storage and Disposal of Empty Packages and Containers

The following was found with respect to storage.

TABLE 4.11 Where Pesticides Are Stored

Storage Area	No. of subjects	Percent
Not indicated[12]	270	70.7 percent
In a covered area outside the home	77	20.1 percent
In the home	29	7.6 percent
Outdoors	6	1.6 percent
TOTAL	382	100.0 percent

The following was found with respect to disposal of empty packages and containers.

TABLE 4.12 Disposal of Empty Packages and Containers

Disposal	No. of subjects	Percent
Do not know/No reply	274	71.7 percent
Buried	30	7.9 percent
Thrown in the garbage	28	7.3 percent
Burned	23	6.1 percent
Left in the field	15	3.9 percent
Reused for another purpose	5	1.3 percent
Other	7	1.8 percent
TOTAL	382	100.0 percent

Through observation and by talking to HEALTH BRIGADE patients, the research team confirmed the existence of agricultural chemical abuse to maintain the region's coca crops. Highly toxic pesticides (Toxicity Category I: Extremely Toxic) are applied weekly. These include organophosphates (e.g. methylparathion), bipyridyl herbicides (e.g. paraquat) and endosulfans (e.g. thiodan).

Frequency of application and lack of protective measures increases the risk of exposure. In addition to mixtures known as "bombs" [13] , inappropriate means such as static irrigation are used.[14] To make matters worse, children and women are sometimes involved in preparing and applying these chemicals.

[12] No indication, since the person interviewed was a child.
[13] A mixture of several pesticides applied simultaneously.
[14] A static irrigation system used to apply agricultural chemicals.

4.5 CLINICAL EVALUATION

All patients served by the HEALTH BRIGADE were subject to a clinical assessment. In response to directed questioning on the occurrence of illness in the last six (6) months, 445 (91.2 percent) claimed to have suffered some type of health problem.[15]

TABLE 4.13 Illnesses Experienced in the Last Six Months

Illness	No. of subjects	Percent
Scabiosis	**158**	**32.4 percent**
Pyodermitis	**122**	**25.0 percent**
Fever syndromes	**61**	**12.5 percent**
Asthma	**53**	**10.9 percent**
Contact dermatitis	**28**	**5.7 percent**
Allergic rhinitis	**16**	**3.3 percent**
Eruptive diseases	**7**	**1.4 percent**
TOTAL	**445**	**91.2 percent**

Most of these diseases are infectious and are not related to contact with agricultural chemicals (except for allergies such as asthma, dermatitis and rhinitis). This eliminates the possibility of their being caused by glyphosate from PECI aerial spraying.

To disprove claims that glyphosate is associated with fetal death, malformation or abortion, specific questions were asked about personal and family gynecological-obstetric background. No positive information was found in this respect.

After the questioning, a definitive diagnosis was printed on the basis of the physical examination. The following were the predominant clinical entities (See Attachment 10).

TABLE 4.14 Definitive Diagnosis

Definitive Diagnosis	No. of subjects	Percent[16]
Intestinal parasitism	112	23.0 percent
Scabiosis	108	22.1 percent
Acute respiratory infection (ARI)	54	11.9 percent
Impetigo	50	10.3 percent

[15] Includes the 403 subjects who claimed to have experienced some type of illness in the four (4) weeks after PECI spraying and those who experienced any type of illness in the last six months.
[16] These percentages are not exclusive. In other words, the same individual could have reported more than one symptom or illness.

Cephalea	40	8.2 percent
Acute diarrheal disease (ADD)	36	7.4 percent
Contact dermatitis	13	2.7 percent
Urinary infections	13	2.7 percent
Anemia	12	2.5 percent
Healthy subjects	38	7.8 percent

Since most are infectious diseases (parasital, viral or bacterial), no connection was found between these illnesses and glyphosate exposure from PECI spraying.

4.6 TOXICOLOGY EVALUATION

The 266 blood samples analyzed for cholinesterase activity were within a normal range for the Colombian population (between 91 and 164 units (∆pH/hour). The average level was 122.7 units (∆pH/hour). This is not surprising and does not rule out continuous overexposure to organophosphate pesticides, even though they join together irreversibly, inhibiting the activity of this enzyme. The body is quite capable of synthesizing new cholinesterases to reestablish their activity.

Although the 489 urine samples were reported as “not detectable” for paraquat and glyphosate, the possibility of occupational overexposure to pesticides cannot be ignored. The pesticides analyzed are not biocumulative. In other words, they are eliminated entirely through feces and urine. Also, they are compounds with low liposolubility and minimum dermal and inhalatory absorption.

5. CONCLUSIONS AND RECOMMENDATIONS

- Despite the number of illnesses observed among the population of Putumayo, there are several reasons why they cannot be attributed to a single chemical substance. The first concerns the limits of a retrospective epidemiological-environmental study. These make it difficult to collect objective evidence of exposure to the substance in question. The existence of biomarkers is also a problem, as is the difficulty of establishing a correlation between glyphosate exposure and the clinical manifestations reported by the subjects. It is, therefore, virtually impossible to establish a cause-effect relationship between exposure to the substance in question and the clinical manifestations attributed to this exposure. Nor can a plausible hypothesis be drawn to explain morbidity attributable to the introduction of a chemical substance of low toxicity and limited environmental dispersion.

- A prospective epidemiological-environmental study is required to determine if health problems and illness are more frequent after aerial spraying with glyphosate and if this supposed increase is related to glyphosate exposure. However, this was not possible, because the study was designed and conducted five months after aerial spraying. The initial case-control model was discarded, leaving a retrospective study as the only option available, with the limitations noted above.

- The information collected for the study reflects only the characteristics of demand for and use of the services provided by the health brigade in nine villages in three municipalities in the Department of Putumayo (Orito, Valle del Guamuez and San Miguel). [17] The sample cannot be characterized as random, because the subjects volunteered in response to a broad invitation.

