PARAQUAT in developing countries

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ABSTRACT

Paraquat, a controversial herbicide, is one of the most used pesticides globally, in most countries without restrictions. It is considered safe by industry and the bulk of regulators worldwide, especially in the context of stewardship programs. However, the few recent studies on exposure assessment and health effects demonstrate that determinants of exposure that were identified thirty years ago still prevail in developing countries. Little is known about systemic absorption of paraquat from occupational exposures. The relations between exposure determinants, levels of external exposure, biomarkers of exposure, and outcomes are far from clear. For example, measured low inhalation levels are inconsistent with frequent episodes of nosebleeds, and it remains uncertain at which inhalation levels nosebleeds occurs and whether these levels may be relevant for systemic uptake. Non-worker populations are also at risk for exposure and health effects, in particular children. High rates of severe acute poisonings, both suicidal and unintentional, have been documented in many countries, also in recent years. There are no strong data that total paraquat poisonings have substantially diminished, and paraquat poisoning clearly remains a severe public health problem in many countries. In addition, topical injuries, including skin problems ranging from mild dermatitis up to severe chemical burns, eye injury, nail damage, and nosebleed, have been observed in proportions as high as 50% of exposed workers in both early and recent surveys. Long-term and delayed health effects may occur, including Parkinson’s Disease, lung effects, and skin cancer. Regulatory agencies have not fully recognized either the inherent toxicity of paraquat for human beings or the particular risks derived from exposures in developing countries. Independent risk assessment in the developing country context and application of the precautionary principle are necessary to prevent the occurrence of adverse affects from dangerous pesticides such as paraquat in susceptible third World populations.
INTRODUCTION
The contact herbicide paraquat (1,1'-dimethyl-4,4'-bipyridylium dichloride) disrupts photosynthesis processes in plants. Paraquat is used in over 120 countries, commonly sold as Gramoxone®, a 20% solution. It is currently the third best-selling pesticide globally, produced by of the world’s largest agrochemical company currently by name SYNGENTA, [www.syngenta.com/en/customer, July 2001]. Paraquat is labor saving and cheap, and therefore especially popular and accessible to farmers in developing countries.

The use of paraquat has been questioned and discussed for decades in international regulatory, NGO, and scientific fora.1-13 Reasons for alarm were frequent suicides, unintentional poisonings in children and adults, and skin and eye injuries. In the late 1980s, manufacturers added a blue pigment, a stenching compound, and an emetic substance to the formulation to make severe unintentional poisonings due to oral intake virtually impossible.14 Industry has repeatedly claimed that paraquat has an excellent occupational safety record, when labeled instructions are followed.14-17 In response to a report on high frequency of suicidal paraquat poisonings in Trinidad,18 the manufacturer recently stated that paraquat suicides are decreasing, and that safe use practices and training have decreased if not eliminated unintentional poisonings. They claim that “banning paraquat could add to the social distress associated with high suicide rates among subsistence farmers, by banning an essential tool to feed their families and enhance their prosperities”.17

Paraquat has been banned or restricted in a number of countries. The US Environmental Protection Agency (EPA) allows its purchase and use solely by certified applicators.19 Paraquat is prohibited in Sweden, Finland, and Austria based on acute toxicity and absence of antidote. In Norway, the manufacturers canceled voluntarily its registration.20 In Germany and in The Netherlands, paraquat was banned because of its persistence in soil. The ban was subsequently lifted.21 Paraquat is being reviewed in the European Union and is in use in 10 of the 15 EU member states [http://europa.eu.int] status of current authorizations in December 2000).

In developing countries, where health hazards of pesticides are pronounced, paraquat is minimally restricted. In Indonesia, its use is restricted to large estates and certified applicators.22 In April 2001, the government of Chile prohibited aerial applications [http://www.sag.gob.cl]. In September 2000, the Central American Ministers of Health signed
an agreement on restricting the most toxic pesticides, including paraquat. The agreement has not been implemented yet.

