FINAL REPORT TO THE WORLD BANK ON PARAQUAT AND POSSIBLE ALTERNATIVES

by

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Summary

Paraquat

Paraquat has particular physical, chemical and biological properties that give advantage to its use as a herbicide. It, however, has relatively high mammalian toxicity which has many facets; not only is paraquat irritant and corrosive to skin, eye and mucous membrane, but it is also specifically toxicity to internal organs after absorption. Fortunately, it is poorly absorbed through skin and from the gastrointestinal tract.

Because the 20% concentrate formulation is corrosive and irritant, splashes or more extensive exposure to the skin and eye can cause severe skin and ocular damage, particularly if not promptly treated. Fortunately, these adverse effects seem to be uncommon and they have been infrequently reported in the literature.

Once the concentrate has been diluted to a normal working dilution, it is correspondingly less irritant and corrosive and, so, far less hazardous. Sufficient dilute solution to cause serious poisoning is unlikely to be swallowed accidentally, even after such ill-advised action as sucking from spray nozzles.

Dermal irritation, the most commonly reported adverse effect of occupational exposure, can occur from prolonged contact with spray solution or wet clothing. Fatal cases or severe dermal poisoning are relatively uncommon and seem to result most often from prolonged contact with clothing contaminated by poor application technique or faulty or improperly maintained equipment. Inadequate dilution of the concentrate or the presence of skin lesions can increase the dermal hazard.

Localised contact or irritative dermatitis, delayed wound healing and nail damage can occur from improper handling or application of the working dilution. Blepharitis and epistaxis, resulting from exposure to the working dilution, may be taken as an indication of poor application practice.

Such adverse effects demonstrate the need for good personal hygiene and proper working technique. These measures are manageable through education and training of the applicators and their supervision in the workplace, where practicable.

Inhalational exposure to paraquat in the workplace with recommended application equipment and rates is negligible since the spray particles from normal high volume application, being relatively large, deposit in the upper respiratory tract and do not reach the lower airways where pulmonary absorption might occur.

Low volume/high concentration application of paraquat is contraindicated because of the greater hazard of dermal exposure to concentrations above that recommended and the possibility of inhalation of fine droplets. Mist blowers also should not be used for applying paraquat for the latter reason.

The use of elaborate protective clothing and equipment is unnecessary in routine application of paraquat, provided proper application practice is followed. The high water solubility of paraquat makes effective dermal cleansing relatively easy by washing. An adequate supply of water for washing and first-aid should be available at all times.

Given its significant acute toxicity and widespread use around the world, it is not surprising that there have been numerous reports of accidental, suicidal or other poisoning by ingestion of paraquat. Accidental paraquat poisonings have most often been due to its ingestion from containers into which it has improperly been decanted.

The acute lethal human dose of paraquat by ingestion is about 3-5 g. The prognosis in paraquat poisoning depends on the amount ingested and the speed with which emergency treatment is initiated. Complete recovery has been achieved in less severe poisoning cases without pulmonary damage.

Worldwide experience is that most paraquat poisonings arise from deliberate ingestion of the 20% concentrate, although dilute solutions also are sometimes taken. The unusual feature of paraquat suicide is its disproportionate occurrence in some countries but not in others. The factors determining choice of a suicidal agent are complex and often unknown. The incidence of paraquat poisoning peaked in the UK in the early 1980s and has declined thereafter. It seems to have peaked somewhat later in Fiji, Malaysia, Japan and Western Samoa. There is a paucity of poisoning incidence data from other countries so that the present magnitude of the problem cannot be assessed on a global basis.

The incorporation of a distinctive colour and stench to the liquid paraquat concentration was intended to provide warning against accidental ingestion.The emetic is now considered to assist only in marginal cases. These measures have reduced the incidence of accidental poisonings and may have contributed to the above mentioned decline in suicide in some countries at least. However, they do not seem to deter those truly determined on suicide.

There have been calls for restriction of the availability of paraquat in countries where paraquat suicide is a problem. Experience in several countries suggest that this measure, by itself, is unlikely to prevent of self-poisoning whilst other highly hazardous poisons remain freely available. Nonetheless, measures to restrict the availability of paraquat remain appropriate where paraquat suicide is a problem and/or satisfactory alternatives are available. Wherever possible, there should be controls on the sale and supply of paraquat concentrate so that it is only available to *bona fide* users.

Development of public policy on the availability of particular pesticides such as paraquat should be based upon knowledge of its risks and benefits. There is a paucity of data on pesticide poisonings in many developing countries. If hazardous pesticides are to be provided or otherwise made available in developing countries, there is a need to gather and collate information on their economic benefit and their costs to man and the environment.

The established use of paraquat as an agent for suicide and its capacity for occupational poisoning indicate that collection and analysis of paraquat poisoning data should be undertaken. Public sector agencies should recognise and assume this responsibility in projects with which they are associated. International agencies such as the International Programme on Chemical Safety should be able to assist in this task.

Public sector agencies should also ensure that for pesticides they procure there is adequate labelling, including appropriate warning statements and directions for safe use and that packaging, protective equipment, and first-aid measures are as required at registration. Application equipment should be appropriate and properly maintained.

The availability of paraquat concentrate, in particular, should be restricted, where possible, to *bona fide* users.

There is a clear need for education and training of all persons with access to paraquat in its safe handling, use and disposal as well as the need to avoid decanting. The concentrate should only be made available in containers of sizes appropriate for the intended use so that excessive amounts are not stored in or around the household.

There is also a further need for community education of the hazards of paraquat mishandling and misuse. Care should be taken that this is done in a way that does not encourage the notoriety of paraquat as an agent for suicide. Genuine concern exists that increasing awareness of paraquat's toxicity could promote imitation of its use for self-poisoning. However, it must be recognised that self-poisoning by paraquat is already a reality in some communities. Increased knowledge of the toxicity of pesticides such as paraquat may discourage those wishing to use it for suicidal gestures and encourage those handling, storing and using it to exercise due care.

The management of paraquat poisoning should be regarded as a medical emergency. Wherever possible, a responsible person should be trained in the administration of Fuller's earth as a first-aid measure. Local medical personnel should be aware of the gravity of paraquat ingestion and its contemporary medical management.

From a public health viewpoint, the use of alternative herbicides to paraquat should be considered wherever paraquat poisoning is likely to become or is an established problem. Wherever paraquat attains notoriety as an agent for suicide, its replacement by a less hazardous alternative should become a public health priority. Whilst such substitution may not always be optimal in terms of agricultural or economic efficiency, it may provide real benefits in terms of a reduced number of human poisonings.

These competing interests are evident in the present situation where misuse of paraquat has given rise to the need to restrict its availability and use. Public health considerations should always take precedence.

Experience has shown, however, that replacement of one pesticide with another is usually not a straightforward matter. Questions of availability, efficacy, costs , acceptability etc almost always arise. The environmental aspects of paraquat's use as a herbicide are generally favourable. Its rapid penetration into plant matter makes it "rain-fast", a feature which is of particular value in tropical agriculture where sudden precipitation commonly occurs. Once in the soil, it is highly bound and not biologically available. It does not transmigrate. Thereafter, it does not significantly affect soil microfauna and is slowly degraded microbially.

Diquat

The other bipyridinium herbicide, diquat, shares many of the physico-chemical and biological properties of paraquat and could be a useful alternative for some applications, although it is generally considered an inferior herbicide to paraquat in tropical agriculture.

From an occupational health viewpoint, diquat is less hazardous than paraquat. Few occupational poisonings due to diquat are reported in the literature. Skin irritation, delayed wound healing, epistaxis and nail damage due to diquat have been reported but not occupational dermatitis or acute eye injury. As for paraquat, inhalational exposure to diquat is insignificant in comparison to dermal exposure.

Only a few cases of diquat poisoning following oral ingestion have been reported. Most were due to self-poisoning with the 20% concentrate. Diquat poisoning causes severe diarrhoea due to gastrointestinal irritation. Serious renal toxicity can develop but not the pulmonary toxicity that characterises paraquat poisoning. The acute lethal human dose for diquat has been estimated to be 6-12 g. Fortunately, diquat has not gained the notoriety of paraquat as a poison for suicide.