- Despite the limitations of a retrospective study, an analysis of CRI data, figures on morbidity and toxicological information on glyphosate indicates that glyphosate sprayed by DIRAN between December 2000 and February 2001 could not have been responsible for the illnesses reported by the study population.

The following should be noted with respect to the findings:

- The prevalence of health problems observed in the study population was similar to the prevalence found in epidemiological reports from years prior to the start of the PECI, both in municipalities targeted by the program (e.g. La Hormiga) and in municipalities in departments where illicit crops have yet to be sprayed for eradication, such as Puerto Wilches and San Vicente de Chucurí in the Department of Santander (See Table 5.1). The findings are consistent with the poor health conditions, poverty, lack of potable water, inadequate personal hygiene, lack of adequate sewage facilities and solid waste disposal, and inadequate food handling found in Putumayo. The rate of unsatisfied basic needs (UBN) was 78.7 percent in 2001.[18] The poverty rate in the department was 68.9 percent in 1998.

TABLE No. 5.1 Morbidity per Outpatient
La Hormiga and Sibundoy in Putumayo and Puerto Wilches and San Vicente de Chucurí in Santander
1992-1996

Municipality	Diagnosis	1992		1993		1994		1995		1996	
		# Visits	M (%)	# Visits	M (%)	# Visits	M (%)	# Visits	M (%)	# Visits	M (%)
La Hormiga	ADD	113	0.25	72	0.16	98	0.26	102	0.34	65	0.21

[17] Between December 2000 and February 2001, PECI/DIRAN eradicated coca crops in these areas through aerial spraying with glyphosate. This sparked controversy and speculation as to how exposure to glysophate might affect the environment and human health.
[18] National Department of Planning. www.dpn.gov.co

(Putumayo)	ARI	88	0.20	63	0.14	81	0.22	103	0.35	71	0.23
	Dermatopathy	49	0.11	28	0.06	42	0.11	65	0.22	51	0.17
	Conjuntivitis	5	0.01	2	0.004	2	0.005	4	0.01	8	0.03
	Cephalea	28	0.06	22	0.05	9	0.02	51	0.17	41	0.13
Sibundoy (Putumayo)	ADD	38	0.35	ND	ND	ND	ND	50	0.42	53	0.44
	ARI	33	0.31	ND	ND	ND	ND	29	0.25	37	0.30
	Dermatopathy	24	0.22	ND	ND	ND	ND	32	0.27	29	0.24
	Conjuntivitis	3	0.03	ND	ND	ND	ND	5	0.04	6	0.05
	Cephalea	1	0.01	ND	ND	ND	ND	1	0.01	2	0.02
Puerto Wilches (Santander)	ADD	94	0.31	137	0.46	98	0.33	151	0.50	80	0.26
	ARI	103	0.34	183	0.61	164	0.55	215	0.72	154	0.51
	Dermatopathy	72	0.24	85	0.28	67	0.22	86	0.29	53	0.17
	Conjuntivitis	9	0.03	14	0.05	5	0.02	10	0.03	5	0.02
	Cephalea	6	0.02	2	0.007	2	0.007	10	0.03	6	0.02
San Vicente de Chucurí (Santander)	ADD	229	0.74	244	0.78	218	0.71	210	0.69	ND	ND
	ARI	104	0.34	119	0.38	182	0.59	186	0.61	ND	ND
	Dermatopathy	87	0.28	117	0.37	144	0.47	138	0.45	ND	ND
	Conjuntivitis	8	0.03	8	0.02	16	0.05	10	0.03	ND	ND
	Cephalea	8	0.03	26	0.08	20	0.07	66	0.22	ND	ND

Source: PECI/PLANCO Advisory Council. Figures on the Department of Putumayo are from the National Health Institute. Figures on the Department of Santander are from the National Health Policy Analysis and Planning Office. SIS103, Ministry of Health.
The population figures are DANE projections based on the adjusted 1993 census.

C Number of Cases
M Morbiidity (percentage)
ADD Acute diarrheal disease
ARI Acute respiratory infection
ND No data

Due to the social and political situation in Colombia and because departmental health officials are slow about reporting data to the National Health Institute (INS), these figures could be incomplete and should be regarded with caution. Figures from recent years are not consolidated and, in some cases, none have been reported. The system was changed in 1997 and departmental officials only report when notification is mandatory, as is the case with diseases transmitted by vectors, those preventable through vaccination and sexually transmitted diseases.

All infectious skin diseases are grouped as dermatopathies, even though WHO differentiates between specific diseases such as dermatophytosis, eczemas, pruritus, allergic dermatitis, other types of dermatitis, etc. According to the INS, this change in procedure is not fully understood, especially at municipal level. As a result, there are problems with records on morbidity.
The municipality of La Hormiga (Valle del Guamuez) has been sprayed heavily by the PECI. On the other hand, Sibundoy (Putumayo), Puerto Wilches and San Vicente de Chucurí (Santander) have never been subject to aerial spraying. Although the Santander region lacks the demographic characteristics, poverty and poor health conditions found in Putumayo, the prevalence of health problems reported by the population as “allegedly due” to aerial spraying is similar or even greater in the municipalities that have not been sprayed.

- The health problems attributed most often by the study population as secondary to glyphosate spraying were gastrointestinal symptoms (diarrhea, vomiting and nausea), skin problems (pruritus or itching, erythema or reddening, vesicles or blisters, burning sensation and pustules), eye problems (burning, reddening or conjunctival injection, pain and pruritus), respiratory symptoms (dyspnea or tiredness, coughing and colds or rhinorrhea), cephalea (headache) and fever. These can have a variety of causes, including infection and allergies, as well as chemical exposure.

