U.S. ENVIRONMENTAL PROTECTION AGENCY

OFFICE OF PESTICIDE PROGRAMS

DETAILS OF THE 2003 CONSULTATION FOR THE DEPARTMENT OF STATE

USE OF PESTICIDE FOR COCA AND POPPY ERADICATION PROGRAM IN COLOMBIA

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EXECUTIVE SUMMARY

CONSULTATION REVIEW OF THE USE OF PESTICIDES FOR COCA AND POPPY ERADICATION IN COLOMBIA (2003)

BACKGROUND

The Department of State continues to assist the Government of Colombia with training, contractor support, financial assistance, and technical and scientific advice for an aerial pesticide spraying program designed to eradicate illicit crops (coca and poppy). The Department of State has again consulted with the Environmental Protection Agency (EPA) on whether "the herbicide mixture is being used in accordance with EPA label requirements for comparable use in the United States" and that "the herbicide mixture, in the manner it is being used, does not pose unreasonable risks or adverse effects to humans health or the environment."

Similar to this year, in 2002 EPA conducted a review of coca eradication activities in Colombia. The Agency has determined that its findings from 2002 remain relevant to the current coca eradication activities in Colombia. For 2003, EPA was asked to also consider the opium poppy eradication program.

2002 REVIEW OF COCA ERADICATION PROGRAM

Last year, EPA reviewed the coca eradication program in Colombia and concluded that there was no evidence of significant human health or environmental risks from the spraying. The Agency did recommend that the Department of State switch to an herbicide product with lower toxicity due to a potential for hazard to the eyes of pesticide mixers/loaders. EPA also requested the Department of State to conduct field investigations of health complaints associated with coca eradication. The Agency further concluded that spray drift was likely to cause phytotoxicity downwind of coca fields. The final primary conclusion was that EPA could not verify the product formulation because the product was being manufactured outside of the U.S.

2003 FINDINGS

The Department of State followed EPA's 2002 recommendation by beginning use of a lower toxicity glyphosate product in its coca and poppy eradication programs and implementing a program to investigate health complaints. As with coca eradication, the use of glyphosate for opium poppy eradication is done aerially. Based on information provided by the Department of State, several conclusions may be reached concerning poppy eradication: total area sprayed is less than for coca eradication, individual poppy sites are smaller and located at higher elevations, and the rate of glyphosate for poppy eradication is lower than that for coca. Based on a comparison of the glyphosate use pattern in Colombia, as described by the Department of State, and use in the U.S., EPA has determined that application rates for both coca and poppy eradication in Colombia are within the parameters listed on U.S. labels.

As for human health concerns, EPA concludes there are no risks of concern from dietary, mixer/loader/applicator or field workers, or bystanders (including children). The concerns for mixer/loader eye irritation discussed in the Agency's 2002 findings have been mitigated by switching to the lower toxicity product. The Department of State and the Government of Colombia initiated two programs to investigate health complaints. Of those cases investigated to date in Colombia, no findings directly link adverse health effects to the spraying.

In regard to potential environmental effects from the coca and poppy eradication programs, EPA concludes that the switch to a lower toxicity product will pose less risk of acute poisoning to wildlife. The Agency believes that the potential for spray drift phytotoxicity is still a factor for both coca and poppy spraying. EPA recognizes that the Department of State is employing Best Management Practices to minimize drift and encourages them to continue these efforts.

EPA cannot verify the quality of the product manufactured, since the actual formulation is done in Colombia. The Agency did, however, review toxicity testing conducted on the spray mixture solution being applied in Colombia and did not find any irregularities.

For 2003, EPA recommends that the Department of State continue programs for investigating health complaints. The Agency also requests that Department of State improve its definition of glyphosate poisoning, provide further documentation of its investigations and how they are conducted, and standardize data collection.

Details of EPA's findings are provided in the attached document.

I. PESTICIDE USE ASSESSMENT

A. Introduction

The Biological and Economic Analysis Division (BEAD) in the Office of Pesticide Programs within the Environmental Protection Agency (EPA) has augmented the 2002 EPA assessment and description of the use of glyphosate in the United States (1) as a basis for comparison to glyphosate use in Colombia for coca eradication with a discussion of changes in the program for 2003. This request has come from the Department of State (DoS) which is required to consult with the EPA before reporting to Congress on the use of glyphosate for the Andean counter drug initiative. This year DoS is required to include glyphosate for control of opium poppy in its consultation. This document compares the described use on opium poppy and coca to use within the US.

B. Summary

The use of glyphosate for control of opium poppy is conducted at 1 lb ai/acre (0.8 lb a.e/acre) and at a spray mixture (product + water diluent + Cosmoflux 411F surfactant) volume of about 5.5 gallons per acre (50 liters/hectare). This application rate is within the label recommendations for the amount of concentrated formulation per acre and the amount of total spray volume per acre for application for glyphosate products registered for use in the US.

C. Background

Glyphosate is the most widely used herbicide in the US (1). It is non-selective in action and is used where total vegetation control is desired. It is used on a variety of sites including agricultural crops, lawns, gardens, forests and utility grounds. Application is made to the target plant's foliage, and after being absorbed, glyphosate circulates within the plant, exerting herbicidal activity systemically. Glyphosate and its use within the US were described in the 2002 EPA assessment. In its assessment report, EPA described the use of glyphosate in the US in the following paragraph:

> "Glyphosate may be used on over 400 crop and non-crop sites. The largest agricultural use sites include soybeans, cotton and field corn. In addition to agricultural use, EPA estimates that 16-22 million pounds of the technical grade active ingredient were applied to non-agricultural sites in 1999 (this is the most recent year for which adequate data are available). This estimate includes both home owner and professional applications as well as use on forested lands. Based on EPA data for 1999, an estimated 1-2 million pounds of glyphosate was applied to forest acres, with more than 650,000 forest acres treated."

In 2002, a description of glyphosate use in forestry sites in the US was included since use for coca eradication would be most similar to the US labeled use for broad-spectrum post-emergence weed control for forestry site preparation and utility rights-of-way. For coca eradication, glyphosate is sprayed from fixed wing aircraft at speeds around 165 mph at 4.4 pounds active ingredient (isopropylamine salt) per acre in about two gallons of spray mixture per acre.

Aerial application of the glyphosate product to non-crop, non-timber, industrial and rights-of-way areas in the US is allowed using fixed wing aircraft and helicopter to control annual and perennial weeds and woody brush and trees. Although application may be made at up to 10 lb ai/year per acre in the US, the typical use rate per application is much lower, averaging less than one pound per acre on major agricultural sites (EPA has no data on average application rate to forest sites). In addition, product labeling recommends application at 3 to 15 gallons of total spray mixture volume per acre for aerial application to forestry sites.

D. Opium Poppy Eradication

Glyphosate used for the opium poppy eradication program is also applied aerially, however its use differs in several ways from the coca eradication program:

1. Total area sprayed is much smaller for poppy eradication. The State Department explains that:

> "Because Colombia cultivates much less opium poppy than coca and spray resources are limited, aircraft spray much more coca than poppy, therefore expending more spray chemicals in coca growing areas than in areas where opium poppy is cultivated. For example, in 2002, eradication aircraft sprayed totals of 122,700 hectares of coca [about 303,000 acres] and 3,000 hectares [about 7400 acres] of opium poppy."

2. Individual poppy spray sites are smaller and located at higher elevations. The State Department states:

> "While difficult to quantify precisely, opium poppy fields generally range from 0.5 to 5 hectares. Opium poppy is ordinarily cultivated at a higher altitude than coca, and thus opium poppy often is cultivated and sprayed in hilly to mountainous terrain."

3. The rate (or dose) of glyphosate for poppy eradication is lower than that for coca eradication. The State Department states:

> "Because the opium poppy is not a woody, hard-to-control species like the coca bush, opium poppy eradication uses a spray mixture with a substantially lower glyphosate content than the spray mixture used for coca eradication."

The Department of State described the concentrate formulation for use in 2003 as containing 41 percent glyphosate salt and 59 percent inert ingredients. The same concentrate formulation is being used for both coca and opium poppy eradication (1). Other similar products with this proportion of active to inert ingredients are registered with the US Environmental Protection Agency for use in the US on forestry and utility rights-of-way sites. A surfactant is added to the diluted spray mixture prior to spraying. This practice improves absorption of the herbicide by the plant and is standard practice for applying glyphosate to forestry sites in the US.

For opium poppy spraying, water, formulated glyphosate, and surfactant are combined in a spray mixture in the following percentages: 94 percent water, 5 percent glyphosate formulation, and 1 percent surfactant. This diluted spray mixture is applied to opium poppy at the rate of 50.0

liters/hectare (or 5.5 gallons per acre) (1). This is equivalent to 1 lb ai/A isopropylamine salt (or 0.8 a.e.)/acre as illustrated in the calculation below.

Calculation of rate of application for opium poppy:

(50 liters spray mixture/1 hectare) (5% glyphosate product/1 liter spray mixture) (4 lbs. ai isopropylamine glyphosate salt/1 gallon formulated product[1])(1 gallon/3.78 liter) (1 hectare/2.47 acres) = 1.1 lb ai/acre

In contrast, the Department of State reports glyphosate use for coca eradication at 10.4 l/ha of glyphosate product which is equivalent to 4.4 lb a.i./acre of glyphosate isopropylamine salt (3.3 a.e./acre) as illustrated in the calculation below.

Calculation of rate of application for coca eradication:

(10.4 liter spray mixture/1 hectare) (4 lbs ai isopropylamine glyphosate salt/1 gallon glyphosate product[1]) (1gallon/3.78 liter) (1 hectare/2.47 acres) = 4.4 lb ai/acre

Although glyphosate is applied aerially to wooded sites, the rate of application is more similar to that for agricultural uses than for forestry uses. Agricultural use of glyphosate is common at rates lower than 0.5 lb ai/A. In contrast, product labels for the use of glyphosate for forestry sites start at rates of 2 lbs ai/A.

E. Conclusions

This application rate for opium poppy eradication is within the glyphosate manufacturer's label recommendations for both the amount of concentrated formulation per acre and the amount of total spray volume per acre . The Department of State informed EPA that the coca use is the same as described in the 2002 assessment, except for a change in product.

REFERENCES

(1) U.S. Environmental Protection Agency, Office of Pesticide Programs, Details of the Consultation for Department of State, Use of Pesticide for Coca Eradication Program in Colombia, August 2002.

(2) Department of State Updated Report on Chemicals Used in the Columbian Aerial Eradication Program. Attachment to a letter from Secretary of State, Colin Powell, to Environmental Protection Agency Administrator, Governor Christine Whitman, April 9, 2003.

(3) Donaldson, D., T. Kiely, and A. Grube. Pesticide Industry Sales and Usage, 1998 and 1999 Market Estimates. June 2002. Biological and Economic Analysis Division, Office of Pesticide Programs, U.S. Environmental Protection Agency.

(4) Agricultural Chemical Usage - 2000 Field Crops Summary. May 2001. US Department of Agriculture. National Agricultural Statistics Service.

II. HUMAN HEALTH RISK ASSESSMENT

A. Introduction

In April 2003, the DoS requested that EPA provide a human health risk assessment for the aerial eradication of coca and poppy in Colombia. To facilitate this request, in addition to the information provided for the previous assessment, the DoS provided a report entitled, Department of State Updated Report on Chemicals used in the Colombian Aerial Eradication Program and submitted acute toxicity tests for the spray mixture used in the coca eradication program assessed previously.

Unless otherwise specified, all information pertaining to the coca and poppy e eradication program s in Colombia was provided to the Agency from three sources: (1) DoS Presentation, DoS Coca Eradication Program, 4/18/02, (2) DoS document entitled Chemicals Used for the Aerial Eradication of Illicit Coca in Colombia and Conditions of Application. (3) DoS report entitled Department of State Updated Report on Chemicals used in the Colombian Aerial Eradication Program.