The prognosis for ingestion of 20% diquat concentrate depends on the amount ingested, prompt initiation of therapy but also the degree of resultant renal damage incurred. Survivors of diquat poisoning seem to exhibit no long-term sequelae.

Diquat concentrate is also sufficiently hazardous to warrant restriction of its availability to *bona fide* users only. The practice of decanting it into other containers should also be actively discouraged.

Diquat shares the generally favourable environmental attributes of paraquat as an agricultural herbicide. It is subject to photochemical degradation in water and on surfaces but should be a suitable alternative for paraquat in some situations. Like paraquat it binds to soil and is not bio-available thereafter.

From a public- and occupational- health viewpoint, diquat is to be preferred over paraquat. It may be a suitable alternative in some situations. Like paraquat, it should only be available for use by *bona fide* agriculturalists, horticulturalists and professional users.

Glyphosate

Glyphosate, is already well established as the major alternative non-selective herbicide to paraquat in many situations. Its uses are expanding due to formulation improvements giving greater efficacy and increasing cost competitiveness.

The acute toxicity of glyphosate itself is low. Its formulation, containing a polyethoxylated alkylamine (POEA) surfactant, is an eye irritant and is also more acutely toxic than glyphosate *per se*. Several hundred deaths attributed to the glyphosate-surfactant formulation poisoning have been reported, mostly from Japan and the Republic of China.

Fortunately, glyphosate has not earned the notoriety of paraquat as an agent for suicide, elsewhere. The approximately 10-fold lower acute human toxicity of the glyphosate concentrate makes accidental poisonings usually less serious than for corresponding ingestion of paraquat concentrate.

Like diquat and paraquat, glyphosate binds tightly to soil and does not transmigrate. It is degraded microbially thereafter. Contamination of watercourses following direct application of glyphosate has been reported but its fate in water is relatively short-lived as it binds to sediments.

Glyphosate is already clearly established as an alternative to paraquat in many situations.

Glufosinate-ammonium

Relatively less information is available on the human toxicology of glufosinate-ammonium, possibly because it has been marketed for a lesser period than the bipyridinium herbicides and glyphosate.

Glufosinate-ammonium apparently has low acute and chronic toxicity. It is unlikely to present a significant occupational hazard with proper application technique but accidental or suicidal ingestion always remains a potential problem as with any herbicide. The available information on glufosinate-ammonium suicides in Japan suggest that a dose of several hundred millilitres of the 20% concentrate is required for complete suicide.

Glufosinate-ammonium is mobile in soil but is readily and extensively metabolised by soil micro-organisms. Its environmental toxicology is favourable and is unlikely to be a problem in use. Glufosinate-ammonium may well prove to be an acceptable alternative to paraquat, particularly from a public health viewpoint.

Conclusion

The above considerations indicate that each of the non-selective herbicides considered here has particular advantages. The is unlikely to be a truly ideal non-selective herbicide suited for all uses. The choice of a herbicide should not, however, be determined by purely agronomic considerations. In situations where human poisonings are a problem, the human cost should be taken into account and priority should be afforded to introducing a less hazardous substitute. Selection of alternatives should be undertaken with collaboration between health and agricultural authorities.

Introduction

The World Bank has initiated a consultancy to examine the use of the herbicide, paraquat, in projects which it may sponsor. In accordance with the Terms of Reference, this report examines the problems associated with the use of paraquat and some possible alternative herbicides and develops some proposals for their future use in publicly sponsored projects.

Objectives of the Consultancy

The terms of this consultancy requires consideration of the following objectives:

1. Assemble available information on the impact of paraquat concentrate and working dilutions on the health of users;

2. Evaluate the effectiveness of existing programmes aimed at reducing the risks and negative health impacts of paraquat and make recommendations which would improve conditions of use and reduce associated health hazards in the future;

3. Undertake a comparative evaluation (opposite paraquat) of positive or negative environmental and health impacts of accepted alternative chemical herbicides; and

4. Recommend future research or other action that the public and private sector agencies involved in the development, registration, manufacturing and distribution of paraquat-based products should undertake to increase dissemination of safety information and provide demonstrable results in safety.

Procedure

To minimise costs and to complete the study within the recommended timeframe, the use of existing data on the impact of paraquat on health would be maximised. Data would be drawn from all possible sources, such as manufacturers of paraquat, national health agencies, environmental/public interest groups and environmental agencies.

A desk review of the available toxicological data, information on user behaviour and exposure levels and environmental aspects of paraquat was undertaken as the first stage of this study. Information reviewed included that obtained from the published literature, that submitted by a principal sponsor of paraquat and other information gathered by the consultant.

The second stage of the study involved visits to Malaysia, the U.K. and U.S.A. to interact with knowledgeable people on the subject and to cross-check information gathered from published literature.

The third stage of the study involved finalisation of the report based on the completed review of literature and findings of the field visit.

Terminology

For consistency, the following terminology is used in this review.

Concentrates of a pesticide is the commercial formulations sold and distributed for agricultural use.

Working dilutions of a pesticide is the diluted solution prepared from the concentrate in accordance with recommended rates of dilution.

Toxicity is defined in its widest sense i.e. to include all adverse effects of a herbicide, including its irritant or corrosive properties,which may not be strictly related to its mechanism of systemic toxicity.

Objective 1

Assemble available information on the impact of paraquat concentrate and working dilutions on the health of users

General Considerations

. Formulation and Use of Paraquat

Paraquat is the 1,1'-dimethyl salt of 4,4'-bipyridine. Only the dication, known as the 1,1'-dimethyl-4,4'-bipyridinium ion, is herbicidally active due to its ability to be reduced to a free radical cation which reacts with oxygen to reform the paraquat ion and concomitantly produce superoxide ion.

Paraquat is highly soluble in water, slightly soluble in alcohols and virtually insoluble in less polar solvents. It is not volatile and is highly corrosive (IPCS, 1991a).

It was first introduced as a broad spectrum, contact herbicide in 1962.This herbicide is now used in over 100 countries. Several aqueous paraquat formulations are available. The most common is a concentrate containing 200 g/L paraquat dichloride ion (20% w/v, "Grammoxone"). A granular formulation, containing paraquat and diquat, each 2.5% w/w, is available for home garden use in the U.K. Other formulations, including admixtures with other herbicides, are also available (Hart, 1987).

Paraquat concentrate usually contain various wetting agents (condensation products of ethylene oxide and an alkyl phenol), spreaders, humectants to promote moisture retention (calcium chloride, glycerol, polyethylene glycol), plant adhesion materials (carboxymethylcellulose, polymethacrylates) and antifoaming agents (Summers, 1980). A stench and/or a dye or an emetic may be added to paraquat concentrate as an alert against ingestion.

The use and utility of the bipyridinium herbicides, paraquat and diquat in agriculture has been comprehensively reviewed (Calderbank, 1968; Summers, 1980).

Paraquat has particular advantage as a non-selective contact herbicide with its rapid speed of action, rainfastness and non-residual activity. It kills green plant tissues but does not affect mature bark enabling its use around trees in orchards and between crop rows to control broad-leaved and grassy weeds. Paraquat is also used in plantation crops (banana, cocoa, palm, coffee, oil-palm, rubber trees etc). On certain other crops (potato, pineapple, sugar-cane, sunflower), it is used as a desiccant. Paraquat is also used for defoliation of cotton (IPCS, 1991a).

Working dilutions of paraquat are prepared by dilution of paraquat concentrates with water to give a working dilution of 1-5 g/L (0.1-0.5% w/v) to be applied by ground sprayer at 200-500 L/ha. Higher volumes may be required for clearance of mature weeds. The spray may be applied downwards onto the foliage by hand-held knapsack-type or other spraying apparatus, by vehicle-mounted sprayers or by aircraft (IPCS, 1984).