- Fever, vesicles, blisters and cutaneous pustules cannot be attributed to glyphosate exposure from PECI spraying. Toxicology research on glyphosate and its formulation aids contains ample evidence of the absence of cutaneous irritating properties. Nor can diarrhea, vomiting or nausea be attributed to the PECI mixture. According to clinical research, these symptoms occur only in cases with ingestion of a relatively high volume of the concentrated preparation sold commercially. Cephalea is an unspecified symptom. Like the others, it is associated with infections that are prevalent in the region, such as intestinal polyparasitism, scabiosis, pyodermitis and acute respiratory infections. (See Table No. 5.1).

- Erythema and reddening of the skin cannot be attributed to contact with glyphosate. According to the IPCS, "In skin irritation studies on volunteers, 0.9 ml of a 9:1 dilution of glyphosate-based preparations in water applied to intact skin for 24 hours produced no change in the skin (Shelanski, 1973). Maibach (1986) tested glyphosate-based preparations and applied 0.1 ml to intact and traumatized skin for 24 hours. Erythema was found on only one of the 24 subjects with intact skin. Four of the subjects with traumatized skin showed some reaction and 10 of the 24 had erythema." [19]The conclusion, in this context, is that exposure to pure glyphosate and/or POEA on traumatized skin unprotected by clothing is required to cause eczema by contact. This further confirms the absence of a cause-effect relationship between DIRAN aerial spraying with glyphosate and the dermal lesions reported by the study population.

- Eye discomfort such as burning, pruritus and reddening, and respiratory symptoms such as coughing and rhinorrhea correspond to the clinical manifestations described in literature as secondary to acute accidental exposure to undiluted glyphosate, and are due to respiratory and ocular mucus irritation. However, in the case of minimal exposure to the PECI mixture through aerial spraying, the dose that could come in contact with ocular, pharyngeal and respiratory mucus is insufficient to produce an appreciable clinical effect.

- Although acute intoxication from ingestion of concentrated glyphosate (undiluted) is associated with gastrointestinal irritations such as nausea, vomiting and abdominal pain, the symptoms reported by the study population cannot be attributed to contact with glyphosate through PECI spraying. This is because ingestion could have occurred only by consuming sprayed water, in

[19] International Programme on Chemical Safety (IPCS). "Environmental Health Criteria 159, Glyphosate." World Health Organization. Geneva, 1994, pg. 89.

which case the dose of the active ingredient would be 3.74 mg/L; that is, 4,813 times less than the dose free of symptoms.[20]

- Only 19.9 percent of those who claimed to have experienced health problems due to PECI aerial spraying (80 subjects) consulted a health professional. The other 323 subjects (80.1 percent) used home remedies, self-prescribed medication or consulted a pharmacist, heath worker or traditional healer. This information seems to indicate the illnesses reported by the population were slight and temporary, improved with analgesics or home remedies, did not require medical care, and evolved satisfactorily within a short period of time. The subjects mentioned only two (2) hospitalizations: one due a serious asthma attack and the other to acute diarrhea accompanied by dehydration. There were no reported deaths related to exposure.

- According to CRI data, 84.9 percent of those who claimed to have experienced illness during the four (4) weeks after PECI aerial spraying were located in the field that was sprayed or in a rural dwelling at a distance of less than one (1) kilometer. There are, however, cases where people claim to have been affected in spite of being located more than one kilometer away. At this distance, exposure to the compound is unlikely, since the maximum measured drift of PECI aerial spraying is 5-10 meters. Most of the subjects who said they suffered no illness or health problems were also in the field at the time of spraying or at a distance of less than one kilometer. If there were a relationship between spraying and illness, we would expect the percentage of those unaffected to increase with distance, not decrease.

- The study leaves no doubt that a wide variety of agricultural chemicals are used to grow coca in the Department of Putumayo. For example, 382 of the 488 subjects (78.3 percent) said they handle a substance of this type (even though farmers and day laborers account for only 18.5 percent of the study population). Ten of the 26 pesticides used by the study population in the last six months belong to Toxicology Category I: “extremely toxic,” with Gramoxone® (paraquat) being the pesticide used most frequently (20.9 percent, 80 subjects).

- Furthermore, 91.1 percent of the subjects who reported using pesticides (348 individuals) employ no means of personal protection. Boots are the main element, but are used only occasionally (4.4 percent, 17 subjects). Pesticides are normally applied with a back pump or *cacorro*, but inappropriate means such as static irrigation are also used. What is worse, exposure to these chemicals can affect the entire family, because women and children help to mix and apply them (67.0 percent of the study population). These products are used frequently (weekly in some cases) and are commonly stored in the home, under beds and near food.

[20] The symptom-free dose for Roundup® is 50 ml (equivalent to 18 g or 18,000 mg of glyphosate as acid).

Recommendations based on the study:

- There is widespread and illegal use of agricultural chemicals in Putumayo, especially to grow coca. Accordingly, the Putumayo Health Department should design and implement an epidemiological surveillance system for mandatory notification of all toxic accidents involving pesticides, as stipulated by Ministry of Health Decree 1843/ 1991.

- Training programs should be designed to provide the community and local authorities with scientific and technical information on pesticide toxicity and safety. Health Department workers require continuing education to diagnose and treat toxic accidents involving pesticides and to be more effective in notifying the pesticide epidemiological surveillance system.

- To facilitate consultation on treatment, all toxic pesticide accidents involving humans should be reported to the Toxicology Advisory Center at the Uribe Cualla Toxicology Clinic in Bogota by calling 9800-116818 or 9800-916818. This effort should be coordinated with DASALUD and the other health institutions in Putumayo. It would also allow the clinic to serve as a reference center for gathering information.