The recommendation for classification by acute hazard of the World Health Organization’s International Program on Chemical Safety (IPCS), followed by most developing countries, endorses a laissez-faire for paraquat by classifying it as a moderately toxic Class II pesticide, based on oral toxicity data in rats. Paraquat was initially considered by the Prior Informed Consent (PIC) Expert Group for inclusion in the list of PIC pesticides of the FAO Code of Conduct, as a pesticide with special problems in developing countries. Heavy industry lobbying however has kept paraquat excluded from the PIC list. The PIC Expert Group suggested during the 1992 FAO/UNEP joint meeting on PIC in Rome, that “FAO consult with PAHO regarding the reported accidents, deaths and incidents in Latin America and consider a consultancy involving visits to five or six countries to investigate the reports of incidents and provide a report on the actual conditions of use”. This consultancy never took place. In 1995, discussions on the PIC Convention stopped any further actions (Barbara Dinham, personal communication). The World Bank agreed to consider not recommending paraquat in World Bank projects, but never implemented this policy.

Deficient working conditions, improper maintenance, climatic conditions, illiteracy, and general poverty make controlled and safe use of paraquat extremely difficult in developing countries. This paper reviews data on use, human exposure, toxicity and health effects of paraquat, focusing on Costa Rica, Central America, and other developing countries, in order to provide an overview of basic data for risk assessment and decision making in developing countries.

USE OF PARAQUAT AND HUMAN EXPOSURE

Use in Central America
Paraquat has for decades stayed among the pesticides imported by highest volume in Central American countries: Belize, Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, and Panama. It is used in for weed control on banana, coffee, plantain, sugarcane, corn, palm heart, ornamentals, trees, citrus fruits, oil palm, macadamia, mango, avocados, and other crops; as a pre-emergent herbicide on crops or for the cleaning of land; as a defoliant on
cotton; for destruction of potato stems and tops; as a post-harvest desiccant on pineapple; in roadside weed control; and around buildings and homes, especially in rural areas (Database IRET-UNA). Paraquat became widespread in the late 1970s. By the end of the 1980s, technical grade paraquat was processed in pesticide formulating factories in the seven Central American countries.25 Being a contact herbicide, spraying of paraquat occurs with high frequency, especially under humid weather conditions with rapid plant growth, for example up every six to eight weeks on banana plantations. Import data, available for Costa Rica from 1981 (Database IRET-UNA), peaked at 750 tons in 1989, followed by a steep decline to 187 tons in 1995. The decrease was related to a substitution for other less toxic herbicides, such as glyphosate. This occurred in particular on the banana plantations, under consumer pressure from abroad, since paraquat could not be used anymore for bananas with an eco-label. At present, the use of paraquat is on the rise again, due to increased use in other crops such as pineapple, with over 420 tons having been imported in 1999 in Costa Rica (Figure 1). No Central American country restricts the agricultural use of paraquat in any manner, with the exception that it is not registered for aerial applications.

INSERT FIGURE 1

**Occupational exposure**

Exposure to paraquat occurs by dermal and ocular contact, by inhalation or by oral intake. Early occupational exposure studies in Sri Lanka, Malaysia and the United States assessed exposure levels of knapsack and field tractor applicators26-29 and occupational exposures for aerial applications.30 More recently also some exposure assessments studies on knapsack applicators have been performed in Sri Lanka31 and Costa Rica.32,33 Table 1 gives an overview of the studies performed. The studies measured dermal, inhalation and/or urinary paraquat levels of applicators and/or plantation workers. In general, dermal exposure levels seemed most important, whereas measured inhalation levels were relatively low. Four out of six studies assessing uptake found paraquat in urine at the end of one or more working days. However, the relations between exposure determinants, levels of external exposure, and levels in urine were far from clear and not investigated with much detail.