USE PATTERN
The glyphosate tank mixture is applied as an over the top aerial foliar application to coca in certain provinces within Columbia. The tank mixture sprayed for eradication of coca in Columbia contains 55% water, 44% of glyphosate herbicide product, and 1% adjuvant (Cosmo-Flux 411F). Up to two applications of the glyphosate tank mixture are sprayed over coca crops at a maximum of 1.25 gallons of product/acre.

According to updated information provided by the DoS, "Apart from changing to a more benign formulation of glyphosate spray mixture, there have been no changes to any of the components of the spray mixture." The only changes in the methodology used in the spray program is the use of a new aircraft, the Four Air Tractor Model 802 (AT-802). These aircraft utilize the identical nozzles (same brand and diameter) in the identical configuration (nozzle angle, droplet size, calibration methods) as the aircraft evaluated in the previous assessment.

The opium poppy spray mixture contains the same components as the spray mixture used in the coca eradication program. According to information provided by DoS, the spray mixture used in the opium poppy eradication program contains a substantially lower concentration of glyphosate than the spray mixture used for coca eradication (1.11 gallons glyphosate/A for coca versus 0.27 gallons glyphosate /A for poppy). This application rate is within the manufacturer's product label recommendations.

The poppy eradication program differs from the coca eradication program in several ways. According to the DoS report, poppy fields are generally smaller than coca fields, ranging from 0.5 to 5 hectares. Also, poppy is often cultivated and sprayed in more mountainous terrain than coca.

As for the previous assessment, in order to assess the hazard of what was sprayed in Columbia, the components of the mixture were evaluated separately.

HAZARD ASSESSMENT

The **Cosmo-Flux 411F** adjuvant used in the glyphosate tank mix is produced by a Colombian company and is not sold domestically. All ingredients of this product are substances that are not highly toxic by oral or dermal routes. They may cause mild eye and skin irritation. Cosmo-Flux 411F consists mainly of (*information not included as it may be entitled to confidential treatment*) with a nonionic surfactant blend primarily composed of (*information not included as it may be entitled to confidential treatment*).

The available hazard data base on experimental animals indicates that the glyphosate technical grade active ingredient (TGAI) has low acute toxicity via the oral and dermal routes. It is a mild eye irritant and a slight dermal irritant. It is not a dermal sensitizer. The requirement for an acute inhalation study was waived since no respiratory or systemic toxicity was seen following subchronic inhalation exposure in rats. In the subchronic and chronic oral toxicity studies (1-year dog, 24-month mouse, 2-year chronic/carcinogenicity rat, and 2-generation rat reproduction), systemic toxicity manifested most commonly as clinical signs, decreases in body weight and/or body weight gain, decreased food consumption, and/or liver and kidney toxicity at doses equal to or above the limit dose (1000 mg/kg/day). No dermal or systemic toxicity was seen following repeated dermal exposures. There was no quantitative or qualitative evidence for increased susceptibility in fetuses following *in utero* exposure to rats and rabbits in developmental toxicity studies or following pre/post-natal exposure to rats in the 2-generation reproductive toxicity study in rats. Effects in the offspring were observed only at or above treatment levels which resulted in evidence of appreciable parental toxicity. The Food Quality Protection Act (FQPA) Safety Factor Committee (SFC) concluded that the safety factor, to protect infants and children, of 10x be removed (reduced to 1x). The Hazard Identification Assessment Review Committee (HIARC) met on March 26, 1998 and, again, on November 20, 2001. The most recent report of the HIARC for glyphosate has the complete assessment of the endpoints selected for dietary exposure and residential/occupational exposure. No endpoints were selected for the acute Reference Dose (RfD) since no hazard attributed to a single dose was identified from the oral toxicity studies, and there are no concerns for developmental or reproductive toxicity. In addition, the HIARC did not identify endpoints of concern for dermal and inhalation exposures for any exposure period (short term 1 to30 days, intermediate term 1 to 6 months, or long term 6 months to lifetime) since no hazard was identified due to the low toxicity of glyphosate. HIARC did identify an incidental oral endpoint for short- and intermediate-term exposure. The chronic dietary RfD of 1.75 mg/kg/day was based on diarrhea, nasal discharge, and mortality in a rabbit developmental toxicity study. Glyphosate was not mutagenic in a full battery of assays. Based on the lack of evidence for carcinogenicity in two acceptable studies in mice and rats, glyphosate is classified as a “Group E” chemical (no evidence of carcinogenicity to humans).

EXPOSURE

An exposure and risk assessment are required for an active ingredient if: (1) certain toxicological criteria are triggered and (2) there is potential for exposure. Upon review and analysis of the hazard database in total, the Agency's HIARC did not identify a hazard of concern for acute dietary, dermal, or inhalation exposures. Therefore, quantitative estimates of risk for these exposure durations have not been conducted.

Acute **dietary exposure** is possible for persons consuming livestock or food crops which have been inadvertently sprayed as a result of the aerial eradication program in Columbia. However, since glyphosate is a contact herbicide that systemically kills plants after absorption through leaves, dietary exposure due to consumption of treated crops is expected to be limited. In addition, since an acute dietary endpoint of concern was not identified in the hazard database, no significant risk due to acute dietary food exposure to glyphosate residues is expected. Based on the fact that a poppy field is sprayed no more than twice to eradicate the crop, no chronic food exposure is expected.

Handler (e.g., individuals mixing the concentrated formulated product to prepare the tank mix and loading the tank mix in the aircraft) exposure is anticipated for short-term (1-30 days) and, possibly intermediate-term (1-6 months) durations based on the frequency of application and duration of the spray program.

Based on the use pattern described by the DoS, short-term dermal post-application exposures are expected for persons re-entering treated coca and poppy fields immediately after spray events. In cases such as glyphosate, where the vapor pressure is negligible, OPP experience with post-application data suggests that inhalation exposure is minimal and does not quantitatively assess post-application inhalation exposure. Intermediate and long-term post-application exposures are not expected due in part to the fact that coca and poppy fields are sprayed no more than twice to eradicate the crop. Additionally, glyphosate is a translocated herbicide which is rain fast within 48 hours after spraying. Therefore, potential exposure to dislodgeable residues of glyphosate after 48 hours is expected to be minimal.

DoS states that pilots are instructed not to spray fields where people are present. Therefore, incidental oral exposure (hand-to-mouth) resulting from individuals being directly sprayed by glyphosate was not quantitatively assessed. Also, it is not current Agency policy to quantitatively assess toddler hand-to-mouth exposure resulting from spray drift. Additionally, HED does not currently perform exposure assessments for toddler non-dietary oral exposures for agricultural scenarios. As a point of comparison, screening level risk estimates for toddler incidental oral exposures (hand-to-mouth) to the U.S. registered residential turf uses of glyphosate have been calculated. Using the same standard screening level assumptions as used in the residential assessment for the U.S. registered turf use and taking the higher application rate into account, the potential risks form incidental oral exposure due to the spraying of glyphosate as part of the coca and poppy eradication program would not exceed HED's level of concern.

There is potential for exposure to persons in nearby areas to those targeted for spraying. However, the technology and other safeguards used in this program are consistent with common approaches in the US for reducing **spray drift**. Therefore, it is likely that drift is minimized in this program if all procedures are adhered to and operational equipment is in working order.

From the review of Colombian glyphosate product human **incident reports** for poppy eradication (evaluated in the previous assessment), it should be emphasized that the overwhelming majority (95%) of the illnesses reported are likely background incidents unrelated to the spraying of herbicide on poppy. The remaining 5% increase could be due to a variety of causes and do not support a conclusion that the spraying of the glyphosate tank mixture was responsible for these complaints. Furthermore, the individual with the highest potential for exposure would be the mixer loader. They are handling the concentrated glyphosate product and the tank mix. The incidence data that has been submitted to the Agency by DoS, does not include any incident reports for those individuals. There are data to suggest that the poppy spray eradication program could have resulted in minor skin, eye, or respiratory irritation, and perhaps headache or other minor symptoms. However, the detailed information on timing of application, history of exposure, and medical documentation of symptoms related to exposure to glyphosate tank mix were not available. Given the limited amount of documentation, none of the data in the report from Colombia provide a compelling case that the spraying of the glyphosate mixture has been a significant cause of illness in the region studied. Prospective tracking of reports of health complaints, documenting times of exposure and onset of symptoms, are recommended during future spray operations to evaluate any potential health effects and ameliorate or prevent their occurrence.

The *glyphosate formulated product* used in the coca eradication program in Colombia contains the active ingredient glyphosate, a surfactant blend, and water. The acute toxicity test of the *glyphosate technical* is classified as toxicity category III for primary eye irritation and toxicity category IV for acute dermal and oral toxicity, and skin irritation. It is not a dermal sensitizer. The product currently used in the coca and poppy aerial eradication program is classified as toxicity category III for primary eye irritation and toxicity category IV for acute dermal and oral toxicity, and skin irritation and is not a dermal sensitizer. The label for the *formulated* product used in the poppy eradication program in Colombia uses “Caution” as the signal word.

The overall conclusion from the earlier review stated that “There is some data to suggest that the spray eradication program could have resulted in minor skin, eye, or respiratory irritation, and perhaps headache or other minor symptoms. However, the detailed information on timing of application, history of exposure, and medical documentation of symptoms related to glyphosate exposure were not available. Thus, the reported symptoms cannot be confirmed to be a result of the spray applications. The information collected gives the impression that any increase in health problems is likely to be relatively small, and the severity of those symptoms is likely to be minor to moderate. Given the limited amount of documentation, none of the data in the report from Colombia provide a compelling case that glyphosate spraying has been a significant cause of illness in the region studied. Some of the reports in Colombia, potentially related to glyphosate tank mix exposure, are similar in nature to those reported in the literature and by

California. These cases report irritation to skin, eyes, and respiratory passages. This suggests that the Cosmo-Flux 411F added to the glyphosate in Colombia has little or no effect on the overall toxicity of the formulated product. Prospective tracking of reports of health complaints, documenting times of exposure and onset of symptoms, are recommended during future spray operations to evaluate any potential health effects and ameliorate or prevent occurrence."

In the 2002 assessment the DoS requested advice on whether the aerial application program may pose unreasonable risks or adverse effects to humans or the environment. The current (2003) assessment considers recent exposure information provided to the Agency for the DoS Colombia poppy eradication program in light of the 2002 assessment. Current information indicates that the Government of Colombia and the U.S. Embassy Bogota have adhered to the EPA advice . . . "Prospective tracking of reports of health complaints, documenting times of exposure and onset of symptoms, are recommended during future spray operations to evaluate any potential health effects and ameliorate or prevent occurrence." The 2003 submission from the "Department of State Updated Report on Chemicals used in the Colombian Aerial Eradication Program" to the EPA indicates that "A visit to the hospital and interviews with doctors there revealed no cases of poisoning or illness attributable to spray chemicals." U.S. Embassy-contracted toxicologists talked to patients and talked to local medical personnel, looking for spray-related cases. . . The report concluded that "Through Medical Civic Action Program (Medcap) and other medical investigations, the U.S. Embassy has never found an instance of spray-related harm to human health.". Missing from their account was a clearly stated case definition for what would constitute a glyphosate-related poisoning. A case definition is required if the conclusion that they have "never found an instance of spray-related harm to human health" is to be supported.
During April 18 briefing, the Department of State agreed to supply the Agency with a full battery of the six acute toxicity tests on the tank mix used in the coca aerial eradication program. That information has been received and reviewed. In summary, the acute toxicity of the spray mixture is category III for eye irritation and category IV for skin irritation and acute dermal, oral and inhalation exposure and is negative for dermal sensitization.

B. Background

EPA regulates pesticides under two statutes, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug, and Cosmetic Act (FFDCA). FIFRA provides the authority to register and review pesticides as well as the authority to suspend and cancel if use poses unreasonable risks. FFDCA provides authority to set maximum residue levels (tolerances) for pesticides used in or on foods or animal feeds.