6. BIBLIOGRAPHY

- *Seguridad Social en Colombia: Series de Publicaciones Científicas* No. 7, Instituto Nacional de Salud/Instituto de Seguro Social, 1986.
- “Encuesta Nacional sobre Conocimientos, Actitudes y Prácticas en Salud (CAP): 1986-1989,” *Seguridad Social* Vol.: (sic), Instituto Nacional de Salud. Bogotá, Colombia: 1990
- PECI / PLANCO – NAS Consulting. “Undécimo Informe Periódico de Actividades de Asesoría.” September 1-30, 2001. Bogotá, October 5, 2001.

- Revelo, M.D. "Mortalidad en el Departamento del Putumayo durante 1999." Head of Epidemiology Department. DASALUD Putumayo; Mocoa, November 2000.
- Law 30 /1986. National Drug Statute and regulatory decrees.
- Government of Colombia. "Plan Colombia: Plan Para la Paz, La Prosperidad y el Fortalecimiento del Estado," April 2000.
- Royen M. Handelblat. "Article on Glyphosate Aerial Spraying of Opium Poppy in Colombia." December 28, 2000.
- Drug Advisory Council, Memorandum: February 1, 2001.
- Instituto Geográfico Agustín Codazzi. Departament of Putumayo. *Diccionario Geográfico de Colombia, 1996.*
- Drug Advisory Council, "Cultivos ilícitos, erradicación e impacto ambiental." Colombia, June 2000. p. 22-24
- Parra, L.E. PECI / PLANCO–NAS Consulting. "Consideraciones generales sobre el uso de plaguicidas en agricultura comercial y el uso de glifosato en la erradicación de cultivos ilícitos de coca en Colombia." Bogotá, September 2001.
- Wayland, J., Laws, E. *Handbook of Pesticide Toxicology. Glyphosate*. Volumen 3. San Diego, California. 1991.
- Giesy, J.P., Dobson, S., Solomon, K.R. "Ecotoxicological Risk Assessment for Roundup Herbicide." Rev Environ Contam Toxicol 167:35-120/2000
- Food and Agriculture Organization of the United Nations. FAO. "FAO Specifications and Evaluations for Plant Protection Products. Glyphosate," 2000.
- International Programme on Chemical Safety (IPCS). "Environmental Health Criteria 159, Glyphosate." World Health Organization. Geneva, 1994.
- Williams, G., Kroes, R., Munro, I. "Safety Evaluation and Risk Assessment of the Herbicide Roundup and its Active Ingredient, Glyphosate, for Humans." Regulatory Toxicology and Pharmacology 2000; 31: 117-165.
- Córdoba, D. "Toxicología. Plaguicidas," in *Manual Moderno Editores*. 4th edition. Medellín, Colombia: 2001. p. 107-166
- Helling, C.S, Lead / Soil Scientist Alternate Crops and Systems Laboratory, PSI, ARS-USDA Beltsville, Maryland. "Comments on the Handlblat Article (Dec 28,2000) on Glyphosate Aerial Spraying of Opium Poppy in Colombia," January 4, 2001.
- United States Environmental Protection Agency EPA. "Reregistration Eligibility Decision Fact Sheet on Glyphosate." September 1996. *Pesticide Industry Sales and Usage*. p. 21. EPA.
- García, F. "Análisis de la información epidemiológica en cinco municipios del Huila, donde hubo fumigaciones con glifosato," Huila Health Department; February 2001.
- Parra, L.E. "Programa de erradicación de cultivos ilícitos por aspersión aérea con el herbicida glifosato, acción fundamental para el avance en la lucha contra la droga."

- Parra, L.E. “Los cultivos ilícitos una causa probada del deterioro ambiental regional y nacional,” Bogotá, June 2001.
- APECI/PLANCO. “Evaluación de exposición a glifosato, POEA, Cosmoflux 411F en el PECI.” July 2001. Bogotá.
- International Programme on Chemical Safety (IPCS). “Environmental Health Criteria 159, Organophosphates,” World Health Organization. Geneva, 1994.
- Wayland, J., Laws, E. *Handbook of Pesticide Toxicology. Organophosphate.* Volumen 2. San Diego, California. 1991.
- Uribe, C. “Guías de toxicología. Intoxicaciones por plaguicidas,” Bogotá, 1997. Unpublished.
- Marrs, T.C. “Organophosphate Intoxication. Pharmacology and Therapeutics,” 1993 58(1): 51-66.
- Health and Safety Executive. “Biological Monitoring of Workers Exposed to Organophosphorus Pesticides,” HMSO Publication Center. London, United Kingdom, 1987.
- Rolando Tinoco - Ojanguren. “Poverty, Production, and Health: Inhibition of Erythrocyte holinesterase via Occupational Exposure to Organophosphate Insecticides in Chiapas, México,” January-February 1998.
- Programa de Vigilancia Epidemiológica en Personas Expuestas a Plaguicidas en Colombia (VEO), Instituto Nacional de Salud, 1981-2001.
- Michel, H. “Standard Methods of Clinical Chemistry,” The American Associaton of Chemists, 3(93): 1961.
- ISS, ANDI, ICA. *Manual de Urgencias Tóxicológicas*. Bogotá, Colombia; 1993
- United States Environmental Protection Agency (EPA), *Diagnóstico y tratamiento de los envenenamientos por plaguicidas*. 4th ed. Philadelphia, USA; 1995.
- International Programme on Chemical Safety (IPCS). “Environmental Health Criteria 159, Endosulfan,” World Health Organization. 1994.
- Córdoba, D. “Toxicología” in *Manual Moderno Editores. Paraquat - Nuevo enfoque terapéutico del paciente intoxicado*. 4th ed. Medellín, Colombia: 2001. p. 167-173.
- International Programme on Chemical Safety (IPCS). “Environmental Health Criteria 39: Paraquat and Diquat,” World Health Organization. Geneva, 1994.
- Ruiz, A., Gómez, C., Londoño, D. “Investigación clínica: Epidemiología clínica aplicada.” p.117-119.
- Aldrich, T.E., Griffith, J., Cooke, C. (Ed) *Environmental Epidemiology and Risk Assessment,* Van Nostrand Reinhold. New York USA. 1993.