. Toxicology of Paraquat

The animal and human toxicology and the environmental fate of paraquat has been extensively reviewed and summarised (Smith and Heath, 1976; Summers, 1980; Onyeama and Oehme, 1984; IPCS, 1984; FAO/WHO, 1987a; Hayes and Laws, 1991).

- Toxicity in Experimental Animals

Studies in experimental animals show that paraquat is poorly adsorbed after oral administration but thence distributed into most tissues with the highest concentrations occurring in kidneys and lungs. Paraquat accumulates slowly in lung tissue due to energy dependent transport mechanisms. Excretion of absorbed paraquat is biphasic due to this pulmonary accumulation and is mainly via the urine and to a lesser extent by bile. There is little biotransformation via N-demethylation or oxidation.

The acute oral toxicity of paraquat is higher in guinea pigs, monkeys, cattle (and man) than in rats and birds. Paraquat introduces characteristic dose-related fibrotic changes in the lungs of mice, rats, dogs and monkeys (and man) but not in rabbits, guinea pigs or hamsters. The acute pulmonary toxicity of paraquat in rats and man is biphasic. In the early destructive phase, the alveolar epithelial cells are extensively damaged. Death may occur in a few days due to pulmonary oedema. In the later proliferative phase, fibroblasts and collagen accumulate in the lungs of surviving mammals (and man), possibly resulting in fibrosis. Death from respiratory failure ensues.

Paraquat was not teratogenic in mice and rats at doses up to 10 mg/kg bw/day. It has been found to delay foetal ossification at higher doses in rats. Paraquat had no effect upon the reproductive performance or development of the reproductive organs of rats. A reduction in the lactation index occurred at a dietary level of 290 ppm dietary paraquat cation in one study. These findings have no direct relevance for man.

Paraquat was not mutagenic, both in the presence and absence of metabolic activation, when tested in the Ames test, mouse micronucleus test, unscheduled DNA synthesis rec-assay and host-mediated assay. Results of a mouse lymphoma cell test were inconclusive. It was clastogenic to human lymphocytes *in vitro* at cytotoxic doses and it induced sister chromatid exchange in Chinese hamster lung fibroblasts.

A lifetime feeding study of paraquat in mice showed no oncogenic potential, although a slightly higher incidence of lung tumours was noted in animals of the high-dose test group dying between 79 and 98 weeks when compared to control mice.

Administration of paraquat in the diet of F-344 rats caused a significantly increased incidence of pulmonary adenomas in the females. These findings indicated a weak, organ-specific, sex-related potential of paraquat to produce benign proliferative changes in the lungs of female F-334 rats. Paraquat also caused cataracts in both male and female rats at higher doses.

The Acceptable Daily Intake for Man, estimated from studies in experimental animals, is 0.004 mg paraquat/kg bw (FAO/WHO, 1987a).

The US Environmental Protection Agency concluded that there was, at best, equivocal evidence of carcinogenicity in male Fischer rats at 7.5 mg/kg/day and that this was associated with irritation due to topical exposure and not with oral exposure (Anon., 1990).

Paraquat degrades to the 4-carboxyl-1-methylpridinium salt. The degradation product has very low toxicity, the acute oral toxicity in rats (LD50) being more than 5000 mg/kg bw (IPCS, 1984). The methosulphate salt is slightly more acutely toxic to rats, the acute oral LD50 being 2,000-4,000 mg/kg bw (McElligott, 1966).

In a 90 day feeding study in rats fed at nominal dietary levels of 5,000, 20,000 and 40,000 ppm, adverse effects were seen only at the high dose (Broadhurst *et al*, 1966).

Dogs, fed 4-carboxy-1-methylpyridinium methosulphate in the diet at 125 or 500 mg/kg bw for 90 days, showed no adverse effects on biochemical or urinary parameters or at histopathology on necropsy (Broadhurst *et al*, 1966). 4-Carboxyl-1-methylpyridinium (as the methosulphate salt) was without mutagenic activity in *Salmonella typhimurium* (strains TA 1535, TA 1537, TA 1538, TA 98 and TA 100) and in *Escherichia coli* (WP2 uvrA pkm 101) with or without S9 microsomes (Callender, 1986).

Dermal Toxicity
Paraquat provokes local irritation to skin and eye of rats and mice which is accentuated by occlusion. This can progress to dermatitis which is characterised by erythema, oedema, desquamation and skin necrosis. Delayed irritancy in rabbits has been reported but paraquat did not cause skin sensitisation in guinea-pigs (IPCS, 1984).

Ocular Toxicity
Instillation of paraquat into the rabbit's eye at high concentration (500 g/L) caused severe eye irritation resulting in corneal opacification, iritis and conjunctivitis. Severe conjunctivitis, iritis and pannus also developed at lower concentrations (IPCS, 1984).

Inhalational Toxicity

Studies in experimental animals have shown that direct instillation of low doses of radiolabelled paraquat into the lung can lead to its rapid uptake and distribution.

Direct installation of 10 µg of ^{3}H-paraquat in saline (0.1 ml) into the left main bronchus of rats led to its rapid systemic distribution. After 15 minutes, 90% of the administered dose was detected in the urine and in tissues, with 50% in the lung. Doses of 10 µg or above produced pathological pulmonary changes like those seen in systemic poisoning (Wyatt *et al*, 1981). Rabbits were even more sensitive (IPCS, 1984).

A 3-week inhalational study of rats exposed to 0.1 µg/paraquat ion/L reportedly showed histopathological changes in the larynx. However, at 0.01 µg/paraquat ion/L there were no pathological changes in the larynx in either the 3 week inhalation study or on exposure for 15, six hour periods. The pharynx was reportedly unaffected in all studies (Grimshaw *et al*, 1979).

Mechanism of Systemic Toxicity

The biochemical effects of paraquat have been reviewed in detail (Autor, 1977; FAO/WHO, 1987a).

Survival of acute paraquat toxicity in animals can lead to the same progressive pulmonary fibrosis that can develop in man. The mechanism of paraquat pulmonary toxicity in animals involves absorption from the gastrointestinal tract into the blood, transport to the lung and accumulation into specific alveolar epithelial cells. Accumulated pulmonary paraquat undergoes redox cycling, consuming the reducing equivalents of the cell and generating superoxide anion. Cell death occurs from either loss of NADPH or lipid peroxidation resulting from the generation of reactive oxygen radicals, or a combination of both processes. Acute alveolitis occurs and if severe, pulmonary fibrosis develops which obliterates the normal alveolar architecture, preventing gaseous exchange and causing death from anoxia (Smith, 1987; Smith, 1990).

Human Toxicity

Dermal Toxicity

The rate of percutaneous absorption of paraquat in man has been quantified experimentally, using radiolabelled paraquat, at 0.03 µg/cm^2 for 24 hour exposure. No differences were discernible in the absorption rate over 24 h at different sites of application, i.e. normal human hand, leg and forearm (Wester *et al*, 1984). Only 0.3% of an applied dose of paraquat (0.64 mg) was absorbed over 5 days from the ventral forearm of volunteers (Wester and Maibach, 1985).

Paraquat is more rapidly absorbed through animal skin than human skin to a degree ranging from 40-1000 fold (Walker *et al*, 1983).

In man, prolonged dermal exposure to liquid paraquat concentrate can produce varying degree of skin erythema, irritation and, in severe cases, blistering, desquamation and skin necrosis. A near fatal case of poisoning following accidental contamination of the skin of a child by paraquat concentrate has been reported. The affected area was not washed until the next day. Necrosis of the skin occurred at the site of exposure (Okoneck *et al*, 1983). Fortunately, reports of such severe effects are uncommon.

Contact dermatitis due to exposure to paraquat has been reported occasionally. According to FAO/WHO (1987),

'Horiuchi and Ando (1980) carried out patch testing on 60 patients with contact dermatitis due to" Grammoxone". In 8 patients (13.3%), positive allergic reactions were established. In another survey with 52 persons, a positive photo-patch test was reported in 11 patients.'