Measured exposure levels and exposure circumstances among backpack sprayers seemed quite comparable in the different studies, with the exception of the remarkably lower levels observed in a study in the US.27 Nevertheless, the interpretation of similar findings of studies
performed in several tropical countries differed considerably. The studies carried out by or in collaboration with Imperial Chemical Industries (currently SYNGENTA) concluded that paraquat is most unlikely to cause serious health problems under correct conditions of use,\textsuperscript{15,26,28,31} despite the fact that in several of these studies between 40 and 50% workers experienced topical injuries.\textsuperscript{26,34} Other researchers concluded that, even when measured levels were unlikely to result in acute or chronic health effects, spray operators were continuously at risk for high exposures that may lead to severe intoxication and injuries. Even on plantations where serious efforts had been made to reduce risks, dangerous situations and events of inadequate handling were registered.\textsuperscript{32,33}

**INSERT TABLE 1**

*Dermal exposure*

Dermal exposure was the most likely route of uptake in studies that reported paraquat in urine (see Table 1). Paraquat is poorly absorbed through intact skin, but penetration is considerably increased by damaged skin, which is of particular concern because paraquat itself is a skin irritant.\textsuperscript{35} Total dermal exposure levels in studies presented in table 1 were assessed by residue analysis on pads and coveralls or from hand washing, with calculations of mg/h or mg/kg of applied paraquat of actual or potential dermal exposure. It is noteworthy that the existing exposure data have only limited value for risk assessment, however they give insight in possible exposure routes and mechanisms. Conceptual models of dermal exposures and new methods for dermal exposure assessment are only recently being developed and underlying mechanisms of exposure scrutinized scientifically.\textsuperscript{36}

On banana plantations, dermal exposures varied rather due to differences between plantations, than differences between applicators or between days.\textsuperscript{32,33} The body parts identified with highest exposure were hands, wrists, back, and scrotum. They included splashing during preparation of the spray solution and open transportation, deposition of spraying mist, contact with spray solution when filling knapsack, leaking of knapsack on back and groin, adjustment of spray equipment, and walking through the sprayed vegetation.

Use of protective clothing is supposed to considerably reduce dermal exposure. However, few studies have evaluated the effectiveness of personal protection or other safety measures.\textsuperscript{33,37} Swan (1969) compared exposure of applicators using normal clothing with workers using
gloves, boots and respiratory protectors. Less positive urine samples were identified in workers using protective equipment (7-14% versus 18-50%) and less skin complaints were reported. Spruit and van Puijvelde (1998) performed a small study to evaluate the use of protective equipment at four banana plantations by means of fluorescent tracer and cotton gauze. All workers (n=8) had received training in safe use of protective equipment. Wearing jeans and an apron on the back seemed to reduce exposure considerably. Dermal exposure levels were lower than those measured by van Wendel de Joode et al. (1996) (see Table 1). Exposure occurred especially in body areas with movements (knees, elbow, wrists) and those becoming wet by transpiration or pressure from belts of the knapsack (armpits and shoulder region). Despite the use of gloves, hands remained exposed due to cross contamination by taking gloves off and on. Occlusion of pesticides by protective devices may result in increased absorption.

**Inhalation**

In general, inhalation exposure is not considered a relevant exposure route, due to the low volatility of paraquat and droplets being too large to enter the small airways during application. Ambient air concentrations are generally well below NIOSH and OSHA limits (0.1 mg/m³ and 0.5 mg/m³ TWA, respectively) (see Table 1). However, van Wendel de Joode et al. (1996) could not exclude that inhalation exposure was relevant for internal exposure. Inhalation exposures measured in this study appeared to be strongly influenced by differences between days, which could be due to variable wind speeds and other weather related conditions. In Costa Rica, the use of motor driven backpacks to spray paraquat is not uncommon. These may produce increase of the fraction of respirable particles. It has also been put forward that the respirable fraction of paraquat may become larger under certain climatic conditions. Several studies suggest that inhalation may play a role in systemic paraquat absorption.

The low inhalation levels measured in the different studies seem inconsistent with the frequent episodes of epistaxis or nose bleeds reported among exposed workers, which are due to local irritation of the upper respiratory tract by paraquat particles. It is possible that inhalation exposure levels are incidentally higher than those reported in the studies of Table 1, since none of the studies with assessment of inhalation exposures mentioned the occurrence of epistaxis during the measurements. However, it remains unclear.
at which inhalation exposure levels epistaxis occurs and whether these levels may be relevant for systemic uptake.