EMBASSY OF THE UNITED STATES OF AMERICA

URIBE CUALLA TOXICOLOGY CLINIC

REPORTED HUMAN HEALTH EFFECTS FROM GLYPHOSATE

ATTACHMENT 1

CLINICAL RESEARCH INSTRUMENT

-CRI-

Department of Putumayo

Bogota, D.C., Colombia
December, 2001

EMBASSY OF THE UNITED STATES OF AMERICA

URIBE CUALLA TOXICOLOGY CLINIC

REPORTED HUMAN HEALTH EFFECTS FROM GLYPHOSATE

ATTACHMENT 2

RADIO ANNOUNCEMENT ON THE HEALTH BRIGADE
PUTUMAYO
JUNE 10-20, 2001

Department of Putumayo

Bogota, D.C., Colombia
December, 2001

RADIO INVITATION
Broadcast by Proyección Estereo

The Putumayo Department of Health and the Uribe Cualla Toxicology Clinic invite the people of:

SIBERIA
CABAÑAS DEL GUAMUEZ
BATGERIA CHURUYACO 1
EL EMPALME
JARDIN DE SUCUMBIOS
PRIMAVERA DEL GUAMUEZ
ALTO GUISIA
SANTA LUCIA and
ARGENTINA

to take advantage of a HEALTH BRIGADE, which will operate at the schools in Orito on June 11-13.

The purpose of the brigade is to conduct a general medical examination of the community and to collect blood and urine samples from people who believe they have been affected by aerial spraying with glyphosate or by exposure to other pesticides.

Bring the entire family: children, adults, the elderly, and especially those who suffered any kind of problem after spraying.

RADIO INVITATION
Broadcast by Emisora Calientísima de Candela Estéreo
A Community Radio Station

The Putumayo Department of Health and the Uribe Cualla Toxicology Clinic invite the people of:

AGUA BLANCA
SAN JUAN
BAJO AMARON
SAN MARCELINO
SAN FERNANDO\LA GUISITA
LIMONAL\CHIGUACO
RISARALDA
EL AGUILA
YARINAL
LA DANTA and
LA CRUZ

to take advantage of a HEALTH BRIGADE, which will operate at the schools in San Miguel on June 14-16.

The purpose of the brigade is to conduct a general medical examination of the community and to collect blood and urine samples from people who believe they have been affected by aerial spraying with glyphosate or by exposure to other pesticides.

Bring the entire family: children, adults, the elderly, and especially those who suffered any sort of problem after spraying.

RADIO INVITATION

The Putumayo Department of Health and the Uribe Cualla Toxicology Clinic invite the people of:

LA ESMERALDA
LOS ANGELES
SAN ISIDRO
EL PLACER
LAS VEGAS
ALTO PALMIRA
COSTA RICA
LA PRADERA and
BRISAS DEL PALMAR

to take advantage of a HEALTH BRIGADE, which will operate at the schools in La Hormiga on June 17-19.

The purpose of the brigade is to conduct a general medical examination of the community and to collect blood and urine samples from people who believe they have been affected by aerial spraying with glyphosate or by exposure to other pesticides.

Bring the entire family: children, adults, the elderly, and especially those who suffered any sort of problem after spraying.

EMBASSY OF THE UNITED STATES OF AMERICA

URIBE CUALLA TOXICOLOGY CLINIC

REPORTED HUMAN HEALTH EFFECTS FROM GLYPHOSATE

ATTACHMENT 3

INVITATION TO THE SEMINAR-WORKSHOP ON PESTICIDES: SAFE HANDLING AND ENVIRONMENTAL IMPACT

Department of Putumayo

Bogota, D.C., Colombia
December, 2001

Bogota, Colombia
22 May 2001

Title
Name
Position
Institution
City

Dear Sir:

The Governor of Putumayo, the Putumayo Department of Health, the Uribe Cualla Toxicology Clinic and the Embassy of the United States of America have scheduled the Seminar-Workshop on Pesticides: Safe Handling and Environmental Impact for June 21, 2001 at the Comfamiliar Auditorium in Puerto Asís, Putumayo.

The event will be conducted by Dr. Camilo Uribe, Scientific Director of the Uribe Cualla Toxicology Clinic, and will feature the participation of Mr. Luis Eduardo Parra, an environmental engineer. At the end of the seminar-workshop, each participant will receive a report on the proceedings.

We look forward to your participation.

Sincerely,

CAMILO URIBE-GRANJA, M.D.
Scientific Director
Director of Advanced Training in Toxicology, Rosario University School of Medicine
President of the Latin American Toxicology Association
Vice President of the International Union of Toxicology (IUTOX)
Chair of Forensic Medicine, Javeriana University School of Law
President of the Colombian Toxicology and Drug Addiction Association

Bogota, Colombia
22 May 2001

Title
Name
Position
Institution
City

Dear Sir:

The organizers of the Seminar-Workshop on Pesticides: Safe Handling and Environmental Impact will contact the authorities and/or representatives of invited institutions to finance the cost of transportation, food and lodging for participants who do not have offices in Puerto Asís.

We look forward to your participation.