Similarly, repeated dermal exposure to paraquat concentrates can produce characteristic discolouration or transverse banding of the nail plate, due to adverse effects on the developing nail (IPCS, 1984). This can even progress to gross deformity of the fingernail and even loss of the nail with prolonged exposure (Botella *et al*, 1985). These local effects, which are not commonly reported and seem to result from prolonged or undue exposure, resolve after cessation of exposure.

In Israel, the absorption of paraquat following 15 cases of single exposure to paraquat solutions accidentally splashed onto the skin or eyes of agricultural workers was investigated quantitatively. The concentration of most these solutions ranged from 0.75% to 20% w/v but was unknown in three cases. Dermal reactions ranged from none to vesicles (skin blisters) and in the worst cases second and third degree burns. There was one case of contact dermatitis. Paraquat was detectable at very low levels in plasma (0.025-0.05 µg/ml) in only 3 of the cases and in urine (0.07-0.25 µg/ml) in 5 cases.

Single exposure of healthy skin to paraquat solutions was found to cause local lesions only and did not lead to systemic poisoning. Paraquat was more likely to be detected in biological fluids when vesicles were present. Significantly, simple erythema on a small body area caused by exposure to paraquat solution was considered unlikely to be of clinical significance (Hoffer and Taitelman, 1989).

Ocular Toxicity

Paraquat liquid concentrate can seriously affect the eye because of its corrosive and irritant properties. After exposure, inflammation of the eye can develop gradually, reaching a maximum after 12-24 h. Pathological changes may be limited to local irritation of the eye and of the eyelid but may progress to destruction of the bulbar and tarsal conjunctiva and of the corneal epithelia. Anterior uveitis can also occur. Visual loss can develop if the severity of the condition is unrecognised and/or is improperly treated (IPCS, 1984; Vale *et al*, 1987).

Fortunately, serious eye damage from ocular contact with paraquat concentrate is uncommon, judging from the limited number of reports in the literature. Two cases of temporary ocular injury due to "Preeglox-L", a diquat/paraquat mixture, have recently been reported from Japan. In each, corneal epithelial damage occurred, despite immediate flushing of the eye with water (Nirei *et al*, 1993).

Inhalational Toxicity
There have been no convincing reports of paraquat inhalation leading to pulmonary toxicity in man (Vale *et al*, 1987). Inhalation of paraquat spray mists can cause local irritation of the nasal mucosa and of the nasopharynx. This can lead to varying degrees of nasal blood loss, ranging from serosanguinous nasal discharge to frank epistaxis ("nose bleed"). Inhalational exposure to paraquat liquid concentrates has not been reported or identified as a significant hazard.

Systemic Toxicity
The systemic toxicity of paraquat has been will described (IPCS, 1984). The toxicological processes of paraquat in man is believed to be similar to that in animals. Lipid peroxidation also occurs in paraquat poisoning (Situnayake *et al*, 1987; Yasaka *et al*, 1981). Its role in the pathogenesis of paraquat toxicity is unclear, since it may occur as a cause or a consequence of cellular damage.

The clinical manifestations of systemic paraquat toxicity in man are well established (IPCS, 1984; Hayes and Laws, 1991; Parkinson, 1980).

Ingestion of paraquat concentrate is the most significant route of exposure leading to poisoning. In extreme situations, dermal exposure can also lead to systemic toxicity. In a typical study of 28 exposures to paraquat between 1972 and 1981, 24/28 patients ingested paraquat. Of these, 17 died. Four who had inhaled paraquat aerosols and/or suffered skin contamination survived (Bismuth *et al*, 1982).

. Paraquat Poisoning

- Dose response of Paraquat Poisoning in Man

Clinically, 3 degrees of paraquat poisoning following its ingestion have been recognised (Vale *et al*, 1987):

- mild poisoning follows the ingestion of less than 20 mg of paraquat/kg bodyweight. Symptoms are localised to the gastrointestinal tract and patients usually recover fully;
- moderate to severe poisoning follows the ingestion of 20-40 mg paraquat ion/kg body weight. Non-specific symptoms may occur together with gastrointestinal irritation prior to the development of renal failure, which may be transient, and fatal pulmonary fibrosis, which may not manifest for days or weeks; and
- acute fulminant poisoning follows the ingestion of large amounts of paraquat more than 40 mg/kg paraquat cation. In addition to local symptoms, multiple system failure occurs, involving cardiac, respiratory, adrenal, renal, pancreatic and neurological systems. Death occurs within hours or days.

Paraquat ingestion causes nausea and vomiting due to its local irritancy of the gut. Its corrosivity causes patients who are moderately or severely poisoned to develop a burning sensation ,soreness and pain in the mouth, throat, chest and abdomen. Ulceration of the mouth, sloughing of the oropharyngeal mucosa, inability to swallow, and aphonia commonly occurs. Prominent pharyngeal membranes and even oesophageal rupture can occur.

Within 24 h of ingestion, the more severely poisoned develop lethargy, a widespread burning sensation, generalised weakness and myalgia, giddiness, headache, anorexia and fever. Renal failure, with or without oliguria, may develop due to acute renal tubular necrosis. Proteinuria, microscopic haematuria, glycosuria, aminoaciduria, phosphaturia, and excessive excretion of sodium and urate can develop. Severely poisoned patients often develop signs of hepatic toxicity, with jaundice and hepatomegaly. Central abdominal pain may occur due to pancreatitis.

Most poisoned patients develop a cough which may be productive and bloodstained. Dyspnoea develops early in severe poisoning due to the onset of the adult respiratory distress syndrome. It is delayed in the less severely poisoned cases where it is due to pulmonary fibrosis. Cardiovascular complications due to toxic myocarditis tend to develop later and are manifested as arrythmias and cardiomegaly. Coma is a common terminal event, although convulsions may occur (Vale *et al*, 1987).

Survivors of systemic paraquat poisoning with pulmonary involvement may develop varying degrees of lung damage, ranging from transient pleural effusions and resolving pulmonary infiltration to persistent radiological changes (Hudson *et al*, 1991).

Of 13 people who survived at least one year after acute poisoning, 2 children and 5 non-smoking adults had some pulmonary dysfunction and one had persistent pulmonary infiltration (Fitzgerald *et al*, 1979). Complete recovery after severe poisoning and radiological resolution has also been reported (Laithwaite, 1976).

- Lethal Dose

The minimum lethal amount of paraquat ingestion for man is stated to be 35 mg/kg (IPCS, 1984) but other estimates of the fatal human dose of paraquat vary from 1-6 g, corresponding to 5-30 ml of the 20% concentrate. Some survivors have ingested larger doses (Hays and Laws, 1991; Howard, 1979; Smith 1988; Sax and Lewis, 1989). The different circumstances of the poisoning incident and the difficulty of estimating the amount actually ingested make accurate estimation difficult. The acute lethal human dose is generally accepted as 3-6 g.

- Toxicokinetics of Paraquat in Man

As in experimental animals, such as the rat and dog, only about 5-10% of swallowed paraquat is absorbed in man. Most is excreted via faeces. The presence of food in the stomach delays absorption. Studies in poisoned patients show that plasma paraquat concentration has a mean distribution half-life of 84 h. The principal route of elimination of absorbed paraquat is via the kidney and follows a biphasic pattern. Tissue paraquat distribution is ubiquitous with an apparent volume of distribution of 1.2-1.6 L/kg. Several organs, including muscle and lung, provide a reservoir for paraquat which slowly redistributes into the blood.

This also accounts for the prolonged urinary excretion of paraquat for several days to weeks after ingestion (Houzé *et al*, 1990; Pond, 1990).

- **Management of Acute Paraquat Poisoning**

The clinical management of paraquat poisoning has been well reviewed (Davies, 1987; Vale *et al*, 1987; Bismuth, 1990; Pond, 1990). As for most poisons, there is no specific antidote. The prognosis depends not only on the degree of exposure or dose but also route of entry, intention, type of formulation and the speed and vigour with which treatment is undertaken.