**Oral exposure**

Oral exposure may occur during work when ingesting paraquat solution by mistake, through splashes in the mouth during mixing and transporting, by eating with contaminated hands, by blowing or sucking spray nozzles, or when eating contaminated food.\(^{12,15,28,32,44}\) In addition, oral ingestion may also occur as a result of swallowing the ‘run off’ on the face caused by droplets when the operator is working in the spray mist.\(^{15}\) Retention of paraquat particles in the nose and mouth, as evidenced by soar throat and nosebleed, may contribute to the internal dose by swallowing.\(^{12}\)

**Nonoccupational exposure: risk for children**

The border between occupational and nonoccupational accidental exposure is not always easy to distinguish. Accidental oral exposure may occur under a variety of circumstances. Confusion of paraquat concentrate or solution due to inappropriate storage in refreshment or liquor bottles has apparently diminished but still occurs. Accidental intake at home is in Costa Rica often in association with alcohol intake.\(^{45}\)

Children’s exposures are of special concern. To determine oral exposure of children from containers for garden use, a US EPA study analyzed paraquat residues of diluted spray on nozzles and nozzle discharge. Based on a LD\(_{50}\) for rats of 100 mg/kg, the maximum observed value for oral exposure would represent 0.14% of the toxic dose for a child of 12.3 kg. The authors concluded that despite the ample safety margin there is a potential hazard, in particular because of higher toxicity in humans than in rats.\(^{27}\) In Costa Rica, between 1991 and 1995, the exposure circumstances of severe and fatal poisoning in children age 1-6 included the cases of two toddlers placing respectively a rinsed spray jet and a bottle top into their mouths, two cases of confusion of bottles stored in the kitchen, two cases of children playing with empty bottles, and a 7-year old sister giving “cough medicine” to a younger brother.\(^{45}\)
TOXICITY DATA AND HEALTH EFFECTS

Acute systemic toxicity
Systemic paraquat poisoning is characterized by burns of the upper digestive tract when ingested, and by multi-organ failure, including the lungs as the main target organ, and liver, kidneys and, less frequently, the central nervous system, heart, suprarenal glands, and muscles. In fatal cases, depending on the dose, death is due to respiratory failure from lung edema within a few days or from lung fibrosis up to over a month after the poisoning event. No antidote or effective treatment is known.\textsuperscript{11,43}

Toxicity data from animal bioassays used by regulatory agencies are not fully consistent. US EPA classifies the acute toxicity of paraquat due to oral intake as Category II, moderately toxic, based on the LD$_{50}$ of 283 and 344 mg/kg in female and male rats,\textsuperscript{19} while WHO-IPCS uses a LD$_{50}$ of 150 in rats as the basis for its classification.\textsuperscript{24} Acute oral toxicity is much higher in other mammals, for example guinea pigs (22-30 mg/kg), monkeys (50 mg/kg), cats (40-50 mg/kg) and dogs (25–50 mg/kg).\textsuperscript{43,46} For humans, the lowest fatal dose recorded is 17 mg/kg.\textsuperscript{43} Still lower doses may be fatal, especially in children.\textsuperscript{12,47}

EPA classifies systemic toxicity of paraquat from dermal absorption as slightly toxic, category III, based on LD$_{50}$ > 2000 mg/kg (no observed mortality dosing rats during 24 hours with 2000 mg/kg).\textsuperscript{19} In other animal bioassays, the dermal toxicity of paraquat has been reported to be much higher with LD$_{50}$ of 80 and 90 mg/kg in male and female rats,\textsuperscript{43} and 236-500 mg/kg in the rabbit.\textsuperscript{43,46} In addition, paraquat is caustic and may, by increased dermal absorption, originate systemic poisonings.\textsuperscript{7,35,48}

US EPA classifies the acute toxicity by inhalation as Category I, highly toxic based on an inhalation LC$_{50}$ of the respirable fraction of paraquat of 1 µg/L. However, since agricultural formulations of paraquat contain few respirable particles and paraquat’s volatility is low as discussed above, EPA does not consider the respiratory toxicity a toxicological endpoint of concern for systemic paraquat absorption and does not consider it in its risk assessment.\textsuperscript{19} Systemic toxicity after respiratory exposures has however been reported.\textsuperscript{12,40,41}
Epidemiology of severe and fatal paraquat poisonings