Section 3 of FIFRA provides authority to register (license for sale and distribution) pesticide products. The label of the pesticide product specifies the use (pest and crop/site), amount of product to be applied, frequency, timing of use, restrictions, storage and disposal practices and precautionary statements. The active ingredient in a pesticide product is the "ingredient which will prevent, destroy, repel, or mitigate any pest." The inert or other ingredient(s) in a pesticide product is "an ingredient which is not active." The registrant must provide data for the Agency

to assess potential environmental and human health risks. The data required to make a safety finding are dependent on the intended use, e.g., food use vs non-food use. The data requirements for pesticides may be found in 40 CFR Part 158. For human health risk assessment, data is required to permit characterization of hazard and exposure.

Data requirements on the chemical identity and composition of the formulated pesticide product, may be found in 40 CFR 158.150. The list of ingredients for a pesticide product and the percent of each ingredient in the formulation are contained in the confidential statement of formula (CSF). The CSF is FIFRA confidential business information (CBI) and is entitled to treatment as trade secret or proprietary information. Agency risk assessments do not typically contain this information.

Residue chemistry data required as per 40 CFR 158.240 support the ability of the Agency to estimate the amount of pesticide that will result in food as a result of application of the pesticide according to the product labels directions for use. The magnitude of the residue studies for crop field trials use the typical end use product as the test material. The livestock feeding studies are required whenever a pesticide residue will be present in livestock feed. The livestock feeding studies evaluate the magnitude of the resulting pesticide residue in meat, milk, poultry, and eggs. The studies are conducted with the technical grade of the active ingredient or the plant metabolites Residue chemistry data are also required to identify any potential metabolites of concern. These data are used to determine the tolerances for the parent and/or metabolites. Additional data is required on environmental fate, degradation, metabolism, and dissipation.

Hazard data required for human health risk assessment are provided in 40 CFR 158.340. The use of the active ingredient (i.e., food use or non-food use) will determine what studies are required. The acute toxicity data on the technical grade of the active ingredient are used for classification and precautionary labeling for protective clothing requirements, and worker reentry intervals. The only studies that are required to be conducted on the manufacturing use product or end use product are the acute toxicity studies. The remaining toxicology studies (e.g., developmental toxicity, reproduction, subchronic, chronic feeding, or carcinogenicity studies) require that the test substance is the technical grade of the active ingredient. Subchronic toxicity studies provide data on potential target organ toxicity and are also used to select dose levels for long term or chronic toxicity studies. Chronic toxicity or carcinogenicity studies are conducted for food use chemicals to determine potential effects following prolonged or repeated exposure that may have a latency period for expression. The test animals are exposed orally for a significant portion of their life span. Developmental toxicity studies are required in two species (usually the rat and rabbit) for food use chemicals. They are conducted to detect alterations in the normal development of fetuses following *in utero* exposure. The 2-generation rat reproductive toxicity study is required to assess potential alterations in gonadal function, estrus cycles, mating, conception, birth, lactation, weaning, as well as growth and development of offspring. The Agency also requires a battery of mutagenicity studies to assess the potential induction of changes in the genetic material of cells. The above studies are required for food use active ingredients. In general, less data is required for non-food use active ingredients and inerts unless a concern has triggered additional testing.

The Agency conducts separate risk assessments for all pesticide active ingredients and has conducted risk assessments for some inerts. The remaining inerts are cleared by the Agency. It should be understood that whenever the inert ingredient was cleared, whenever the tolerance exemption was established, the inert met the standards of the time.

Inert ingredients, also known as "other ingredients," are the carrier for the active ingredients which allow the product to deliver the active ingredient at a specific rate and ensure proper distribution during application. Currently there are over 3200 inert ingredients cleared by EPA for use in various domestic pesticides products. There are two major classifications: non-food use (such as lawn care products and bathroom cleaners), and food-use, which require an exemption from the requirement of a tolerance and can also be used in non-food products.

The Agency has a newly developed methodology for evaluating low or low/moderate toxicity chemical substances by way of a screening process that incorporates elements of a tiered approach . Use of this process will permit the Agency to clear more chemicals of low to moderate toxicity for use in pesticide products. The Agency is aware that some chemicals may be used as inert ingredients in some formulations and as active ingredients in other formulations. EPA believes this methodology is appropriate for evaluating some low toxicity chemicals regardless of whether they are categorized as active or inert ingredients. The new process will permit the Agency to be able to conduct more in-depth evaluations of other ingredients that are of potentially higher toxicity. Chemicals of higher toxicity that cannot be appropriately addressed in the lower tiers would be evaluated in a manner substantially similar to that of an active ingredient. Later as the Agency begins to review chemical-specific or surrogate information in the open literature, the preliminary tier determination may be revised.

Inert ingredients that are exempt from tolerance are listed in 40 CFR 180.1001 (c). The inert ingredients in the glyphosate formulation have been approved by the Agency. The components of the adjuvant (Cosmo-Flux 411F) that have been sprayed on coca plants in Colombia, have also been determined to be approved for use on food by the Agency.

The two federal statutes for regulating pesticides in the US give EPA limited authority to regulate the sale, or use of adjuvants in the US. EPA has authority to regulate an adjuvant if it is purposely included in the manufacturing process of a pesticide product in which case the chemical would be regarded as an inert ingredient. In the US as with all countries, adjuvants are commonly used and added to pesticides as wetting agents, spreaders. emulsifiers, antifoamers, and penetrants. These may contain surfactants, solvents, or other types of chemicals to achieve the desired purpose.

An adjuvant is a subsidiary ingredient or additive product added to a pesticide in a mixture that aids the effectiveness of the primary or active ingredient. Adjuvants are most commonly added to tank mixes of pesticide products prior to application to the site to be treated. Adjuvants are not subject to FIFRA registration, as no pesticidal claims are made. Pesticide manufacturers choose whether or not to address on their product labels the use of adjuvants with their product(s). However, when added to a tank mix for application to a food or feed crop/site, the

individual components must be cleared under FFDCA. While adjuvant products are not registered on the federal level, they are subject to registration under some state laws. The states of Washington and California are two states that register adjuvants. The adjuvant (Cosmo-Flux 411F) used in the glyphosate tank mix is produced by a Colombian company and is not sold domestically. The Department of State has agreed to provide the Agency with acute toxicity data performed on the actual tank mix that has been sprayed in Colombia.

C. Historical Regulatory Information

The glyphosate product currently used in the Colombian aerial eradication program was registered in August 1994. It was intended to replace the glyphosate products on the market that were in toxicity category I and II for eye irritation with a product that was category III for eye irritation. The currently used product also offered improves rain fastness and is currently one of the major glyphosate products used in agriculture in the US. In August 2002, the registrant submitted a label for ground and aerial application to kill undesirable vegetation in a variety of non-agricultural sites.

D. Hazard Identification

Hazard identification is the first step in the risk assessment process. The objective is to qualitatively characterize the inherent toxicity of a chemical. Scientific data are evaluated to establish a causal relationship between the occurrence of adverse health effects and exposure to a chemical. Because high quality controlled toxicology studies on humans are frequently unavailable, regulatory scientists rely on animal data to estimate hazard to support regulatory decision making. Prior to and subsequent to initial registration, the Agency has required the registrants of glyphosate products to submit appropriate studies according to contemporary study requirements and testing protocol requirements.

Glyphosate Technical

The available hazard data base on experimental animals indicates that glyphosate has low acute toxicity via the oral and dermal routes with LD_{50}s > 5000 mg/kg. It is a mild eye irritant and a slight dermal irritant. It is not a dermal sensitizer. The requirement for an acute inhalation study was waived since no respiratory or systemic toxicity was seen following subchronic inhalation exposure in rats. In the subchronic and chronic oral toxicity studies (1-year dog, 24-month mouse, 2-year chronic/carcinogenicity rat, and 2-generation rat reproduction), systemic toxicity manifested most commonly as clinical signs, decreases in body weight and/or body weight gain, decreased food consumption, and/or liver and kidney toxicity at doses equal to or above the limit dose (1000 mg/kg/day). No dermal or systemic toxicity was seen following repeated dermal exposures. There was no quantitative or qualitative evidence for increased susceptibility in fetuses following *in utero* exposure to rats and rabbits in developmental toxicity studies or following pre/post-natal exposure to rats in the 2-generation reproductive toxicity study in rats. Effects in the offspring were observed only at or above treatment levels which resulted in evidence of appreciable parental toxicity. Glyphosate was not mutagenic in a full

battery of assays. Based on the lack of evidence for carcinogenicity in two acceptable studies in mice and rats, glyphosate is classified as a "Group E" chemical (no evidence of carcinogenicity to humans).

Components of the Glyphosate Product

1. Polyoxyethylene alkylamine (POEA). POEA is a compound that is used as a surfactant with many glyphosate formulations. In a safety evaluation and risk assessment of glyphosate, the Roundup formulation and the surfactant POEA, Williams *et al.* (2000) reported that POEA can cause severe skin irritation and be corrosive to the eyes. In subchronic oral studies, POEA was mainly a gastrointestinal irritant in rats at high doses (~ 100 mg/kg/day) and in dogs at lower doses (30 mg/kg/day). In a developmental toxicity study in rats, POEA did not cause any developmental effects up to 300 mg/kg/day, but did induce maternal toxicity at 100 and 300 mg/kg/day (Farmer *et al.*, 2000). The concentrated formulated Roundup product can also be strongly irritating to the eyes and slightly irritating to the skin (Williams *et al.*, 2000).

2. (*information not included as it may be entitled to confidential treatment*). (*information not included as it may be entitled to confidential treatment*) are substances that are not highly toxic by oral or dermal routes and are not irritating to the skin. They may cause mild, transient eye irritation. Many *(information not included as it may be entitled to confidential treatment*) are known not to be sensitizers (*information not included as it may be entitled to confidential treatment*). The molecular weight of a *(information not included as it may be entitled to confidential treatment*) determines its biological properties, and, thus, its toxicity. The lower molecular weight (*information not included as it may be entitled to confidential treatment*) tend to be more toxic than the higher-weighted (*information not included as it may be entitled to confidential treatment*) and are absorbed by the digestive tract and excreted in the urine and feces, while the higher molecular weight *(information not included as it may be entitled to confidential treatment*) are absorbed more slowly or not at all *(information not included as it may be entitled to confidential treatment*). (*information not included as it may be entitled to confidential treatment*) have low acute and chronic toxicity in animal studies. No significant adverse effects have been noted in inhalation toxicology studies, carcinogen testing, or mutagen assays. High oral doses have resulted in toxic effects to the kidneys and loose feces (*information not included as it may be entitled to confidential treatment*). Topical dermal application of (*information not included as it may be entitled to confidential treatment*) to burn patients with injured skin has resulted in toxicity. (*information not included as it may be entitled to confidential treatment*).

Cosmo - Flux 411F (Adjuvant)

The Cosmo-Flux 411F adjuvant product used in the glyphosate tank mix is produced by a Colombian company and is not sold in the U.S. The Agency is not in possession of toxicity data from direct dosing of test animals with Cosmo-Flux 411F. However, the Agency has made safety findings based on the toxicity of the individual components. As stated above, sale or use of spray adjuvant products in the U.S. are generally not regulated by EPA. However, the DoS

has provided the EPA with a copy of this product's label and a description of the product ingredients. To be able to provide an opinion on hazard characterization of the Cosmoflux ingredients, the EPA relied on available technical information from various sources. Cosmo-Flux 411F consists mainly of (*information not included as it may be entitled to confidential treatment*) with a nonionic surfactant blend primarily composed of (*information not included as it may be entitled to confidential treatment*). All ingredients of this product are substances that are not highly toxic by oral or dermal routes. They may cause mild eye and skin irritation. All components of the adjuvant have been approved for use in/on food by EPA (40 CFR 180.1001.