All cases of paraquat poisoning require prompt medical attention. Treatment of paraquat ingestion will be effective only if begun early, preferably in the first two hours whilst the paraquat is still being absorbed. According to the clinical situation, the gastrointestinal tract can be decontaminated by gastric lavage and absorbents, administered orally, (Fuller's Earth, Bentonite, charcoal or even soil or clay) to bind unabsorbed paraquat. Purgation with mannitol should then follow. The effectiveness of this therapy depends largely upon the amount of ingested paraquat and the time elapsed prior to its initiation. Monitoring of plasma concentrations and urinary excretion can indicate the prognosis.

Eye contamination warrants particularly prompt first-aid and appropriate medical attention.

- **Incidence of Paraquat Poisoning**

The incidence of paraquat poisoning differs between countries. However, the magnitude of the problem is difficult, if not impossible, to determine because of different requirements for notification and recording of cases of poisoning in many countries (IPCS, 1984).

Paraquat poisoning is a far greater problem in some countries than in others.There are wide variations in the number of fatalities per million population e.g. 0.004/million in the U.S.A. and 47/million in Fiji. The disparity in mortality rate, ranging from 0.6% (U.S.A.) to 58% (Fiji), suggests differing proportions of accidents and suicides (Onyon and Volans, 1987).

Accidental Paraquat Poisoning

Early cases of paraquat poisoning were mostly accidental. Victims often accidentally consumed liquid concentrate decanted into smaller unmarked or incorrectly labelled containers, such as beer, wine or soft drink bottles. The first reported cases of accidental paraquat poisoning occurred in 1964 in Ireland and New Zealand. By 1970, some 600 fatalities had been reported (IPCS, 1984).

. Case Reports of Accidental Poisoning

Case reports describing poisoning by paraquat have been reported worldwide and summarised (WHO,1984; Hayes and Laws, 1991). Accidental poisoning most often follows ingestion of paraquat when mistaken for a beverage. Decanting of the concentrate into a food or beverage container, little or no labelling and improper storage, all contributed to such accidents. Accidental poisoning from dermal exposure is reported less commonly. The following examples illustrate the types of situations, including accidents or misuse, where paraquat poisoning has occurred by accident or misuse.

- Liquid Concentrate

Fatal poisoning followed use of paraquat liquid concentrate as a pediculocide. A 22 year old African man presented with sepsis of his scrotum which healed only slowly with treatment. He subsequently revealed he had intentionally applied paraquat concentrate to his underwear to control pubic lice. At autopsy, his lungs showed the fibrosis and epithelial proliferation characteristic of paraquat poisoning. Paraquat was not detected in his urine.

Similar cases have been reported elsewhere. A villager in Papua New Guinea applied paraquat concentrate to his beard and scalp to rid himself of lice. He presented three days later complaining of painful "sores" in his hair and beard. He developed shortness of breath, cyanosis and jaundice. He died six days after he had applied the paraquat. Post-mortem examination confirmed multiple organ toxicity consistent with paraquat poisoning. The mode of exposure probably included a combination of ingestion, inhalation and absorption through the skin. Although the container of the paraquat concentrate was clearly labelled as a poison and carried detailed instructions for its safe handling and use in English, these were meaningless to a native of Papua New Guinea (Binns, 1976). A similar case was reported subsequently (Wohlfahrt, 1982).

A fatal case of paraquat poisoning from prolonged dermal exposure to paraquat concentrate arising from breakage of a bottle carried in a farmer's trouser pocket has also been described (Waight and Weather, 1979).

These cases illustrate the hazard of dermally applied paraquat concentrate, the consequences of ignorance of its hazards and the need for education about the hazards of pesticides and the dangers of their misuse, particularly in developing countries (Onogom *et al*, 1974).

- Granular Formulation

A series of 14 cases of poisoning by ingestion of granular formulations containing paraquat 2.5% w/w and 2.5% diquat w/w have been described. The resulting illness was milder than with paraquat liquid concentrate, although some fatal poisonings resulted. The painful necrotic lesions of the mouth and pharynx, usually found after ingestion of paraquat liquid concentrate, were not seen. Little renal impairment occurred. Significantly, "paraquat lung" did not occur, although three of the fourteen patients had transient pulmonary changes on X-ray.

The milder degree of poisoning with granular paraquat formulation may result from the absence of the corrosive effects which occur with the liquid concentrate, the presence in the granules of the purgative, magnesium sulphate, and the volume of fluid ingested at the time of poisoning (Fitzgerald and Barnville, 1978). In another study, the mortality rate in those who ingested solution prepared from the granules was only 4%, compared to 65% from ingestion of the liquid concentrate (Proudfoot *et al*, 1987).

Suicidal Paraquat Poisoning

During the 1970s, the clinical and pathological features of paraquat poisoning changed. Paraquat poisoning resulted increasingly from suicidal, rather than accidental ingestion. Patients died more often of multiple organ toxicity within five days of concentrate ingestion, because larger amounts were ingested intentionally in suicide than for accidental poisoning (Carson and Carson, 1976; Fitzgerald *et al*, 1978; Vale *et al*, 1987). Typical suicidal ingestion of paraquat concentrate has a higher fatality rate than that resulting from accidental poisoning due to the larger amounts ingested.

The following information provides insight into factors associated with paraquat suicide in several countries.

. Paraquat Suicide in Several Countries

- Australia

The average annual suicide incidence from all causes in Australia is relatively stable at about 13 per 100,000. There are about 20 deaths each year from ingestion of therapeutic agents and/or pesticides, arising in a population of 17.5 million(Australian Bureau of Statistics, 1993).

Paraquat is classified as a dangerous poison and is restricted to agricultural and horticultural uses, although the granular formulation was available for home garden use until 1985. In the period 1971-1993, there were a total of 60 poisoning incidents associated with paraquat of which 29 were fatal. Sixty percent of the poisonings (36 cases) were classified as suicide or attempted suicide, leading to 20 deaths (16 males, 4 females). The 7 accidental deaths all occurred in males (Drew, 1993).

- Costa Rica

A retrospective survey of Costa Rican poisoning statistics between 1980 and 1986 found that some 3,330 persons had been hospitalised for pesticide poisoning and that there were 429 deaths. Anti-cholinesterases were reported to cause 71% of the occupational accidents, 63% of the hospitalisations and 36% of the deaths. Paraquat was reported to have caused 21% of the occupational accidents, 24% of the hospitalisations and some 60% of the deaths. Hospitalisations and deaths were

13 and 11 times, respectively, more frequent amongst agricultural workers than the general population. Of the occupational poisonings, 90% occurred amongst agricultural workers, 87% during the application of pesticides and 13% during the mixing, carrying or cleaning of equipment or during work in or near areas being treated or sprayed or after re-entry into recently sprayed crops. Most (91%; 1175/1294) of the occupational poisonings occurred in farm labourers and the independent farmers, often spraying with poorly maintained equipment or spraying in inappropriate conditions such as wind, rain or high temperature.

Many of the non-occupational accidents were considered to be the consequences of inadequate control of pesticides. Improper storage leading to confusion with food, beverages, liquor or medicines occurred in 40% (224/565) of the identified accidental cases. Suicide comprised 62% (123/198) of the deaths in which the cause of poisoning was defined (Wesseling *et al*, 1993).

- **Fiji**

Paraquat was introduced into Fiji in 1964 and was registered under the Pesticides Act in 1970 (Groundar, 1984).

In Fiji, the high incidence of suicide has long been a public health problem, particularly amongst persons of Indian origin who comprise about half of the population. There were 90 certified suicides for 1971-1972. All female deaths were due to hanging. In the males, 91.6% hanged themselves and 8.4% died from other causes. 91% the suicides were in persons of Indian origin, 7% in Fijians and 2% in other races. There was a significantly higher suicide rate in rural areas than in the towns. There were no cases of paraquat suicide in this period (Taylor *et al*, 1985).