Thousands of paraquat poisonings and fatalities have been reported in case reports, case series, surveys and through surveillance systems, in particular in developing countries. Table 2 illustrates incidence and mortality for paraquat poisoning in selected countries, including epidemics with a very high fatality rate in Asia and Latin America, including Malaysia, Fiji, Japan, Sri Lanka, Surinam, Mexico, Costa Rica, Trinidad y Tobago, and Samoa. Incidence and mortality rates vary enormously according to patterns of paraquat use, prevention and control programs, type of register, and reporting practices. Despite likely underreporting, in some developing countries rates were between 10 and 300 fold those reported in the USA, UK, Ireland or Finland. Recent figures available for Central America and the Pacific Islands are of similar magnitude as in many countries in the 1980s. Despite precautionary measures, the incidence of fatal paraquat poisonings, particularly suicides, increased in Costa Rica during 1992-1998 as compared to the period 1980-1986. Reports of severe unintentional poisonings and suicides have continued to appear also from many other countries.

The surveys in Table 2 refer mainly to suicidal poisonings, but many include also cases of unintentional paraquat poisoning. The annual incidence rate of severe hospitalized paraquat poisonings in Costa Rica is estimated at 44 per million inhabitants, and the incidence of fatal paraquat poisonings at 15 per million during 1980-1986. Seventy five percent were accidental and occupational poisonings. Forty-eight percent of the paraquat fatalities with an identified cause were unintentional, mostly after accidental ingestion but also after occupational exposure. Severe paraquat poisonings and fatalities in children have been reported, ranging from accidents with extremely low doses up to homicides.

Although by far the majority of paraquat poisonings occur by oral intake, a number of severe and fatal occupational and accidental poisoning reports after skin absorption are available. One report concerned an unintended death following vaginal absorption. It has been alleged that systemic effects do not occur at recommended dilution rates. However, in 1983 a fatal case was reported of a farmer having applied a paraquat solution diluted according label instructions (0.5% solution of paraquat) during 3.5 hours that resulted in skin exposure due to
a leaking knapsack. The farmer died within a week after application due to paraquat induced systemic intoxication. Wesseling et al (1997) described fifteen unintentional fatal paraquat poisonings, of which five were due to contact with diluted spray solution.

Irritation of skin and eyes

US EPA concluded that paraquat causes moderate to severe eye irritation (Toxicity Category II) and minimal dermal irritation (Category IV), based on toxicity experiments in rabbits. In fact, dermal lesions observed in workers range from mild irritation to blistering and ulceration (second and third degree chemical burns), often in the genital area. Eye injuries may range from blepharitis and conjunctivitis to ulcerations or keratosis of the cornea; and nail damage due to prolonged hand contact with paraquat ranges from localized discoloration to temporary nail loss.

Skin, nail, and eye lesions have been reported, including in children. Workers in formulating factories were at high risk. A survey among 18 paraquat formulation workers in the UK found that 14 (78%) had experienced nail damage, nosebleed, blepharitis, or skin lesions with delayed healing. In Malaysia, 15 out of 18 formulators presented topical lesions, such as dermatitis or chemical burns (50%), and eye injury or blepharitis (39%). Few data from epidemiological studies or surveillance systems are available on topical injuries among agricultural workers. In California between 1971 and 1985, 231 paraquat-related cases of illness were reported, 38% being systemic poisonings and 62% topical injuries, less than 10 topical cases per year. However, skin burns and eye lesions from paraquat exposure are common among herbicide sprayers in developing countries, where no accurate statistics are available. In a number of the previously mentioned exposure assessment studies paraquat-related topical injuries were mentioned. In Malaysia, in one study approximately 50% and in another study 44% (12/27) of paraquat sprayers experienced skin or eye injuries during fourteen and twelve week spraying programs, respectively. In Costa Rica, out of 11 paraquat sprayers on banana plantations three mentioned blistering of skin on hands, thighs, legs, back, and scrotum; two experienced eye irritation, three nail damage, three epistaxis, and one a burning sensation in the nose, during the preceding year.