Sincerely,

CAMILO URIBE-GRANJA, M.D.
Scientific Director
Director of Advanced Training in Toxicology, Rosario University School of Medicine
President of the Latin American Toxicology Association
Vice President of the World Toxicology Federation (IUTOX)
Chair of Forensic Medicine, Javeriana University School of Law
President of the Colombian Toxicology and Drug Addiction Association

REPORTED HUMAN HEALTH EFFECTS FROM GLYPHOSATE

ATTACHMENT 4

INVITATION LIST
SEMINAR-WORKSHOP ON PESTICIDES: SAFE HANDLING AND ENVIRONMENTAL IMPACT

Department of Putumayo

Bogota, Colombia
December 2001

EMBASSY OF THE UNITED STATES OF AMERICA

URIBE CUALLA TOXICOLOGY CLINIC

REPORTED HUMAN HEALTH EFFECTS FROM GLYPHOSATE

ATTACHMENT 5

AGENDA
SEMINAR-WORKSHOP ON PESTICIDES:
SAFE HANDLING AND ENVIRONMENTAL IMPACT

Department of Putumayo

Bogota, D.C., Colombia
December, 2001

OFFICE OF THE GOVERNOR OF PUTUMAYO, THE PUTUMAYO DEPARTMENT OF HEALTH, THE URIBE CUALLA TOXICOLOGY CLINIC AND THE EMBASSY OF THE UNITED STATES OF AMERICA

SEMINAR-WORKSHOP ON
PESTICIDES: SAFE HANDLING AND ENVIRONMENTAL IMPACT

VENUE: COMFAMILIAR AUDITORIUM, PUERTO ASIS
DATE: JUNE 21, 2001
TIME: 9:00 A.M.

FOR: Health professionals in the public and private sectors, including physicians, nurses, nurse's aids and I.S.S. rural health workers in San Miguel, La Hormiga, Orito, Puerto Guzmán, Mocoa and Puerto Asís

09:00-10:00 a.m.	General Introduction to Toxicology General Measures in Acute Intoxication Lecturer: Dr. Camilo Uribe
10:00-11:00 a.m.	Organophosphate Pesticides Definition, Action Mechanism, Clinical Manifestations, Diagnosis and Treatment Lecturer: Dr. Camilo Uribe
11:00-12:00 a.m.	Glyphosate Definition, Action Mechanism, Clinical Manifestations, Diagnosis and Treatment Lecturer: Dr. Camilo Uribe
12:00-2:00 p.m.	**Lunch**
2:00-3:00 p.m.	Bipyridyls: Paraquat Definition, Action Mechanism, Clinical Manifestations, Diagnosis and Treatment Lecturer: Dr. Camilo Uribe
3:00-4:00 p.m.	Other Pesticides Pyrethrins - pyrethoids, carbamates, organochlorates Fungicides: Dithiocarbamates- thiocarbamates, chlorophenol Dinitrophenols. Herbicides: Phenoxyacetics, etc. Lecturer: Dr. Camilo Uribe Dr. Olga Lucía Melo

4:30-5:30 p.m.	Environmental Impact of Organophosphates, Bipyridyls, Glyphosate and Other Pesticides Lecturer: Dr. Luis Eduardo Parra
5:30-6:30 p.m.	Round Table Questions and Answers Moderator: Dr. Camilo Uribe

OFFICE OF THE GOVERNOR OF PUTUMAYO, THE PUTUMAYO DEPARTMENT OF HEALTH, THE URIBE CUALLA TOXICOLOGY CLINIC AND THE EMBASSY OF THE UNITED STATES OF AMERICA

SEMINAR-WORKSHOP ON
PESTICIDES: SAFE HANDLING AND ENVIRONMENTAL IMPACT

VENUE: COMFAMILIAR AUDITORIUM, PUERTO ASIS
DATE: JUNE 23, 2001
TIME: 9:00 A.M.

FOR: The governor, mayors, municipal representatives and police inspectors from San Miguel, La Hormiga, Orito and Puerto Guzmán, UMATA Directors, the Secretary of Agriculture, the Secretary of Education, ecclesiastic authorities, officials of the Colombian Agricultural Institute (ICA), NGOs and community leaders.

09:00-10:00 a.m.	General Introduction to Toxicology General Introduction to Pesticides Studies on Pesticide Toxicity Lecturer: Dr. Camilo Uribe
10:00-11:00 a.m.	Organophosphate Pesticides Definition, Action Mechanism, Clinical Manifestations, Diagnosis and Treatment Lecturer: Dr. Camilo Uribe
11:00-12:00 a.m.	Glyphosate Definition, Action Mechanism, Clinical Manifestations, Diagnosis and Treatment Lecturer: Dr. Camilo Uribe
12:00-2:00 p.m.	**Lunch**
2:00-3:00 p.m.	Bipyridyls: Paraquat Definition, Action Mechanism, Clinical Manifestations, Diagnosis and Treatment Lecturer: Dr. Camilo Uribe

3:00-4:00 p.m.	Other Pesticides Pyrethrins - Pyrethoids, Carbamates, Organochlorates Fungicides: Dithiocarbamates- thiocarbamates, chlorophenol Dinitrophenols. Herbicides: Phenoxyacetics, etc. Lecturer: Dr. Camilo Uribe Dr. Olga Lucía Melo
4:30-5:30 p.m.	Environmental Impact of Organophosphates, Bipyridyls, Glyphosate and Other Pesticides Lecturer: Dr. Luis Eduardo Parra
5:30-6:30 p.m.	Round Table Questions and Answers Moderator: Dr. Camilo Uribe