A decade later there were 163 suicides annually, an increase of 80%, compared with a population increase of 19%. Most (88.3%) of the suicides were amongst Hindus who outnumbered Muslims (males 14:1; females 8:1). This proportion was greater than the Hindu, Muslim ratio in the general population (5:1). Hanging remained the most common method of suicide (males 60%; females 77%) but paraquat accounted for most of the remainder of the deaths (Haynes, 1984).

Table 1: Paraquat Poisoning in Fiji, 1981-1988

Year	Paraquat Ingestion	Deaths	Survivors (%)
1981	37	14	23 (62)
1982	44	14	30 (68)
1983	39	17	22 (56)
1984	83	34	49 (59)
1985	59	27	32 (54)
1986	66	33	33 (50)
1987	93	28	65 (70)
1988	113	18	95 (84)

Data presented in Table 1 indicate that the incidence of fatal paraquat poisoning in Fiji peaked in 1984-1986 and subsequently declined, although the number of ingestions continued to rise in the period. The case survival rate tended to increase in this period indicating less ingestion and/or improved therapy (Davies, 1993).

Data from Fijian Ministry of Health for 1981-1988 show a markedly greater excess of paraquat poisoning in persons of Indian origin than in Fijians (Table 2).

Table 2: Paraquat Deaths by Ethnic group, Fiji 1981-1988

Ethnic Group	Deaths (%)
Fijian	22 (12)
Indian	16 (87)
Other	2 (1)
Total	185 (100)

- Republic Of Ireland

There were 92 deaths and 44 survivors of paraquat poisoning (mortality 68%) in Ireland in the decade 1967-1977. Poisoning was intentional in 77 cases (57%) and accidental in 40 (29%). The fatality rate in intestinal poisonings was 73% and it was 42% in accidental poisonings.

The number of cases increased after 1967, with the incidence of intentional poisoning doubling after 1975. Males outnumbered females by 4:1. Accidental poisoning was particularly common and intentional poisoning occurred across a wide spectrum of occupations.

Estimates of the lethal volume of paraquat ingested indicated that, of 62 cases of poisoning, all 10 cases taking less than 5 ml of concentrate survived; one fatal case took 5-10 ml and 37 died from taking 11-20 ml. Only 28 survived ingestion of 21-30 ml and there were no survivors of ingestion of greater volumes.

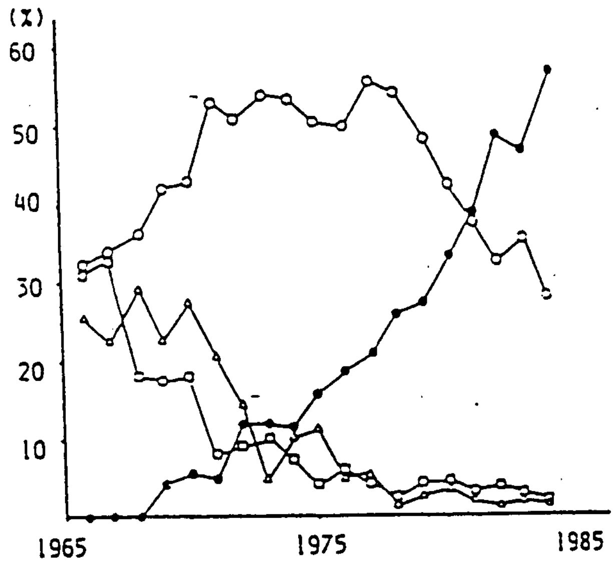
The subsequent reduction in the number of accidental poisonings followed legislative restriction of the availability of paraquat liquid concentrate to the general public and additional label warnings (Fitzgerald *et al*, 1978).

- Japan

Japan experienced an epidemic of paraquat poisoning in the 1980s (Naito and Yamashita, 1987).

Figure 1 shows the changing pattern of pesticide poisoning in Japan from 1965-1985 (Ikebuchi, 1987). Most of the deaths were attributed to pesticides. As the incidence of paraquat poisoning increased, there was a corresponding decrease in the incidence of poisoning by other pesticides.

Figure 1: Pesticide Poisoning in Japan, 1965-1985



Circumstances of pesticide poisonings in Japan ●—●: paraquat, o—o: phosphorus pesticides (except parathion), Δ—Δ: chlorinated pesticides, ▫—▫: parathion

(Source; Ikebuchi, 1987)

Information provided by the Japanese Ministry of Health and Welfare is that the incidence of paraquat poisoning declined after the mid-1980s following the combination of measures that were undertaken at that time. These are reviewed in Objective 2.

Table 3: Suicide Trends in Japan, 1983-1990

Year	Total Suicide Deaths	Total Pesticide Deaths	Total PQ/DQ Deaths
1983	24,985	1386	398
1984	24,344	1422	551
1985	23,383	1890	965
1986	25,667	2631	1202
1987	23,831	2232	1043
1988	22,795	1804	727
1989	21,125	1161	577
1990	20,088	1068	471

- Malaysia

A changing pattern of use of pesticides for suicide has been reported in Malaysia. Sodium arsenite, formerly used as a herbicide on western rubber estates, was the poison most commonly associated with suicide from 1963 to 1967, if not before. Formic acid was the next most commonly used poison (Amarasingham and Lee, 1969).

By 1972, organophosphorous insecticides (316 cases) had overtaken sodium arsenite as the most commonly ingested poison (271 cases). Formic acid remained the second most commonly used agent (295 cases) but the use of herbicides and fungicides began to rise. Of 82 cases of deaths from herbicides and fungicides, 68% were due to paraquat (Amarasingham and Hee, 1976). Between 1977 and 1981, paraquat was responsible for 31% of all poisoning cases, with a 79% mortality rate (Onyon and Volans, 1987).

Demographic and psychiatric aspects of 96 suicide attempts were studied in the Klang district of Malaysia in 1977. Indians were over-represented, comprising 66% of cases, although they were the minority ethnic group. The Chinese and Malays comprised 20.2% and 11.7% respectively. Three quarters of the sample were aged between 15 and 24 years and females outnumbered males (3:1). The rate was higher in those of lower socioeconomic class. Self-poisoning was by far the most common cause of suicide (97%). The agent used varied amongst the ethnic groups. Insecticides were the most common agent, being used by almost a third of all cases. Other agents chosen were tranquillisers and hypnotics (24%), detergents (15%), methyl salicylate liniment (12%) and weedicide (6%). The source of the insecticide was almost entirely domestic. Three cases bought the insecticide prior to their attempt. The cases using "weedkiller" were all from agricultural estates where the poison was readily available (Murugesan and Yeoh, 1978).

An association between suicide rate and ethnicity was again evident in a study of 30 cases of paraquat poisoning hospitalised in Kuala Lumpur in 1978-1988. Indians formed the largest group (20 cases), equally male and female. There were 6 Chinese and 4 Malay (all female) cases. Most patients were aged 15-29 years. 21 (66%) cases were suicidal and the rest accidental. The common precipitants of suicidal poisoning were a quarrel or abdominal pain in females and depression in males. The accidents were due to consumption of paraquat from unlabelled bottles or cups. It was recommended that the decanting of paraquat should be illegal and that there should be close supervision of estate workers where paraquat was commonly used (Chan and Cheong Izham, 1982).

A study of suicide and parasuicide in the Cameron Highlands of Malaysia for the period 1973-1984 showed that 81% of cases were in persons of Indian origin (largely Tamils), although they formed only 25% of the population. The average annual rate of Indian suicides was 172.3 per 100,000 susceptible population over 15 years compared to the overall suicide rate for all races in the district of 66.9 per 100,000. About 94% of the suicides and 66% of the parasuicides were by ingestion of agricultural chemicals. Most suicides involved ingestion of organophosphorus insecticides but about 15% ingested paraquat, mostly in the latter 5 years. Parasuicides involved not only agricultural poisons but also household agents and medicines (Manian, 1988).