Components of CosmoFlux (Considered as CBI)

1. (*information not included as it may be entitled to confidential treatment*). The (*information not included as it may be entitled to confidential treatment*) can cause dermal and ocular irritation and, in high doses orally, can cause significant toxicity. However, small amounts are not a concern and these substances have been approved as food additives by the FDA and are exempt from tolerances by EPA on certain commodities.

2. (*information not included as it may be entitled to confidential treatment*). The other major component of Cosmo-Flux 411F, (*information not included as it may be entitled to confidential treatment*), is not considered highly toxic. It may cause mild eye and skin irritation. The corresponding monoester, (*information not included as it may be entitled to confidential treatment*), has low subacute, subchronic and chronic oral toxicity and is used as a direct food additive and a component in cosmetics. The higher molecular weight triester is less likely to be absorbed orally or dermally and most likely of less toxicological concern. The other minor components, are not known to be highly toxic compounds and would not be of toxicological concern at the concentrations and conditions in which they are used.

E. Dose Response Assessment

Dose response analysis is the second step in the risk assessment process i.e.; characterization of the quantitative relationship between exposure (dose) and response based on studies in which adverse health effects have been observed. The objective is to identify endpoints of concern which correspond to the route and duration of exposure based on the exposure patterns.

HED selects doses and endpoints (effects of concern) for risk assessment via an internal peer review process. HED uses a standing Committee - the Hazard Identification Assessment Review Committee (HIARC), to consider the available hazard data (studies required to be submitted by registrants in 40 CFR part 158 and open peer reviewed literature) to identify endpoints for use in risk assessment.

Ideally, each safety study identifies a dose level that does not produce a biological or statistically significant increased incidence of an adverse effect or no observable adverse effect level (NOAEL). The threshold dose is the smallest dose required to produce a detectable effect. Below this dose, there is no detectable response.

On **March 26, 1998 and, again, on November 20**, **2001** the HED HIARC met to examine the hazard data base and identify dietary endpoints for Females 13-50 years old, as well as the General Population, the chronic reference dose. The HIARC also considered toxicological endpoints for incidental oral exposure appropriate in residential exposure risk assessments.

The most recent report of the HIARC for glyphosate has the complete assessment of the endpoints selected for dietary and residential/occupational exposures. OPP calculates acute (24 hour or single day) and chronic (continuous lifetime exposure) RfDs for the purposes of calculating dietary risk for food and drinking water. The RfD is calculated by dividing the appropriate no observed adverse effect level by a ten fold factor for interspecies variability ("average" human sensitivities might be up to 10 times that of lab animals) and a ten fold factor for intraspecies variability (i.e., some individuals within a population might be 10 times more sensitive than the "average" person).

For glyphosate, no endpoints were selected for the acute RfD since no hazard attributed to a single dose was identified from the oral toxicity studies, and there are no specific concerns for toxic effects on the developing fetus or infants and children. In addition, the HIARC did not identify endpoints of concern for dermal and inhalation exposures for any exposure period (short term- 1 to30 days, intermediate term- 1 to 6 months, or long term- 6 months to lifetime) since no hazard was identified due to the low toxicity of glyphosate. The chronic dietary RfD of 1.75 mg/kg/day was based on diarrhea, nasal discharge, and mortality in a rabbit developmental toxicity study. A summary of the doses and toxicological endpoints selected for various relevant exposure scenarios are summarized in Table 1.

Table 1. Glyphosate Endpoint Selection Table

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary (24 hour or single exposure)	An effect of concern attributable to a single dose was not identified from the oral toxicity studies; there are no concerns for developmental or reproductive toxicity.		
Chronic Dietary (continuous lifetime exposure)	NOAEL = 175 uncertainty factor (UF) = 100	Maternal toxicity based on clinical signs (diarrhea and nasal discharge)resulting in mortality of some dams at 350 mg/kg/day	Developmental toxicity -Rabbit
		Chronic RfD = 2.0 mg/kg/day	
Incidental Oral, Short- (1-30 days), and Intermediate-(1-6 months) Term	NOAEL= 175	Maternal toxicity based on clinical signs (diarrhea and nasal discharge)resulting in mortality of some dams at 350 mg/kg/day	Developmental toxicity -Rabbit
Dermal, Short-, Intermediate-and Long-Term	No hazard was identified, therefore quantification of dermal risk is not required. No systemic toxicity was seen at the Limit Dose (1000 mg/kg/day) following repeated dermal applications to New Zealand White rabbits.		
Inhalation, Short-, Intermediate-, and Long-Term	Quantification of inhalation risk is not required because 1) no hazard was identified in the 28 day inhalation toxicity study in rats - NOAEL = **0.36** mg/L (highest dose tested (HDT)); lowest observable adverse effect level (LOAEL) not established based on 6 hours/day, 5 days/week for 4 weeks and 2) due to the physical characteristics of the technical (wetcake), exposure to high levels of the active ingredient is unlikely via the inhalation route, so there was no purpose to test at higher doses.		

Glyphosate Food Quality Protection Act (FQPA) Considerations

On August 3, 1996 the FQPA amended FIFRA and FFDCA. Section 408(B)(II)(C) of FFDCA addresses exposure of infants and children. Under this provision EPA must apply the default 10X safety factor when establishing, modifying, leaving in effect or revoking a tolerance or exemption for a pesticide chemical residue, unless the EPA concludes, based on reliable data, that a different safety factor would protect the safety of infants and children. Risk assessors, therefore presume that the default 10X safety factor applies and should only recommend a different factor, based on an individualized assessment, when reliable data shows that such different factor is safe for infants and children that it does not rely on a default value or presumption in making decisions under Section 408 where reliable data are available that support an individualized determination.

The OPP FQPA Safety Factor Committee (SFC) makes specific case-by-case determinations as to the need and size of the additional factor if reliable data permit. Determination of the magnitude of the overall safety factor or margin of safety involves evaluating the completeness of the toxicology and exposure databases and the potential for pre- or post-natal toxicity. Individualized assessments may result in the use of additional factors greater or less than, or equal to 10X, or no additional factor at all. (*OPP Guidance Document on Determination of the Appropriate FQPA Safety Factor(s) in Tolerance Assessment, 2002*)

The HIARC addressed the potential enhanced sensitivity of infants and children from exposure to glyphosate as required by the FQPA of 1996 at the March 26, 1998 meeting and reaffirmed the decision at the November 20, 2001 meeting. The HIARC concluded the following:

< Based on the available data, there was no evidence of quantitative and qualitative increased susceptibility to *in utero* and/or postnatal exposure to glyphosate in rats or rabbits.

< Based on a weight of evidence consideration, the HIARC decided **not** to require the conduct of a developmental neurotoxicity study with glyphosate to evaluate the potential for developmental neurotoxic effects because there was no evidence of neurotoxicity and neuropathology in adult animals.

The **FQPA SFC met on April 6, 1998** to evaluate the hazard and exposure data for glyphosate. The FQPA SFC concluded that the safety factor of 10x be removed (reduced to 1x) since there is no evidence of quantitative or qualitative increased susceptibility of the young demonstrated in the prenatal developmental studies in rats and rabbits and pre/post natal reproduction study in rats. In addition the toxicology data base is complete, a developmental neurotoxicity study is **not** required, and the dietary (food and drinking water) exposure assessments will not underestimate the potential exposures for infants and children.

F. Exposure Assessment

The exposure assessment is the third step in the risk assessment process. The objective is to determine the source, type, frequency, magnitude, and duration of actual or hypothetical contact by humans with the agent of interest. To conduct this assessment EPA relied upon the information provided by DoS from three sources: (1) Department of State (DoS) Presentation, DoS Coca Eradication Program, 4/18/02, (2) DoS document entitled Chemicals Used for the Aerial Eradication of Illicit Coca in Colombia and Conditions of Application. (3) DoS document entitled Department of State Updated Report on Chemicals used in the Colombian Aerial Eradication Program. These data were used in accordance with standard policies and procedures used by the Agency in conducting pesticide exposure assessments.

Dietary Food Exposure

Acute dietary exposure is possible for persons consuming livestock or food crops which have been inadvertently sprayed as a result of the aerial eradication program in Colombia. However, since glyphosate is a contact herbicide that systemically kills plants after absorption through leaves, dietary exposure due to consumption of treated crops is expected to be limited. Since a coca field is sprayed no more than twice to eradicate the crop, no chronic food exposure is expected. Based on an evaluation of the hazard database, the Agency did not identify a toxic effect attributed to a single oral dose. Therefore, an acute dietary risk assessment was not performed. No significant risk due to dietary exposure to glyphosate residues is expected.

Occupational Handler and Post-application Exposure

Use Pattern Information

Use on coca for based on information supplied by DoS for the previous assessment on coca: The tank mixture sprayed for eradication of coca in Colombia contains 55% water, 44% of glyphosate herbicide product, and 1% adjuvant (Cosmo-Flux 411F). No more than two applications of the glyphosate tank mixture are sprayed over coca crops at a maximum of 1.25 gallons/acre (equivalent to 1.1 gallons/Acre of glyphosate product, 0.03 gal/Acre of Cosmo-Flux 411F, and 0.12 gal/acre of water). DoS also stated that the average field size for coca in Colombia is 3-5 hectares (approximately 7-12 acres). The program for aerial eradication of coca treats a maximum of 1000 acres/day, during 3-5 missions/day.

Updated information for the use on coca and poppy (Department of State Updated Report on Chemicals used in the Colombian Aerial Eradication Program).):

"4. Changes in chemical composition and spraying methods since 2002 report: Apart from changing to a more benign formulation of glyphosate spray mixture, as discussed earlier, there have been no changes to any of the components of the spray mixture. For some time in 2002, the Government of Colombia lowered the application rate of glyphosate for coca eradication from the traditional rate of 10.4 liters per hectare to 8.0 liters per hectare. After extensive ground truth evaluation, it was determined that the lower rate was ineffective for killing coca. Thus the application rate returned to its former rate of 10.4 liters per hectare, which was the rate reported in the Department's Report on Issues Related to the Eradication of Illicit Coca in Colombia in 2002 -- the rate that EPA evaluated when analyzing the potential for risks of adverse effects on human health and the environment posed by the coca eradication program. The only changes in the methodology used to spray coca since the time of the last report is the addition of a new type of spray aircraft to the spray fleet. Four Air Tractor Model 802 (AT-802) aircraft are currently being used to spray coca, and another four will be delivered this year. These aircraft are manufactured in the US for agricultural crop spraying and utilize the identical nozzles (same brand and diameter) in the identical configuration (nozzle angle, droplet size, calibration methods) as the OV-10 and T-65 spray aircraft. AT-802 flight speed during eradication operations is 165 m.p.h.

5. Differences between opium poppy spraying and coca spraying:

The Secretary of State was not required to determine and report to Congress on any aspects of the opium poppy eradication program in FY2002, and thus the Department did not provide information to EPA on the chemicals and methodology of poppy spraying. Like the coca spray mixture described in the "Report on Issues Related to the Eradication of Illicit Coca in Colombia," the opium poppy spray mixture contains three components: water, an EPA-registered formulation of the herbicide glyphosate, and a surfactant (Cosmo-Flux 411F). Because the opium poppy is not a woody, hard-to-control species like the coca bush, opium poppy eradication uses a spray mixture with a substantially lower glyphosate content than the spray mixture used for coca eradication . For opium poppy spraying, water, formulated glyphosate, and surfactant are combined into a spray mixture in the following percentages: 94 percent water, 5 percent glyphosate formulation, and 1 percent Cosmo-Flux 411F. This diluted mixture is applied to opium poppy at the rate of 50.0 liters/hectare (or 5.46 gallons per acre). This application rate is within the glyphosate manufacturer's label recommendations for both the amount of concentrated formulation per acre and the amount of total spray volume per acre.