In Costa Rica, a number of surveys on occupational injuries among wage-earning workers have been carried out by the Central American Institute for Studies on Toxic Substances between 1982 and 1996. A summary of the results is presented in Table 3. In absolute
numbers, hundreds of paraquat injuries occur each year in Costa Rica, most of them in the banana producing Atlantic Region. The majority (60%) of victims presented skin burns or dermatitis and 26% chemical eye injuries. The remaining 14% represented systemic poisonings, nosebleeds and nail damage. Incidence rates decreased over time, 1996 being the lowest (0.5 per 1000 banana workers during a one-month period). Most injuries concentrated on herbicide applicators, with a monthly rate of 26.7 and 13.3 per 1000 for 1993 and 1996, respectively.

**Long-term and delayed health effects**

EPA California acknowledges evidence of chronic effects from long-term exposures in lung, liver, kidneys and eyes in rats, dogs and mice. US EPA recognizes lung effects and dermal lesions. Paraquat does not appear to be mutagenic, but is weakly genotoxic. Developmental and reproductive effects occur at doses higher than the maternal toxicity dose. However, paraquat crosses the placenta. Fetal death in pregnant women poisoned by paraquat and neonatal death after induced delivery have been reported. Neurotoxicity has not been evaluated by regulatory agencies. Animal bioassays and clinical and pathological scrutiny of human poisonings revealed behavioral dysfunction and histologic changes in the brain. Paraquat has been linked with Parkinson's disease. A synergistic mechanism with ethylene bisdithiocarbamate fungicides has been proposed.

A number of studies failed to find lung damage in workers with prolonged exposure to paraquat in the United Kingdom, Malaysia, and Sri Lanka. However, in several studies diagnostic tools, such as review of clinical records and X-ray and clinical examinations, were insensitive, or the exposures were much lower than in other occupational settings in developing countries. Thus, a study in Nicaragua reported a dose-response gradient between intensity of exposure, as measured by history of skin lesions and the prevalence of respiratory symptoms. In South Africa, clinical and histological lung lesions were observed among exposed workers who had skin injuries. Arterial oxygen desaturation during exercise has been associated with long-term paraquat exposure. This test was not used in the earlier nonpositive studies. SYNGENTA is now funding a US$ 677,000 project to evaluate long-term lung effects among paraquat exposed workers in Costa Rica (http://obgyn.net.ads. Health & Medicine Week, May 14, 2001).
**Carcinogenicity**

The International Agency for Research on Cancer (IARC) has not evaluated paraquat for carcinogenicity. In the 1980s, US EPA concluded that there was some evidence for carcinogenic effects from paraquat based on a study in rats with excesses of adenomas and carcinomas in the lung, and squamous cell carcinomas in the forehead. Pathologists disagreed on how many of the proliferative lung lesions were neoplasias and, in the end, the lesions were considered secondary to chronic inflammation processes. Following a claim of industry that the tumors of the forehead appeared locations and could therefore not be considered as a single entity, the statistically significant excesses disappeared after stratification, and the results were reinterpreted as negative. EPA California concluded that the tumors were not the result of oral intake of the powdered feed containing paraquat, but several members of the review committee felt that the tumors could have been the result of topical contact with the feed. On various arguments, paraquat’s Class C (limited evidence in animals and lack of data in humans) was downgraded to Class E (evidence of non-carcinogenicity in humans) with no consideration of human evidence.

In Taiwan, squamous cell carcinoma of the skin has been associated with combined exposure to sunlight, paraquat, actinic keratosis, and solar lentigo among workers in 28 paraquat factories. In Costa Rica, a geographic study on geographical study found excesses of different skin cancers (lip, penile cancer, non-melanomous skin cancer and skin melanoma) in coffee growing regions, as well as an excess of skin melanoma in men in the banana producing Atlantic region, both crops with extensive paraquat use. A cohort study among Costa Rican banana workers also found an increased risk for skin melanoma.