In a series of 94 paraquat poisonings in Perak State, 73.4% were suicidal, 13.8% accidental and 5.3% occupational. Most (80%) occurred in persons aged 10-40 years, equally male and female, of whom 81.9% were Indians, 12.8% Chinese and 5.3% Malays. The low incidence in the Muslim Malay population was attributed to religious prohibition of suicide (Wong and Ng, 1984).

In the experience of the Medical Unit, General Hospital, Kuala Lumpur, for 1987, there were 603 cases of poisoning of which 298 cases were associated with pharmaceuticals, 185 with household products, 95 with pesticides, including 35 with herbicides. About half of the cases (49%) were intentional ingestion (suicide or parasuicide) and 39% were accidental. Poisoning was most common amongst those of Indian descent (41%), followed by Chinese (33%) and Malays (22%).

Intentional poisoning was most common amongst the Chinese followed by the Indian sector. Accidental poisoning was most common amongst the Indian followed by the Malay sector. It was suspected that intentional self-poisoning amongst the Malays was under-reported and accidental poisoning over-reported because of the stigma associated with suicide in the Muslim population (Tarik,1989).

According to Lum *et al*, (1993), most pesticide poisonings in Malaysia from 1979 to 1986 were due to paraquat with 49.1% being intentional and 37.8% accidental. Areas that include large numbers of plantations and farms where pesticides were likely to be used in quantity tend to record high levels of mortality due to pesticide poisoning. Mortality from pesticide poisoning correlates strongly with suicidal intent.

Information compiled from inpatient records of Government hospitals and provided by ICI Agrochemicals (Malaysia) indicate that the incidence of suicide with paraquat in Malaysia peaked in 1988 and has declined thereafter. In 1988 there were 418 deaths due to pesticide poisoning: 386 deaths were due to paraquat, 18 due to organophosphates, 9 others, 3 due to glyphosate and chlorinated organic insecticides and unknown pesticides respectively.

Data presented in Table 4 show that, in 1991, there were 893 admissions for pesticide poisonings (278 deaths; 31.1%) in Malaysia of which 494 (55.3%) were associated with paraquat. Of the latter, 338 poisonings were classified as suicide or attempted suicide (204 deaths; 73.4% of paraquat poisonings). Accidental exposure to paraquat resulted in far fewer admissions (129; 26.1%). There were no deaths attributed to occupational exposure to paraquat whilst the number of accidental occupational paraquat exposures resulting in hospital admission was low (13; 2.6%). For comparison, there were 102 hospital admissions due to organophosphate poisoning which resulted in 17 deaths. There were 47 admissions and 2 deaths due to glyphosate.

Table 4: Pesticide Poisoning in Malaysia in 1991

Pesticide	Suicide		Accident				Homicide		Unknown		Total	
			Occupational		Other							
	A	D	A	D	A	D	A	D	A	D	A	D
Paraquat	338	204	13	0	116	40	1	0	26	9	494	253
Organophosphate	62	14	8	0	24	1	0	0	8	2	102	17
Glyphosate	22	2	3	0	16	0	0	0	6	0	47	2
Other	78	4	4	0	106	1	0	6	9	1	250	6
Total	500	224	81	0	262	42	1	0	49	12	893	278

A: Admission
D: Death

– Source: Hospital admission data, as compiled by ICI Agro chemicals (Malaysia)

- Papua-New Guinea

Paraquat poisoning was reported to be a serious and growing problem in Papua New Guinea in the early 1980s. A series of 41 cases, involving accidents and suicides, was described in 1981 (Wohlfart, 1981).

While most of these poisonings were intentional, many were accidental due to the drinking of paraquat from unlabelled containers (Mowbray, 1986; Mowbray, 1988). Addition of an emetic and stench to paraquat concentrate in 1981 as well as an educational campaign has reportedly reduced the incidence of paraquat poisoning in Papua New Guinea but details were not given (Mowbray, 1988).

- Sri Lanka

Sri Lanka has one of the highest suicide rates in the world. Suicides are most frequent in young adults, both male and female. Compared to the U.S.A., the suicide rate for males aged 15-24 years in Sri Lanka is nearly four times greater; the female rate is nearly 13 times greater. The most common mode of suicide is ingestion of liquid pesticides (Berger,1988).

Poisoning due to deliberate ingestion (70%) is the most common method of suicide because of the easy availability of pesticides (Berger, 1988; Fernando, 1989). In 1986, pesticide poisoning was the sixth leading cause of death in State hospitals comprising 5.45% of all deaths. 57% of cases of poisoning admitted to hospital and 66% of resultant deaths were due to pesticides.

In 1979, the morbidity rate for pesticide poisoning was 79 cases per 100,000. The highest incidences of poisonings occurred in the principal agricultural districts (De Alwis and Salgado, 1988). In the period 1975-1980, the annual number of deaths ranged from 938 to 1,112. Suicide and occupational exposure were the most common causes of poisoning and were most often (73.7% of poisoning deaths) due to organophosphorus insecticides (Jeyaratnam *et al*, 1989).

A study of the mortality in Sri Lanka from agrochemical poisoning during the period 1975-1983 showed that about 75% of agrochemical deaths were due to ingestion, with accidental and occupational poisoning forming the balance. The number of deaths during the period varied from 900-1500 annually with 1521 deaths being recorded in 1983. The highest incidence of poisoning occurred in the principal agricultural districts. Over a 3 year period, 1983-1986, only 4% of the deaths autopsied in urban Colombo were due to agricultural chemicals but these comprised 45-50% of the suicides. Organophosphates accounted for 57.7% of all the cases of agrochemical poisoning whilst paraquat accounted 21.2% of cases. Most occurred in young adults with a male to female ration of 2:1. The popularity of agricultural chemicals for suicidal poisoning was ascribed to their free availability, indiscriminate sale without restriction and their high toxicity (De Alwis and Salgardo, 1988).

In a study in 1986-1987 in the Galle district of southern Sri Lanka, a well defined agricultural district, there was a marked increase in the overall suicide incidence by poisoning after 1980. The incidence of poisoning was 75 per 100,000 and the death rate was 22 per 100,000. The preferred self-poisoning agent was an agrochemical (88% of all deaths); for these suicides paraquat was the most prominent agent (61%) followed by organophosphates (11%) and then acetic acid, (10.5%). The mortality rate with paraquat was 68%. It was less with insecticides (27.7%, mostly organophosphates) and acetic acid (32.6%). The use of paraquat for suicide was probably because it was more freely available in Galle than in other parts Sri Lanka where the use organophosphate insecticides for suicide predominated.

In Galle, suicide was associated with a grief reaction or reactive depression in 255 of cases. An impulsive act by a youth following a provocation caused in 12% of the suicides. Completed suicide may not always have been intended. It was suggested that one way of reducing suicide in Sri Lanka would be to foster interpersonal relationships between the young and the elders in the society so that they young would seek assistance from the elders in situations of conflict. Strict controls on the sale and distribution of potent agrochemicals such as paraquat were considered warranted as was education of the community about the proper and safe storage of agricultural chemicals at home (Hettiarachchi *et al*, 1988; Hettiarachchi and Kodithuwakku, 1989a).

A subsequent study of motivation in 97 consecutive cases of self-poisoning showed no greater suicidal intent than has been reported from developed countries, 55.7% wished to die at the time of the act but only 27% retained this attitude afterwards. Attempted manipulation of the attitude of others towards the patient was a common motive. The act of poisoning was not planned in most cases and the most common precipitating cause was interpersonal dispute (50.5%; domestic problems or a "love affair"). Psychiatric illness was associated with 13.4% of cases. Other causes were alcoholism in males (7%), death of a loved one (6.1%), financial difficulty (4.1%). Failure in examinations, social embarrassment and organic illness accounted for 2.1%.

Since interpersonal disputes between family members were the main cause of self-poisoning, efforts to prevent suicide should aim to improve family relationships. Whilst it may be possible to modify attitudes to discourage self-poisoning and encourage the seeking of help before a crisis develops, the impulsive nature of self-poisoning makes this difficult (Hettiarachchi and Kodithuwakku, 1989b).