Opium poppy spraying differs from coca spraying in several ways. Because Colombia cultivates much less opium poppy than coca and spray program resources are limited, aircraft spray much more coca than opium poppy, therefore expending more spray chemicals in coca growing areas than in areas where opium poppy is cultivated. For example, in 2002, eradication aircraft sprayed totals of 122,700 hectares of coca and 3,000 hectares of opium poppy. Opium poppy is generally cultivated in plots that are smaller than the average coca field. While difficult to quantify precisely, opium poppy fields generally range from 0.5 to 5 hectares. Opium poppy is ordinarily cultivated at a higher altitude than coca, and thus opium poppy often is cultivated and sprayed in hilly to mountainous terrain. For these reasons, the T-65 is the only aircraft used to spray opium poppy because it has a smaller wingspan (and spray swath) than the OV-10 or AT-802 and because it is a more agile aircraft capable of staying close to the ground in more steeply graded, rugged terrain.

Because of the challenges of mountain spraying, pilots undergo an extended training program before they are qualified to perform actual opium poppy spray operations in Colombia. As the Department of State reported in 2002, coca eradication pilots must have approximately 3,000 total flight hours before they are considered for the spray program and can receive preliminary training in illicit crop eradication. Most of these pilots also have at least 1,500 hours of commercial aerial application (crop dusting) experience. In addition to these requirements, opium poppy spray pilots must undergo 40 hours of follow-on training specific to the topography, wind conditions, and cloud cover that they will experience in their area of operations".

Handler Exposure

Exposure is expected for workers mixing and loading the glyphosate formulated product and tank mix, and applicators applying the pesticidal mixture via fixed-wing aircraft. Mixers, loaders, and applicators (handlers) have the potential for dermal exposure to the concentrate glyphosate formulated product or tank mix from droplets contacting the skin. There is also the potential for inhalation exposure to the concentrated glyphosate formulated product or mixed formulation from

breathing in aerosolized spray droplets.

According to the DoS, the mixer/loaders are trained on the label requirements for handling the chemicals in the spray mixture, first aid, and use of personal protective equipment (PPE). The required PPE according to the label includes long-sleeved shirts and long pants, waterproof gloves, shoes and socks, and protective eyewear. PPE is expected to mitigate potential exposure to handlers.

Exposure to handlers is anticipated for short-term (1-30 days) durations. There also may be the possibility for intermediate-term(1-6 months) handler exposure for individuals mixing, loading, and applying the glyphosate mixture to multiple fields for more than 30 days. However, the Agency does not have information pertaining to the duration of coca and poppy spray programs or number of days spent mixing, loading, and applying the glyphosate mixture.

An occupational handler exposure and risk assessment is required for an active ingredient if: (1) certain toxicological criteria are triggered and (2) there is potential exposure to handlers (i.e., mixers, loaders, applicators, etc.) during use. Upon review and analysis of the hazard database in total, the Agency's HIARC did not identify a hazard of concern for dermal or inhalation short- and intermediate-term exposures. Therefore, quantitative estimates of risk for short-term dermal and inhalation have not been conducted. No significant handler risk is expected.

Post-application Exposure

According to the DoS, Colombian coca plants (Erythroxylum species) are woody perennial shrubs native to the Andean region. Coca plants have leaves with waxy cuticles which retard herbicide uptake in the plant. The coca bushes grow to approximately chest level and are harvested mainly by leaf pulling, 4 to 5 times per year. Coca plants grow from seedlings to a harvestable plant in 12 to 18 months. Representatives from DoS indicated that, growers will prune the coca plants, immediately after spraying, in order to salvage the coca crop. Specifically, since glyphosate is a contact herbicide that works systemically to kill the plant after absorption through the leaves, workers may enter fields immediately after spraying in order to prune or pull off the coca leaves in order to prevent the coca plant from dying.

In the US, most uses of glyphosate are applied to kill weeds and other non-desirable vegetation–annual and perennial grasses and herbaceous plants and woody plants and trees on crop and non-crop lands. In general, glyphosate is not applied in the US to destroy or kill the raw agricultural commodity. The intended US uses are for undesired vegetation in and around crop fields, forests, industrial areas and residential areas.

DoS states that pilots are instructed not to spray fields where people are present. Therefore, based on the use pattern described by the DoS, potential short-term dermal exposures are expected for persons pruning, or leaf pulling treated coca plants immediately after spray events. These activities are expected to result in dermal exposure from treated foliage contacting the skin. In cases such as glyphosate, where the vapor pressure is negligible, HED experience with post-

application data suggests that inhalation exposure is minimal and therefore, HED does not quantitatively assess post-application inhalation exposure. Since poppy is sprayed at a much lower application rate than coca, potential exposures related to re-entering treated poppy field is expected to be similar or lower than those associated with the use on coca.

Intermediate- and long-term post-application exposures are not expected due in part to the fact that a coca and poppy fields are sprayed no more than twice. Additionally, glyphosate is a translocated herbicide which is rainfast (unable to rinsed off by water) within 48 hours after spraying. Therefore, potential exposure to dislodgeable residues of glyphosate after 48 hours is expected to be minimal. Glyphosate has no residual soil activity. Results from the first 12 months of bare ground field dissipation trials from eight sites show that the median half-life (DT50) for glyphosate (Roundup) applied at maximum annual use rates (7.95 lb a.i./acre, 10.7 lb a.i./acre) was 13.9 days with a range of 2.6 (Texas) to 140.6 (Iowa) days. Acceptable aerobic soil, aerobic aquatic and anaerobic aquatic metabolism studies demonstrate that under those conditions at 25ºC in the laboratory glyphosate degrades rapidly with half-lives of approximately 2, 7 and 8 days respectively. The reported half-lives (DT50) from the field studies conducted in the coldest climates, i.e. Minnesota, New York. and Iowa, were the longest at 28.7, 127.8, and 140.6 days respectively indicating that glyphosate residues in the field are somewhat more persistent in cooler climates as opposed to milder ones (Georgia, California, Arizona, Ohio, and Texas). The climate in Colombia would favor a shorter half life than the colder regions of the US. Thereby, HED believes glyphosate would not be persistent or be available for intermediate-term or long-term post-application exposures in the Colombian climate.

A post-application exposure and risk assessment is required for an active ingredient if: (1) certain toxicological criteria are triggered and (2) there is potential exposure. Upon review and analysis of the hazard database in total, the Agency's HIARC did not identify a hazard of concern for these durations or routes of exposure. Therefore, quantitative estimates of risk for short-term dermal and inhalation have not been conducted. No significant post-application risk due to glyphosate exposure is expected as a result of this use.

Incidental Oral Exposure (Hand-to-Mouth)

Since DoS states that pilots are instructed not to spray fields where people are present, incidental oral exposure (hand-to-mouth) resulting from being directly sprayed by glyphosate was not assessed. Also, it is not current Agency policy to quantitatively assess toddler hand-to-mouth exposure resulting from spray drift. Additionally, HED does not currently perform exposure assessments for toddler non-dietary oral exposures for agricultural scenarios. Therefore, non-dietary incidental oral exposure was not quantitatively assessed for the use of glyphosate in Colombia.

As a point of comparison, screening level risk estimates for toddler incidental oral exposures (hand-to-mouth) to the U.S. registered residential turf uses of glyphosate have been calculated. All resulting risks for toddler incidental oral exposure do not exceed HED's level of concern. The assumptions for toddler incidental oral exposures, (based on the maximum application rate of

1.62 lbs acid equivalent (ae)/acre), are expected to be conservative. For example, it is assumed that there is no dissipation of transferable residues, so that toddlers are exposed to day of treatment residues for each day of exposure. Even though the maximum application rate for the aerial eradication program is higher (3.3 lbs ae/Acre), using the same standard screening level assumptions as used in the residential assessment for the U.S. registered turf use and taking the higher application rate into account, the potential risk would not exceed HED's level of concern.

As indicated in the turf assessment, glyphosate was directly applied to residential lawns and did not result in exposures of concern to HED. Although spray drift is always a potential source of exposure to residents nearby aerial spraying operations, AgDrift® (a spray drift model) consistently predicts drift from applications is only a fraction of the applied rate (lb ai/acre). Based on this assessment, HED believes that it is unlikely that there is a higher potential for risk of exposure to spray drift from agricultural operations.

G. Potential Exposure From Spray Drift

Due to spray drift, there is potential exposure for persons in nearby areas to those targeted for spraying. Exposure through drift is not expected to exceed that which is identified in the exposure characterization provided above and in the ecological risk assessment below.

The coca eradication program operating in Colombia has incorporated several features designed to minimize the potential for off-target drift, provide quality assurance on a mission-by-mission basis, and evaluate the performance of the program to the extent possible given current conditions. Three types of aircraft are used in the program including the Ayres Corporation T65 Thrush, modified OV10D Bronco aircraft converted from military observation use to spray aircraft, and the Air Tractor AT802. The T65 and AT802 are common to the agricultural sector in the US. The nozzles are Accu-Flow as described at the April 18, 2002 briefing to the Agency. The droplet spectra characteristics, under use conditions for these nozzles, produce a very large droplet which has a volume median diameter (VMD) between 300 and 1500 microns. Use of droplets this size is consistent with minimizing spray drift in agriculture in the US. A surfactant (Cosmo-Flux 411F) is also used in the spray solution along with water and the glyphosate formulated product. The use of spray adjuvants (in this case Cosmo-Flux 411F) in pesticide product formulations and/or the spray solution is also consistent with common agricultural practices in the US.

The quality assurance standard operating procedures incorporated into the program are also consistent with standard agricultural practices. These include reconnaissance of the spray sites, use of global positioning satellite technology (GPS), and criteria for aborting missions (e.g., based on climatological conditions or presence of persons or livestock in the treatment areas). Reconnaissance of spray sites is intended to define the treatment zones through the use of sophisticated GPS mapping which is then overlaid with GPS spray records from missions to evaluate performance. GPS technology is used for planning, assessments of mission performance, and for archival purposes to evaluate potential claims against the program.

Finally, to a limited extent where feasible, on-site ground inspections for spray efficacy and potential adverse effects are performed. Reports suggest approximately 90 percent efficacy in the spray swath and minimal collateral damage to surrounding vegetation (e.g., aerial photos of treated areas) based on information supplied by the DoS at the April 18, 2002 briefing.

The Agency did not complete a quantitative risk analysis of the drift potential of glyphosate in the water/surfactant solution used in this program. However, the technology and other safeguards used in this program are consistent with common approaches in the US for reducing spray drift. Therefore, it is likely that drift is minimized in this program if all procedures are adhered to and operational equipment is in working order. At the April 2002 briefing, it was indicated to the Agency that quantitative spray drift studies had been completed by the DoS in conjunction with the University of Georgia. These were not supplied to the Agency nor were they considered in this evaluation. Additionally, it should be noted that the information considered by the Agency were done so without review of the primary source (e.g., the method by which the VMD was determined was not described, written application protocols describing target site conditions when applications would be aborted were not provided, and methods for scoring or measuring off-target damage were not provided).

Based on information contained in the report provided to OPP in 2003 entitled Department of State Updated Report on Chemicals used in the Colombian Aerial Eradication Program, it appears that there are no differences in the method used for poppy eradication significant enough from the coca eradication program, evaluated last year, that would show a cause for concern on drift related issues. By all accounts, DoS is approaching drift reduction in a systematic manner that is based on the same kinds of recommendations that would commonly be used in agriculture. It is also important to consider the drift issue in the context of concerns over human health. As indicated above in the exposure discussion, a qualitative assessment for glyphosate indicated that there were no risk concerns even for children playing in areas that have been treated at rates equivalent to those that would be expected within the treated areas. Spray drift would only lessen these exposures, again, which are already not of concern. As such, the Agency has no concern for spray drift from a human health perspective.

H. Incident Data Review: A Study of Health Complaints Related to Aerial Eradication of Poppy in Colombia

The following incident data were evaluated as part of the 2002 assessment for the use of glyphosate in the coca eradication program. Since the incidence data pertains to areas where poppy was sprayed, it is considered pertinent to the current review and is included below.