**RISK ASSESSMENT AND REGULATORY RECOMMENDATIONS**

Decision-making processes in developing countries tend to be less transparent than in industrialized countries. In Latin American countries, national regulatory authorities habitually assign a compound into acute toxicity categories according to the WHO-IPCS recommendations for hazard classification. Other international bodies and agreements, such as FAO food tolerances and the Prior Informed Consent (PIC) of the FAO Code of Conduct are considered in registration. Latin American countries are strongly influenced also by US EPA, although as a rule only in broad terms, “to ban or not to ban”. Any pesticide
forbidden, never registered, or with a voluntary cancellation by the manufacturer may still have food tolerances. The main driving regulatory restrictions for developing countries today are the food tolerances related to the agricultural exports.

The EPA toxicity classifications and risk management decisions are of limited use in Latin America. First, the toxicity classifications by EPA as well as other major regulatory bodies are based on standard experimental testing protocols in strict laboratory conditions. Second, when assessing the risks, toxicity data are integrated with exposure data, collected under conditions of good agricultural practices that have little resemblance with the circumstances prevailing in developing countries. Available epidemiological evidence of human health effects from outside the USA has been considered only marginally at best. Third, EPA restrictions are adopted south of the US border only in cases of a total ban including food tolerances. This is not the case with paraquat. More subtle risk assessment details, including a robust RUP (Restricted Use Pesticide) status of paraquat in the US, are not incorporated into national legislations in the South. A considerable proportion of paraquat in Central America is imported from the US, without major warning about the restricted regulatory status.

Risk management of paraquat in the US and elsewhere relies largely on safety instructions on the label. Adversities that are consequence of not complying with label instructions are not considered the manufacturers responsibility. In developing countries, the application of paraquat in accordance with correct procedures as indicated on the label seem unrealistic, even in the presence of industry efforts to promote safe and effective use of paraquat by education and training.\textsuperscript{22,116} A label may indicate many good agricultural practices, but the possibility to follow these instructions in the field may be very low. In addition, the effectiveness of training programs performed by industry is not evaluated in proper terms of exposure, health effects, or risk reduction.\textsuperscript{117} The key issue is that in Central America, and in most other developing regions as well, insight in the risks from exposure in the local context and the know how are lacking. Risk assessment concepts or strategies as the precautionary principle are not applied when it comes to registering the use of a pesticide such as paraquat.

CONCLUSIONS AND FINAL REFLECTIONS

- Paraquat is one of the most used pesticides globally and in most countries without restrictions.
- Relatively few exposure and hardly any intervention studies have been performed.
• The understanding of exposure determinants such as climatic circumstances, types of crops, or application methods is limited. It is clear, nonetheless, that paraquat often is applied under hazardous conditions and that in developing countries application techniques have not considerably improved during the last thirty years. Transport systems are still open systems, application equipment easily fails resulting in high exposures.

• Possibilities to reduce exposure by wearing protective clothing seem limited. The effectiveness of control measures under tropical conditions remains largely unevaluated.

  ▪ Relatively few recent surveys on paraquat poisonings are available. It is uncertain whether this reflects a decline in severe poisoning or partially loss of interest in the problem.

  ▪ Suicides increased in Costa Rica in the 1990s compared to the 1980s. Recent reports on suicides come also from other developing countries.

  ▪ Despite incompleteness of data and consequent difficulties of interpretation and comparison, paraquat still represents a severe public health problem.

  ▪ Occupational and nonoccupational hazards may materialize at any time in a developing country.

  ▪ The responsibility for suicidal use of paraquat rests also on the manufacturer. Unrestricted access to a liquid, of which a very small amount may be fatal, makes a suicidal or parasuicidal decision easy.

  ▪ Regulatory agencies have not fully recognized either the inherent toxicity of paraquat for human beings or the particular risks derived from exposures in developing countries.

  ▪ Independent studies of occupational exposure assessment and health effects are needed.

  ▪ The impact of interventions, such as industry stewardship programs, should be properly evaluated.

  ▪ If the precautionary principle would be applied in developing countries for the regulation of pesticides, many of the prevailing problems would be prevented.

  ▪ The Central American Institute for Studies on Toxic Substances (IRET) will initiate an independent health risk assessment for paraquat in the Central American context.
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Figure 1: Tons of paraquat imported in Costa Rica: formulated and technical grade solution between 1981 and 1999; active ingredient between 1992 and 1999.