EMBASSY OF THE UNITED STATES OF AMERICA

URIBE CUALLA TOXICOLOGY CLINIC

REPORTED HUMAN HEALTH EFFECTS FROM GLYPHOSATE

ATTACHMENT 6

CHRONOLOGY OF FIELD WORK
THE PUTUMAYO HEALTH BRIGADE
June 10-20, 2001

Department of Putumayo

Bogota, D.C., Colombia
December, 2001

CHRONOLOGY OF FIELD WORK

REPORTED HUMAN HEALTH EFFECTS FROM GLYPHOSATE
JUNE 2001

June 7-8	Travel from Bogota to Puerto Asís
	Hiring land transportation for the medical team
	Reservation and confirmation of accommodations for the medical team
June 9	Receipt of material for field work
June 10	
8:30	Arrival of the medical team - El Dorado International Airport, Bogota
9:30-11:00	Air travel from Bogota to Puerto Asís
11:00-12:00	Delivery of work elements and material to the field coordinator
12:00-13:00	Lunch
13:00-16:00	Travel by land from Puerto Asís to Orito
16:00	Check in at the hotel in Orito
19:00	Dinner
June 11	
5:30-8:30	Travel by land from Orito to the village of El Empalme
8:30-9:00	Installation of the medical team at the school in El Empalme Meeting with the health worker
9:00-9:30	Breakfast
9:30-12:30	Patient evaluation - El Emplame *CRI administration *Case history * Sample collection
12:30-13:30	Lunch
13:30-18:00	Patient evaluation - El Empalme * CRI administration * Case history * Sample collection
19:00	Meeting to evaluate the session
20:00	Dinner
June 12	Travel by land from El Empalme to the village of Jardín de Sucumbios
6:00-7:00	Installation of the medical team at the school in Jardín de Sucumbios Meeting with the health worker
7:30-8:00	Breakfast
8:00-12:30	Patient evaluation - Jardín de Sucumbios * CRI administration * Case history * Sample collection

12:30-13:30	Lunch
13:30-18:00	Patient evaluation - Jardín de Sucumbios *CRI administration * Case history * Sample collection
19:00	Meeting to evaluate the session
20:00	Dinner
June 13	
5:30-6:00	Travel by land from Jardín de Sucumbios to the village of Siberia
6:00-7:00	Installation of the medical team at the school in Siberia Meeting with the health worker
7:00-7:30	Breakfast
7:30-12:30	Patient evaluation - Siberia * CRI administration * Case history * Sample collection
12:30-13:30	Lunch
13:30-18:00	Patient evaluation - Siberia * CRI administration * Case history * Sample collection
19:00	Meeting to evaluate the session
20:00	Dinner
June 14	
5:30-7:00	Travel by land from Siberia to Orito
7:00 - 7:30	Breakfast
7:30-8:30	Delivery of the samples at the Ecopetrol South District for shipment from Orito to Bogota
7:30-8:30	Travel by land: Orito-San Miguel- San Marcelino
12:00-12:30	Installation of the medical team at the school in San Marcelino Meeting with the health worker
13:00-14:00	Lunch
14:00-18:00	Patient evaluation - San Marcelino * CRI administration * Case history * Sample collection
19:00	Meeting to evaluate the session
20:00	Dinner
June 15	
5:30-6:30	Travel by land from San Marcelino to the village of Chiguaco
6:30-7:00	Installation of the medical team at the school in Chiguaco Meeting with the health worker
7:00-7:30	Breakfast
7:30-12:30	Patient evaluation - Chiguaco * CRI administration * Case history * Sample collection
12:30-13:30	Lunch
13:30-14:30	Travel by land from of Chiguaco to the village of Yarinal

14:30-15:00	Installation of the medical team at the school in Yarinal Meeting with the health worker
15:00-18:00	Patient evaluation - Yarinal * CRI administration * Case history * Sample collection
19:00	Meeting to evaluate the session
20:00	Dinner
June 16	
5:30-6:30	Travel by land from Yarinal to the village of Bajo Amarón
6:30-7:00	Installation of the medical team at the school in Bajo Amarón Meeting with the health worker
7:00-7:30	Breakfast
7:30-12:30	Patient evaluation - Bajo Amarón * CRI administration * Case history * Sample collection
12:30-13:30	Lunch
13:30-14:30	Travel by land from Bajo Amarón to the village of El Aguila
14:30-15:00	Installation of the medical team at the school in El Aguila Meeting with the health worker
15:00-18:00	Patient evaluation - El Aguila *CRI administration * Case history * Sample collection
19:00	Meeting to evaluate the session
20:00	Dinner
June 17	
5:30-6:30	Travel by land from El Aguila to La Hormiga
6:30	Samples sent to the Ecopetrol South District for shipment from Orito to Bogota
7:00-7:30	Travel by land from La Hormiga to the village of La Esmeralda
7:30-8:00	Installation of the medical team at the school in La Esmeralda Meeting with the health worker
8:00-8:30	Breakfast
8:30-12:30	Patient evaluation - La Esmeralda * CRI administration * Case history * Sample collection
12:30-13:30	Lunch
13:30-18:00	Patient evaluation - La Esmeralda *CRI administration * Case history * Sample collection
19:00	Meeting to evaluate the session

20:00	Dinner
June 18	
5:30-6:00	Travel by land from La Esmeralda to the village of Los Angeles
6:30-7:00	Installation of the medical team at the school in Los Angeles Meeting with the health worker
7:00-7:30	Breakfast
8:00-12:30	Patient evaluation - Los Angeles * CRI administration * Case history * Sample collection
12:30-13:30	Lunch
13:30-18:00	Patient assessment - Village of Los Angeles * CRI administration * Case history * Sample collection
19:00	Meeting to evaluate the session
20:00	Dinner
June 19	
5:30-6:30	Travel by land from Los Angeles to the villager of El Placer
6:30-7:00	Installation of the medical team at the school in El Placer Meeting with the health worker
7:00-7:30	Breakfast
7:30-12:00	Patient evaluation - El Placer * CRI administration * Case history * Sample collection
12:00-13:00	Lunch
13:00-14:00	Travel by land from El Placer to the village of Las Vegas
14:00-14:30	Installation of the medical team at the school in Las Vegas Meeting with the health worker
14:30-18:00	Patient evaluation - Las Vegas * CRI administration * Case history * Sample collection
19:00	Meeting to evaluate the session
20:00	Dinner
June 20	
5:30-8:30	Travel by land: Las Vegas - La Hormiga - Orito
8:30	Delivery of samples to the Ecopetrol South District for shipment from Orito to Bogota
8:30-9:00	Breakfast
9:30-12:30	Travel by land from Orito to Puerto Asís
13:00-14:00	Lunch
14:00	Hotel check in at Puerto Asís
16:00	Overall evaluation of the field work