The report, prepared by the Department of Narino, Municipality of El Tablon De Gomez, makes a concerted effort to identify any health problems that might be related to use of the glyphosate tank mix in aerial eradication programs. The study was commissioned by the U.S. Embassy in Bogota and conducted independently by Dr. Camillo Uribe, Director of Clinica Uribe Cualla, the national poison control center. Sections of this report are summarized below with the sections numbered in **bold** corresponding to the original report.

An exact comparison of the epidemiological data in Colombia (which is from aerial application to poppy) relative to the conditions of use, presented at the April 18, 2002 briefing (for aerial application to coca) by DoS to OPP risk assessors, would have limitations and uncertainties. The briefing did not address the conditions of use for poppy. At that time DoS also did not provide human incident data for the coca eradication program. Subsequent to this briefing DoS did communicate that the application rate for poppy was lower than that for coca. According to the DoS, the use pattern of the glyphosate mixture on poppy also differs from the use on coca. Other details of the differences between the two spray programs have not been supplied to the Agency. Specifically, the Agency has no information as to the exact makeup of the tank mixture sprayed on poppy, or whether the same glyphosate product and adjuvants used in the coca eradication program were used in the poppy eradication program. Therefore, generalized conclusions drawn from human incident data as a result of application to opium poppy, in comparison to conditions of use for the coca eradication program should be made with caution.

1.1 Description of studied area

This report primarily concerns the area around the municipality of El Tablon in southern Colombia. The total population is given as 16,770, of which 89% is categorized as rural. The main crops in this area include coffee, corn, wheat, oats, potatoes, and illicit opium poppy. It is known that a variety of other pesticides, more toxic than glyphosate, are used on these crops. The municipality has three health centers, including Aponte, which is the focus of this report. The Aponte health center is staffed by a medical doctor, a nurse, and a nurse's aide. Aerial eradication of the illicit opium poppy reportedly occurred in this region in June, July, and November of 2000.

1.2 Morbidity and mortality in the municipality of El Tablon

The Narino Departmental Health Institute provided summary morbidity and mortality information for the El Tablon De Gomez area and the Aponte settlement for the year 1999. Data for the year 2000 had not yet been officially released, but estimates are provided. These data are reported here to provide an approximate description of glyphosate tank mix exposure upon use on coca fields in Columbia. However, no quantitative conclusions can be drawn from these data. Six illnesses likely to be related to pesticide exposure were identified and tabulated. They include, acute diarrhea, acute respiratory infection, dermatitis, intoxication, conjunctivitis and headache. The authors note that the first three illnesses listed (diarrhea, respiratory infection, and dermatitis) are likely to be related to problems with inadequate nutrition, housing, and lack of health services. The basis for this listing of symptoms is not specified, but it does agree with the list of symptoms likely to result from exposure to glyphosate products based on Poison Control Center data, California surveillance reports, and the world literature. Total morbidity for 1999 and estimated morbidity for 2000 are given in the Table below for El Tablon De Gomez and the Aponte Settlement below. Note, however, that the overwhelming majority of these illnesses did not occur at the time of spraying and, therefore, could not be related to spray exposure.

Table 2. Morbidity reported in the El Tablon De Gomez of Colombia in 1999 and estimated for 2000.

Pathology	1999	2000 Estimated
Acute diarrhea	146	186
Acute respiratory infection	568	506
Dermatitis	209	265
Poisoning/Intoxication	1	4
Conjunctivitis	75	85
Headaches	139	151
Total for 6 suspected illnesses	1,138	1,197

Table 3. Morbidity reported in the Aponte Settlement of Colombia in 1999 and estimated for 2000.

Pathology	1999	2000 Estimated
Acute diarrhea	181	190
Acute respiratory infection	199	222
Dermatitis	210	180
Poisoning/Intoxication	4	4
Conjunctivitis	87	104
Headaches	78	95
Total for 6 suspected illnesses	759	795

The Aponte settlement is contained within the El Tablon De Gomez area, where there has been a concern for herbicide spraying-related health effects. The figures in the report are listed by five separate age groups. This reveals, that the majority of the cases of diarrhea and respiratory infection occurred in children less than five years old, as would be expected given the known demographics of those health effects. Nationwide data show that 53% of intoxications are suicides or suicide attempts, but it is not clear how many of the four poisonings listed above might be suicidal or, more importantly, are due to other products such as medications. In both Tables 2 and 3 there is an increase of 5% from 1999 to the estimate for 2000 for the total of the six suspected illnesses. Given that spraying is reported to have occurred in 2000 and not in 1999, this suggests that the overwhelming majority (95%) of illnesses reported would be background incidence unrelated to the spraying of herbicide. The remaining 5% increase could be due to a variety of causes and do not support a conclusion that the glyphosate tank mixture was responsible for these complaints.

1.3 Epidemiological monitoring system and mandatory notification

In addition to the summary of general morbidity in the population, there is a mandatory health reporting system in Colombia for 34 illnesses including pesticide poisonings. The review of these records found no reports of pesticide poisoning for the municipality of El Tablon in the year 2000 or the first 9 weeks of 2001. Weekly reports were examined to determine how many pesticide poisonings were reported each month. It did not appear that the times of spraying correlated with reports of pesticide intoxication.

Table 4: Reports of Pesticide Intoxication provided to the Narino Department of Health Institute, Epidemiology Section January 12, 2000 through March 7, 2001.

Month/Year	Number of Poisonings	Month/Year	Number of poisonings	Poisonings occurring at time of spraying
January 2000	0	July 2000	11	9
February 2000	0	August 2000	6	
March 2000	8	September 2000	12	
April 2000	13	October 2000	8	
May 2000	7	November 2000	13	6
June 2000	15	December 2000	2	
--	-	Jan. 2001	7	
--	-	Feb. 2001	19	
--	-	Mar. 2001	0	

Out of a total of 125 reported pesticide poisonings in 61 weeks, 15 occurred during 5 weeks when spraying eradication occurred. Given the variation in the data, this could easily be due to chance and be unrelated to exposure from the spraying of the glyphosate tank mixture. More work is required to determine whether locations of the 15 suspect poisoning matched the location and timing of spraying.

In 2000, the Narino Department of Health requested all municipalities to report the human health effects of pesticide spraying. Ten municipalities supplied the reports. They are:

Three municipalities including Tablon de Gomez, Barbacoas, and Magui reported no cases. However, the reports were completed prior to the November spraying in Barbacoas and Magui and prior to (or perhaps during) the July and before the November spraying in Tablon de Gomez.

Buesaco reported one patient with sore throat, numbness in limbs, and conjunctivitis in June.

In Tumaco, six case of patients with conjunctivitis and dermatitis were reported as of October 6, 2000.

In San Pablo, 50 cases of dermatitis, conjunctivitis, respiratory conditions, and digestive problems were reported after as of October 6, 2000.

In La Cruz, two cases of allergic rhinitis, two cases of dermatitis, and five cases of conjunctivitis were reported as of October 6, 2000.

San Jose de Alban did not report any specific cases, but the scientific coordinator and chief nurse noted an increase in gastrointestinal, dermatological and respiratory conditions. The exact quantity of these conditions in relation to spray times was not given.

El Rosario reported five cases of conjunctivitis and rhinitis that might have been related to spraying carried out on July 31.

San Pedro de Cartago reported an increase in gastrointestinal symptoms but no quantitative relationship between illnesses and spray times was provided.

The absence of any reports of pesticide poisoning combined with the information from the ten municipalities is difficult to interpret. The glyphosate formulated product is known to cause irritation to the skin, eyes, mucous membranes which may account for some of the reports of sore throat, conjunctivitis, dermatitis and other conditions described above. However, it is not possible to evaluate these reports in any detail due to the lack of any information on how many of these cases experienced exposure immediately prior to their illness and lack of information on investigation of potential alternative causes. This anecdotal information does not provide any substantial evidence of health effects due to the spraying of the glyphosate tank mixture in Colombia. Many of the reports are consistent with exposure to glyphosate products by the dermal route, as reported in California and the literature. So, it is possible that some cases could be related to the aerial eradication program.

To provide context for comparison, the California Pesticide Illness Surveillance Program (1982-2000) data for glyphosate were reviewed for this risk assessment. This analysis demonstrated interesting findings. Starting in 1992, the glyphosate product was reformulated in the US to reduce the amount of surfactant which posed a hazard to the eye. From 1982 through 1991, there were 221 illnesses involving the eye or 22.1 cases per year. From 1994 (allowing 2 years for the product to be introduced into trade and widespread use) through 2000, there were 65 illnesses involving the eye or 9.3 cases per year, a decline of 58%. Therefore, these data support the finding that the reformulated glyphosate product used since 1992, have resulted in a significant drop in illnesses. Overall, the total illnesses due to glyphosate declined by 39% from the 1982-1991 time period to the 1994-2000 time period, largely due to the reduction in eye injuries.

2.2 Review of report of January 22, 2001 visit to the municipality of El Tablon de Gomez.

A commission visited the municipality of El Tablon on January 22, 2001 and spoke with Dr. Tordecilla and reviewed health records of his patients. A number of records of skin conditions were noted for the months of October, December 2000, and January 2001. The exact number of cases, selection criteria, and method of analysis was not specified in the summary report. Nevertheless, the commission concluded

"that the information available permitted the commission to consider only the possibility of an association between exposure to pesticides and the effects". The commission noted that it lacked the technical expertise, the data on dates and locations of spraying, and therefore could not conclude whether the observed conditions were related to pesticide exposure.

2.3 Interviews with Narino department health officials regarding the spraying

Employees of the Narino Department Health Institute were interviewed. A Fatima Health Promoter, thought the children were most affected, suffering gastrointestinal problems and eye irritation. One possible route of exposure was the village water fountains which supply some of the drinking water. The most common symptoms in children, according to the Health Promoter, were stomach aches and vomiting, which were different from the most common symptoms of glyphosate exposure reported by Lee et al. (2000), sore throat and nausea. This inconsistency suggests that some cause other than glyphosate products was responsible for the children's complaints. The Health Promoter reported one case of a boy with skin lesions like sores after the spraying. The Health Promoter was particularly concerned that peasants receive more health care from the government.

A nurse's aide reported that three or four patients with burning eyes, headache, and dizziness were seen at her health center. One boy with a respiratory infection was sent to another health center, later died. Medical records were sought to substantiate this report but there was no clinical history, autopsy or other information to support glyphosate spraying as a factor. She referred a patient with urinary problems to the hospital. Subsequent review of the medical records of this case did not find reference to glyphosate tank mix exposure and suggested an infectious origin. There were also cases of dermatitis, headache, abdominal pain and gastrointestinal symptoms, but she could not say whether the symptoms were related to exposure to the spraying of glyphosate tank mixture.

Another nurse's aide reported by telephone that her impression was that the number of dermatological consultations had increased. However, there was no clear association with glyphosate tank mix exposure and many of the reasons for the consultations were the same as in previous years when glyphosate was not used, so no clear relationship between the spraying and these dermatological conditions was identified.

Reports of anecdotal evidence by nurse's aides and the health promoter have not established a link between the spraying of glyphosate tank mix and health effects. Follow-up to determine the timing and evidence of exposure and examination of other potential causes of these effects was not performed. These interviews do not add significant evidence about the health risks from the use of glyphosate tank mixture in Colombia, more in depth study is needed.

2.5 Review of records of patients treated at Aponte Health Center - Sept. 2000 to Jan. 2001

There were 29 cases reported by Dr. Tordecelli and clinical records were obtained for 21 of them. Two other reports of skin lesions were sought but could not be confirmed. After careful review of the 21 records, it was determined that all but four cases were likely due to other causes. Most had skin conditions known to be related to bacteria or parasites, not chemical exposures and the onset of their symptoms did not correspond with the times of spraying. There were seven patients whose symptoms

started after spraying and three of these were conditions known to be caused by bacteria or parasites. For the remaining four cases possibly related to the spraying of glyphosate tank mixture, one was an allergic reaction that had been seen in this patient before when there was no spraying. A second and third case were contact eczema that is endemic in this region and thought to be more likely due to an infectious origin. One of these two cases did not initiate until 52 days after the last spraying. The fourth case was dermatitis on the thigh which would typically be protected by clothing and thereby protected from aerial spray applications. This reviewer agrees with the conclusion that "the twenty-one clinical histories . . . reveals that any relationship between aerial eradication with the herbicide glyphosate (tank mixture) and the skin conditions treated in Aponte is unlikely".

In summary, the evidence collected and presented in this report cannot confirm that the glyphosate tank mixture used in Colombia as the likely cause of illness in the surrounding community. There is suggestive evidence in the form of reported increases of morbidity and reports from municipalities that some cases of relatively mild complaints could have occurred in relation to the spraying eradication program. Some of the reports appear to be similar to those reported in the literature and by California. These cases report irritation to skin, eyes, and respiratory passages and suggest that the Cosmo-Flux 411F added to the glyphosate product in Colombia has little or no effect on the overall toxicity of the formulated product.

Rather than review incomplete medical records, it would be better to collect information prospectively. For example, if pesticide poisoning is a mandatory reporting condition, a form documenting the exposure, health effects and medical data on each case could be designed and used to establish whether any particular conditions might be related to spraying the glyphosate tank mixture. Without prospective collection of data and follow up, it is difficult to evaluate potential health effects of the glyphosate tank mixture sprayed in Colombia. Better records of the time of exposure relative to the onset of symptoms would also enhance interpretation of the incidence data.

I. Updated Incident Data Review

The purpose of the current review is to consider recent exposure/incident information provided to the Agency for the DoS Colombia coca and poppy eradication program in light of the 2002 assessment of reported health complaints. The "Department of State Updated Report on Chemicals used in the Colombian Aerial Eradication Program" submitted this year, mentions two activities, quoted below:

> "The spray program tracks human health complaints in two ways. The first is to initiate an immediate investigation, often including clinical evaluation of the patient(s), upon notice to the U.S. Embassy of a problem . . . To investigate complaints of toxic exposure allegedly caused by spraying, [the Embassy's Narcotics Affairs Section] retains the services of two of Colombia's leading toxicologists, including the director of Colombia's national poison control center, the Uribe Cualla Centro de Asesoramiento Toxicologico . . . ". Subsequent to the 2002 EPA assessment, "two complaints have been reported to the U.S. Embassy. In September 2002, the Embassy received a complaint of multiple cases of poisoning from spraying coca in Puerto Asis (Putumayo department). A visit to the hospital and interviews with doctors there revealed no cases of poisoning or illness attributable to spray chemicals."

A detailed report on this visit was provided in the 2003 submission: "Investigative report on cases of possible human health effects in Puerto Asis" by Jorge Hernan Tobon, M.D., September 19, 2002. Review of this report confirmed that only two hospitalized cases were located that could have been the source of the complaint. One was a 13-year old child diagnosed as suffering from organophosphate poisoning, not from glyphosate exposure. And the other was a three-year old child who developed symptoms of asthma at some time after several sprayings near her village. However, the coincidental development of symptoms without supporting evidence from other sources that glyphosate might be a contributor to asthma, make this case an unlikely result of exposure to the herbicide. In the opinion of the specialist treating the child, glyphosate was not the cause of her illness.

The second prospective approach is quoted from "Department of State Updated Report on Chemicals used in the Colombian Aerial Eradication Program":

> The Government of Colombia and the U.S. Embassy Bogota have also taken a proactive approach to investigating any human health concerns manifest in areas where the spraying takes place. Both governments have collaborated to create a robust Medcap to search out cases of harm to health allegedly caused by spraying. During these public health interventions that are timed to take place in areas where coca eradication has recently taken place, U.S. Embassy-contracted toxicologists talk to patients and talk to local medical personnel, looking for spray-related cases. . . .

As a result of the effort described above 1,029 patients were interviewed by Medcap medical personnel, had their medical conditions assessed, and received complimentary health care. None of the cases reviewed were found to be related to the eradication spraying program. Tabular information shows that between 120 and 260 patients were interviewed in relation to five separate spray operations. The report concluded that "Through Medcap and other medical investigations, the U.S. Embassy has never found an instance of spray-related harm to human health."

The report also mentions a separate news report that attributed spread of tuberculosis and questioned whether case of harelip and cleft palate in newborns might be related to spraying. Given the infectious nature of tuberculosis and the known genetic factors associated with the two birth defects, the likelihood of glyphosate having any role in these illnesses is extremely remote at best. The Agency is not aware of any information linking glyphosate to cleft palate in rats or rabbits.

Conclusions Regarding Incident Reports

Current information indicates that the Government of Colombia and the U.S. Embassy Bogota have adhered to the EPA advice ... "Prospective tracking of reports of health complaints, documenting times of exposure and onset of symptoms, are recommended during future spray operations to evaluate any potential health effects and ameliorate or prevent occurrence." The 2003 submission from the "Department of State Updated Report on Chemicals used in the Colombian Aerial Eradication Program" to the EPA indicates that "A visit to the hospital and interviews with doctors there revealed no cases of poisoning or illness attributable to spray chemicals." U.S. Embassy-contracted toxicologists talked to patients and talked to local medical personnel, looking for spray-related cases... The report concluded that "Through Medical Civic Action Program (Medcap) and other medical investigations, the U.S. Embassy

has never found an instance of spray-related harm to human health.". Missing from their account was a clearly stated case definition for what would constitute a glyphosate-related poisoning. A case definition is required if the conclusion that they have "never found an instance of spray-related harm to human health" is to be supported.

It would be useful to continue these efforts and further document the manner in which follow-up is performed. Standardized collection of data on patients and their symptoms is recommended, so that future analysis can look for patterns across patients not only to identify related cases, but perhaps identify new effects previously unsuspected and that might be associated with low-level exposure to glyphosate spray drift.

J. Risk Characterization

Risk characterization combines the assessments of the first three steps to develop a qualitative or quantitative estimate of the probability, that under the assumed conditions or variables of the exposure scenario, that harm will result to an exposed individual. Risk is equal to hazard multiplied by exposure. For the scenarios that are relevant to the subject use, the Agency has not identified toxic effects attributable to a single oral exposure, short- or intermediate-term dermal, or short- or intermediate-term inhalation exposures. Therefore, no quantitation of exposure or risk was performed. Nonetheless, it is appropriate to qualitatively characterize the potential for risk concerns for this use.

From the review of glyphosate product incident reports for the use on poppy, it should be emphasized that the spraying reported to have occurred in 2000 and not in 1999 suggests, that the overwhelming majority (95%) of the illnesses reported would be background incidents unrelated to the spraying of herbicide. The remaining 5% increase could be due to a variety of causes and do not support a conclusion that the spraying of the glyphosate tank mixture was responsible for these complaints. Furthermore, the individual with the highest potential for exposure would be the mixer loader. They are handling the concentrated glyphosate product and the tank mix. The incident data that has been submitted to the Agency by DoS, does not include any incident reports for those individuals. There is some data to suggest that the poppy eradication program could have resulted in minor skin, eye, or respiratory irritation, and perhaps headache or other minor symptoms. However, the detailed information on the use, timing of application, history of exposure, and medical documentation of symptoms related to exposure to glyphosate tank mix were not available. The evidence collected and presented in the epidemiology report cannot confirm that the glyphosate tank mixture used in Colombia as the likely cause of a single illness. There is suggestive evidence in the form of reported increases of morbidity and reports from municipalities that some cases of relatively mild complaints could have occurred in relation to the spraying eradication program. Some of the reports appear to be similar to those reported in the literature and by California. These cases report irritation to skin, eyes, and respiratory passages and suggest that the Cosmo-Flux 411F added to the glyphosate product in Colombia has little or no effect on the overall toxicity of the formulated product. The information so far collected indicates that any increase in health problems is likely to be relatively small at most and the severity of those symptoms is likely to be minor to moderate at most.

The Amazon Alliance and Earth Justice submission in 2002 provided little, if any, information on the number of persons affected, age and sex, symptoms of illness, or diagnosis or treatment received. Without

such information EPA cannot even begin to characterize the extent and pattern of the health effects claimed to result from glyphosate application. Given the limited amount of documentation, none of the data in the report from Colombia provide a compelling case that the spraying of the glyphosate mixture has been a significant cause of illness in the region studied. Prospective tracking of reports of health complaints, documenting times of exposure and onset of symptoms, are recommended during future spray operations to evaluate any potential health effects and ameliorate or prevent their occurrence.

Current information indicates that the Government of Colombia and the U.S. Embassy Bogota have adhered to the advice provided by the Agency in 2002 ... "Prospective tracking of reports of health complaints, documenting times of exposure and onset of symptoms, are recommended during future spray operations to evaluate any potential health effects and ameliorate or prevent occurrence." The 2003 submission from the "Department of State Updated Report on Chemicals used in the Colombian Aerial Eradication Program" to the EPA indicates that "A visit to the hospital and interviews with doctors there revealed no cases of poisoning or illness attributable to spray chemicals." U.S. Embassy-contracted toxicologists talked to patients and talked to local medical personnel, looking for spray-related cases... The report concluded that "Through Medical Civic Action Program (Medcap) and other medical investigations, the U.S. Embassy has never found an instance of spray-related harm to human health.". Missing from their account was a clearly stated case definition for what would constitute a glyphosate-related poisoning. A case definition is required if the conclusion that they have "never found an instance of spray-related harm to human health" is to be supported.

It would be useful to continue these efforts and further document the manner in which follow-up is performed. Standardized collection of data on patients and their symptoms is recommended, so that future analysis can look for patterns across patients not only to identify related cases, but perhaps identify new effects previously unsuspected and that might be associated with low-level exposure to glyphosate spray drift.

The *glyphosate formulated product* currently used in the coca eradication program in Colombia contains the active ingredient glyphosate, a surfactant blend, and water. The acute toxicity test of the *glyphosate technical* and *formulated product* indicate that both are classified as category III for primary eye irritation and category IV for acute dermal and oral toxicity, and skin irritation and are negative for dermal sensitization. The label for the *formulated* product used in the eradication program in Colombia includes the "Caution" signal word.

During April 18 briefing, the Department of State agreed to supply the Agency with a full battery of the six acute toxicity tests on the tank mix used in the coca aerial eradication program. That information has been received and reviewed. In summary, the acute toxicity of the spray mixture is category III for eye irritation and category IV for skin irritation and acute dermal, oral and inhalation exposure and is negative for dermal sensitization.

K. Summary Conclusions

- There are no risks of concern for glyphosate, *per se*, from the dermal or inhalation routes of exposure, since toxicity is very low.

- The components of the adjuvant Cosmoflux 411F are not highly toxic by the oral and dermal routes; they have been approved for use in/on food by the Agency.
- Glyphosate is not highly toxic. Based on the conditions of glyphosate use described by DoS, there is likely minimal exposure or concern for acute and chronic dietary or incidental oral risks.
- Due to the change of glyphosate product used in the Colombian Aerial Coca and Poppy Eradication program and the submission of the acute toxicity tests for the tank mix, there is no longer concern for acute eye toxicity.
- Based on the information received to date for the use on poppy, exposure is expected to be similar or lower than the previously assessed use on coca.

REFERENCES

(*information not included as it may be entitled to confidential treatment*).

HIARC Report for Glyphosate (TXR No. 0050428, 22-JAN-2002)

Glyphosate in/on Pasture and Rangeland Grasses, Roundup Ready® Wheat, and Nongrass Animal Feeds. (DP Barcode: D280831, 20-FEB-2002)

Evaluation of 6 acute toxicity studies conducted on test material identified as Spray–Charlie. (DP Barcode: D289806, 13-MAY-2003)

Farmer, D.R., T.A. Kaempfe, W.F. Heydens and W.R. Kelce. 2000. Developmental toxicity studies with glyphosate and selected surfactants in rats. Teratology 61(6): 446.

(*information not included as it may be entitled to confidential treatment*).