17:00	Visit to the Comfamiliar Auditorium Inspection of audio-visual aids
19:00	Dinner
June 21	
7:30	Breakfast
9:00-12:00	First session with health personnel
12:00-14:00	Lunch
14:00-18:00	Second session with health personnel
19:00	Dinner
20:00	Evaluation of the first day of conferences
June 22	
7:30	Breakfast
9:00-12:00	First session with non-health personnel
12:00-14:00	Lunch
14:00-18:00	Second session with non-health personnel
19:00	Removal of materials, return of auditorium
19:30	Dinner
20:00	Evaluation of the second day of conferences
June 23	
7:30	Breakfast
9:30	Departure from the hotel
10:00	Arrival at the Puerto Asís Airport
11:30-13:30	Air travel from Puerto Asís to Bogotá

EMBASSY OF THE UNITED STATES OF AMERICA

URIBE CUALLA TOXICOLOGY CLINIC

REPORTED HUMAN HEALTH EFFECTS FROM GLYPHOSATE

ATTACHMENT 7

PROTOCOL
CHAIN OF CUSTODY FOR TOXICOLOGY LABORATORY SAMPLES

Department of Putumayo

Bogota, D.C., Colombia
December, 2001

PROTOCOL FOR THE CHAIN OF CUSTODY

Dr. Alejandra Salcedo was the only person authorized to open and close the coolers at the beginning and end of each session. She was designated by the Medical Coordinator, Dr. Camilo Uribe, to verify the presence and condition of all samples listed on the form for each cooler. The coolers were supervised by members of the team throughout collection, storage and shipment of the samples.

SAMPLE COLLECTION

1. Urine

Each subject (individual-sample) was given a plastic container packed in a sealed bag. The container was used to collect 50 cc of urine from a single miction, under the supervision of one of the team members (physician or nurse's aid). The patient returned the container to the supervisor, who labeled the sample with the respective code and attached an adhesive safety strip. The sample was then placed in the appropriate cooler for storage and transport at a temperature of 2º C. The date, time, patient code and evaluator 's signature were entered on a form when the sample was turned over.

2. Blood

Ten cc of venous blood were drawn from each subject. The sample was collected in a heparinized tube and labeled with the respective code. An adhesive safety strip was attached to the tube, which was then packed in the appropriate cooler for refrigeration and transport at a temperature of 5º C. The date, time, patient code and evaluator's signature were registered on a form when the sample was turned over.

After the samples were collected at each location, the coolers were sealed and a final closure certificate was drawn up for each one, listing the number of samples inside, their codes, and the date and time the cooler was closed. The certificate was signed by the person in charge.

SHIPMENT

The nursing and bacteriological staff at the hospitals in Orito and La Hormiga collaborated by refrigerating the samples collected during each session. At night, the samples were stored in coolers at the hospital's clinical laboratory or at the offices of the vaccination program. Blood samples were refrigerated at 5º C and urine samples at 2º C. Before each session, the coolers were picked up at the hospital and a registration form initiated.

Dr. Salcedo turned the coolers with the samples and the chain of custody form over to the person in charge of their shipment. Dr. Glinis Díaz, who manages the

Orito Hospital, was responsible for transporting the samples from Orito to Bogotá. She traveled on a commercial flight. For the trip from Puerto Asís to Bogota, the coolers were delivered to a member of the National Police, who traveled with Ms. Suzanne Sheldon after the seminar on June 21. The sealed coolers were turned over to these individuals with the chain of custody form, which was signed upon receipt and delivery of the samples.

At the airport In Bogotá, the samples were turned over to an employee of the Uribe Cualla Toxicology Clinic, who took them to institution for official delivery to Dr. Billy Armando Vargas, Head of the Uribe Cualla Toxicology Laboratory.

The coolers were opened in the presence of Dr. Fernando Flores, a delegate of the National Food and Drug Surveillance Institute (INVIMA). He watched Dr. Vargas verify the contents for subsequent analysis.

EMBASSY OF THE UNITED STATES OF AMERICA

URIBE CUALLA TOXICOLOGY CLINIC

REPORTED HUMAN HEALTH EFFECTS FROM GLYPHOSATE

ATTACHMENT 8

EVALUATION OF THE SEMINAR-WORKSHOP ON PESTICIDES: SAFE HANDLING AND ENVIRONMENTAL IMPACT

Department of Putumayo

Bogota, D.C., Colombia
December, 2001

EVALUATION OF THE SEMINAR-WORKSHOP ON PESTICIDES: SAFE HANDLING AND ENVIRONMENTAL IMPACT

1. HEALTH SECTOR PARTICIPANTS
Puerto Asís, June 21, 2001

	Excellent	Good	Average	Poor	Total Votes
Dr. Camilo Uribe	36	-	-	-	36
Dr. Luis E. Parra	19	15	2	-	36
Program Content	27	9	-	-	36

2. NON-HEALTH SECTOR PARTICIPANTS
Puerto Asís, June 22, 2001

	Excellent	Good	Average	Poor	Total Votes
Dr. Camilo Uribe	26	1	-	-	27
Dr. Luis E. Parra	7	10	7	3	27
Program Content	21	6	-	-	27

EMBASSY OF THE UNITED STATES OF AMERICA

URIBE CUALLA TOXICOLOGY CLINIC

REPORTED HUMAN HEALTH EFFECTS FROM GLYPHOSATE

ATTACHMENT 9

FREQUENCY TABLE

Department of Putumayo

Bogota, D.C., Colombia
December, 2001