(information not included as it may be entitled to confidential treatment).

US Environmental Protection Agency, Office of Pesticide Programs May 9, 2002: Guidance Document on Methodology for Determining the Data Needed and the Types of Assessments Necessary to Make FFDCA Section 408 Safety Determinations for Lower Toxicity Pesticide Chemicals.

Williams, G.M., R. Kroes and I.C. Munro. 2000. Safety evaluation and risk assessment of the herbicide Roundup and its active ingredient, glyphosate, for humans. Reg. Toxic. Pharm. 31: 117-165.

III. ECOLOGICAL RISK ASSESSMENT

A. Introduction

At the request of the Department of State (DoS), the Office of Pesticide Programs (OPP) of the U.S. Environmental Protection Agency (EPA) provides here an ecological risk assessment for the aerial coca and poppy eradication programs in Colombia. The Environmental Fate and Effects Division (EFED) performed a risk assessment for coca eradication in response to a similar request by DoS in 2002. That assessment concluded that the active ingredient glyphosate itself would likely pose little risk to non-target terrestrial and aquatic animals, but that non-target terrestrial plants would likely be damaged some distance from the intended spray area due to spray drift of glyphosate.

The proposed use of glyphosate on coca will be little changed from that described in 2002, with the exception of the use of a different glyphosate product in 2003. This will reduce the potential for eye irritation, and therefore may provide some benefit to people and terrestrial animals exposed to the spray. Other aspects of the proposed use remain the same, including the use of adjuvant CosmoFlux 411F. Therefore, as detailed below, the expected risks and uncertainties in EPA's environmental risk assessment remain essentially the same as described the previous year.

The request for a risk assessment for the use of glyphosate to control poppy production is new for 2003. However, as described below, the expected risks and uncertainties corresponding to this use are nearly identical to those for the coca use. The application rate of glyphosate is less for poppies than for coca, and therefore the risk to terrestrial animals is expected to be low. The potential for glyphosate runoff may be much greater for poppies, since the sprayed fields can be located on mountainsides. However, as detailed in the 2002 assessment for coca eradication, the concentration of active ingredient glyphosate that might be derived even from direct application to a small pond should not result in significant risk to non-target aquatic animals or plants. Therefore, runoff from the poppy or coca sprays would not be expected to pose a significant risk to non-target aquatic organisms.

The primary risk that might be associated with the poppy eradication program is that from spray drift to non-target terrestrial plants. As with coca applications, application to poppy fields will require application at speeds and application heights greater than might be desirable for drift control, due to the safety precautions needed for eradication sprays down a potentially forested mountainside. The added factor of steep slopes make it likely that spray drift from the lower rate poppy sprays could extend a greater distance than that from the coca eradication sprays which are understood to occur on more level terrain.

B. Ecological Risk Characterization

The following risk characterization for the coca eradication use is adapted from the 2002 ecological risk assessment for the use of glyphosate herbicide as part of the U.S. supported aerial eradication program of coca in Colombia:

The use of a glyphosate spray for coca and poppy eradication is unlikely to cause adverse effects to

terrestrial or aquatic animals but is likely to pose a substantial risk to nearby non-target plants. Vegetative vigor toxicity laboratory tests performed using a formulated glyphosate product (glyphosate acid WP 48.3%) on North American crops indicated toxicity to terrestrial plants with applications of less than 1.0 lb of the isopropylamine salt of glyphosate per acre, which corresponds to 0.75 lb acid equivalents (a.e.) per acre. The coca use rate is 1.11 gallons glyphosate/acre (3.34 lb acid equivalents/acre) for direct, aerial application to coca. A second application is possible if fields are replanted, or the first is determined after 3 to 6 months to have been inadequate. Because poppies are reportedly more sensitive to glyphosate, a lower application rate of 0.27 gallon/acre (0.8 lb a.e./acre) is used in spraying for poppy eradication. The DoS reports that the spray mixture for poppy eradication would include 5% formulated glyphosate, 1% Cosmo-Flux 411F, and 95% water (as opposed to 44%, 1% and 55%, respectively for the coca spray). The product claimed by the DoS to be used ib Colombia is widely used in the US on a variety of agricultural commodities and non-agricultural sites.

EPA used the AgDRIFT model to estimate potential spray drift. The model suggests that non-target plants hundreds of feet away may be exposed to a fraction of glyphosate applied to coca or poppy fields. Some of the important application parameters for estimating spray drift levels from coca and poppy eradication application are shown in Table 1.

Table 1. Important application parameters for defining off-target spray drift levels in coca and poppy eradication.

Application parameter	Coca spraying	Poppy spraying	Effect on off-target exposure
Application rate	3.34 lb a.e./acre	0.8 lb a.e./acre	Lower application rates result in lower off-target exposure
Flight speed during application	200 mph	135-145 mph	Lower flight speeds result in less secondary droplet break up, larger droplets, less drift, and lower off-target exposure
Estimate wind speed range	0-10 mph	0-4 mph	Lower wind speeds results in less movement of spray droplets off-target (i.e. lower drift)
Estimated droplet size range	300-1500 mm	300-1000 mm	Larger droplets are less prone to be blown off-target
Estimated release heights	<100 feet	30 -120 feet	Lower release heights result in shorter fall times for droplets and less opportunity to be blown off-target
Boom width	not available	70% of wingspan	Narrow boom widths result in fewer droplet being caught in wing tip vortices and lower drift levels
Slope	not available	not available	Drift can be carried farther when winds are blowing down steeper slopes

Figure 1.

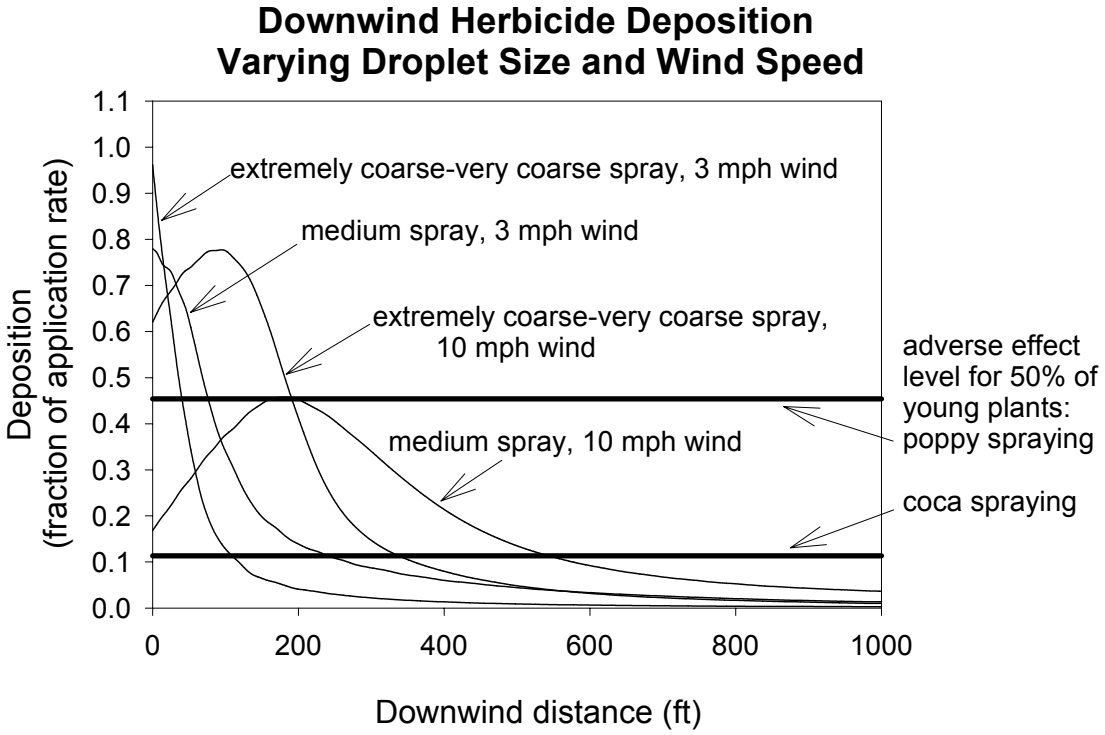

Figure 1 shows the lowest levels of drift are associated with applications using the extremely coarse to very coarse sprays at a 3 mph wind speed. The highest levels of drift are associated medium sprays at wind speeds of 10 mph. Downwind deposition levels from coca and poppy spraying is likely to be bounded by these estimates. The "effect level for 50% of young plants" is based of glyphosate toxicity studies on ten young crop plants. Older plants are generally less sensitive to herbicides than young, rapidly growing plants. At the level corresponding to approximately 11% and 44% of the coca and poppy application rates, respectively, 50% of plants species would be expected to show measurable reductions in dry weight. With a 10 mph wind, plants would be expected to be exposed at this 50% affect level up to 200 feet downwind of poppy spraying and 550 feet downwind of coca spraying. Of the affected plants some would likely recover while more sensitive plants may die, have reduced reproductive success, or reduced yields (crop plants).

There is uncertainty whether crops or other plants in Colombia, whether similar to crops tested in the US or not, would be affected similarly at the same exposure levels. However, since glyphosate is an effective, broad spectrum herbicide, risk to non-target plants outside of the application zone would be expected. The Agency's Ecological Incidents Information Sytem (EIIS) database includes several hundred reports of possible non-target plant incidents in the US attributed to use of glyphosate.

The use of the active ingredient glyphosate itself in poppy and coca eradication would not pose a significant direct risk to terrestrial or aquatic animals, although secondary adverse effects from the loss of habitat in the spray area are likely. Neither acute nor chronic adverse effects were observed in mammalian and avian laboratory toxicity tests submitted to the EPA by US industry, using the active ingredient alone.

Mortality was observed in fish and aquatic invertebrate studies. However, the resulting acute LC_{50} values (concentrations at which half the test animals died), and lowest effect levels for chronic effects, were in parts-per-million. Toxicity endpoints for aquatic plants also ranged from 0.85 to 39.9 ppm. Considerably lower surface-water exposure, in the parts-per-billion, could be expected from the use on coca or poppy using runoff simulations from Agency exposure models PRZM and EXAMS. The Agency considered an even more conservative scenario, estimating the concentration that would result from the direct application of 3.75 lb acid eq./acre of glyphosate to a 1-acre, 6-foot deep pond. The calculated maximum concentration of 230 ppb is well below the toxicity values measured for aquatic organisms in the laboratory.

It is possible that much greater exposure could occur from direct overspray of water bodies much smaller than a 1-acre, 6-foot deep pond, but such simulation is not a standard component of Agency risk assessments. The product label for glyphosate prohibits such direct overspray of water bodies, but it is possible that some ecologically important water bodies too small or ephemeral to appear on maps could be sprayed directly in a project as large as the coca eradication program.

Although the measured toxicity and estimated exposure indicate that only non-target terrestrial plants are likely to be adversely affected by the use on coca and poppy, there are important uncertainties that should be considered. One of these is the extrapolation of North American data to the conditions and wildlife found in Colombia. The toxicity of a pesticide to different classes of animals and plants can vary widely among species within an individual ecosystem. The Agency uses the test species as surrogates for other North American species not tested, but has little experience with tropical flora and fauna. Similarly, laboratory and field estimates of the environmental fate of pesticides, including potential surface-water contamination, are performed with North American soils, hydrology and climate data. The uncertainty of extrapolating North American exposure and effects data to this risk assessment would most effectively be reduced by identification of characteristics which define sensitive tropical ecosystems.

An important uncertainty in this risk assessment concerns differences in the tank mix used in Colombia from those used in the US. The Agency does not have ecological toxicity information on adjuvant Cosmo-Flux 411F, which is neither manufactured nor sold in the US. However, all of the individual components (surfactants) which comprise the adjuvant are substances with low oral and dermal mammalian toxicity. The toxicity of the blend of these surfactants is not known; although the Agency often requires formulation toxicity data for non-target plants and aquatic organisms, tank-mix adjuvants are not required to be included in these studies.