Although the suicide rate from self-poisoning is high in Sri Lanka, the national incidence of self-poisoning is lower than in some western countries with a comparatively lower mortality rate. This is attributed to the high incidence of use of agricultural chemicals for self-poisoning in Sri Lanka. In contrast, less toxic drugs are more often taken for suicide in western countries. In the 97 prospective cases of self-poisoning studied previously (Hettiarachchi and Kodithuwakku, 1989a), 60.8% of cases knew the name of the poison they ingested, 46.3% knew its potential lethality but only 9.2% knew the lethal quantity. Most became aware through other poisoning (18.5%) whilst others became aware through the mass media (14.4%).

The choice of an agricultural chemical as the self-poisoning agent was attributed to their availability and knowledge, or lack of knowledge, of its toxicity. Agrochemicals are readily available with nearly half of the subjects having obtained the poison from home. Some determined cases, mostly males, purchased the poison with suicidal intent. Females wishing to make a suicidal gesture tended to take substances available in the home. Consequently, it was argued that stricter legislation on the sale and distribution of these poisons should reduce their availability for self-poisoning. Similarly, education of farmers about the proper storage and encouragement of proper disposal of excessive amounts may also reduce their availability for self-poisoning (Hettiarachchi and Kodithuwakku, 1989c).

The inadequate availability of Fuller's Earth in peripheral hospitals for treatment of paraquat poisonings is a problem in Sri Lanka (Fernando, 1993).

- **Surinam**

A similar pattern of substitution of suicide agents to that described in Malaysia occurred in Surinam following the prohibition there, in 1980, of sale of concentrated acetic acid which previously was a favoured agent for suicide, along with hanging.

Subsequently, there was a rapid rise in poisonings due to pesticides, particularly paraquat. By 1985, the incidence had risen to 21 cases per 100,000 population. Overall, males (64%) outnumbered females and the male case mortality rate (79%) was higher than for females (57%). The case survival rate was typically low, about 20% at one hospital. Hindustanis were over-represented amongst those attempting suicide, and accounting for twice as many cases as would be expected on the basis of the ethnic composition of the population.

Reportedly, the mortality rate fell to 6.8 per 100,000 in 1986 when the availability of paraquat was curtailed due to economic reasons. Consequently, restriction of the availability to professional users only was advocated (Anon., 1986; Perriens *et al*, 1989).

- United Kingdom

Paraquat poisoning has been a significant problem in the U.K. The first fatalities due to paraquat poisoning were recorded in 1966. Over the period 1965-1975, paraquat fatalities in England and Wales began to increase, particularly after 1971. In 1984, 31 deaths were recorded. Over the period 1966-1984, 428 deaths were attributed to paraquat, 75% male and 25% female. In this period, for comparison, 77% of all suicide deaths and 65% of accidental deaths occurred in males. The trend in Scotland was similar, rising from 1 case in 1967 to 10 cases in 1975.

The National Poisons Information Service (NPIS) has monitored suspected human exposure to paraquat in the U.K. since the 1960's and from 1981 onwards has been conducting a detailed study. Data on 209 paraquat fatalities showed a predominance of males (72%) and deliberate intent (85%). There was a disproportionate number of fatalities in agricultural areas. Most (71%) involved paraquat liquid concentrate but 22% were due to granular formulations. Of 209 fatalities, 204 were due to ingestion. However, information regarding occupation was available for only 69 cases but, of these, only 39% had an occupation that gave ready access to paraquat concentrate (Onyon and Volans, 1987).

In the period 1980-1988, 1,635 suspected exposures to paraquat were identified by NPIS. The majority of paraquat incidents involved adults, i.e. those aged greater than 12 years. This is in marked contrast to age profile for the total inquiries to the NPIS where there is usually a higher percentage of children amongst poisoning cases.

The majority of patients (71%) over the whole survey were males. The greatest overall proportion of cases were suicide (45%). Exposure was accidental in 29.7% of cases.

In both adults and children the majority of exposures were by ingestion and most deliberate exposures were by the oral route (98%). The annual number of ingestions declined in 1985 and thereafter. The number of exposures by other routes has remained fairly constant but, because of the decline in ingestions, they now represent a greater proportion of the reported cases.

No ingestions were described as occupationally related; the number of accidental ingestions were slightly less than accidental dermal, inhalational or ocular exposures. Of the occupational exposures, the most frequent effects noted after occupational exposure were irritation of the mouth and throat and vomiting. No patients suffered renal, hepatic or lung damage after occupational exposure.

Most of the adults who died had deliberately ingested paraquat 225 (87%). Three people died as a result of deliberate injection. Eight adults died as a result of accidental ingestion: two as a result of ingesting paraquat from bottles into which the concentrate had been decanted and which had no warning label (Northall *et al*, 1993).

- **United States of America**

Paraquat poisoning is relatively uncommon in the U.S.A. where it is a restricted pesticide which should only be available to licensed users.

Of 1,864,188 human exposures reported in 1992 to U.S. A. poisons information centres, there were only 114 exposures to paraquat. Of these, 107 were recorded as accidents and 7 as intentional exposures.There was only 1 fatality (Litivitz *et al*, 1993).

- **U.S. Samoa and Micronesia**

Paraquat poisoning is also uncommon in American Samoa despite an increase in suicide incidence of 7.6/100,000 during 1968-1980 to 11.8/100,000 during 1980-1984. Hanging was the most common method of suicide and self-poisoning was uncommon - 2 of 20 cases. There were no recorded deaths from paraquat during 1982-84 and no hospital admissions due to paraquat poisoning from January 1983 to July 1985.

There was an 8-fold increase in suicide in US Micronesia in the two decades since 1960, mostly in the 15-24 age group. Alcohol was a contributing factor in about half of the cases, although alcoholism and psychiatric disorder was uncommon. Hanging accounted for 85% of cases of suicide, with firearms and poisons ranking a very distant second and third (Taylor *et al*, 1985).

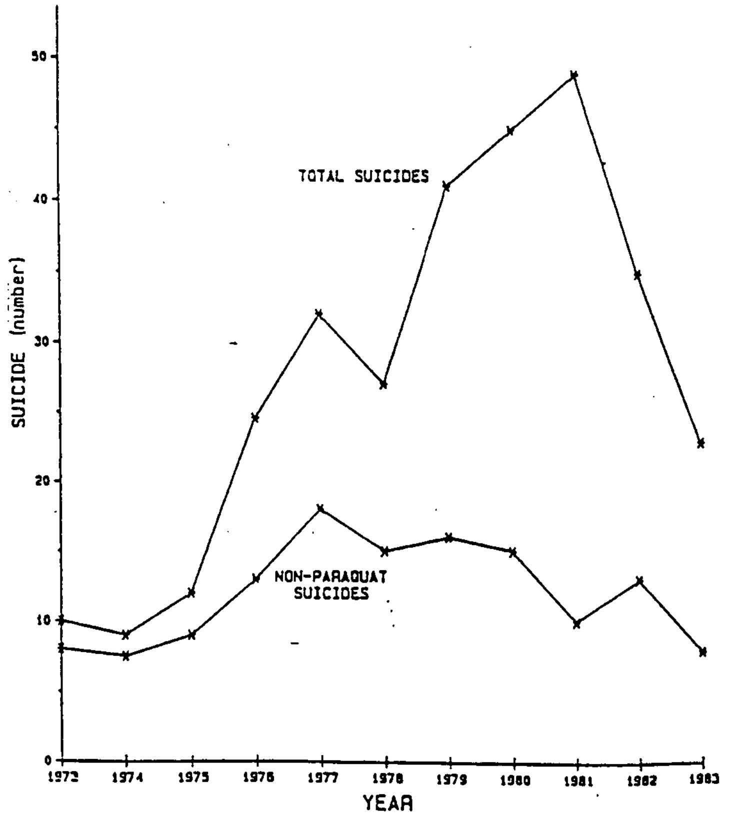
- **Western Samoa**

Whilst a high suicide rate has long been a problem in Western Samoa, the incidence of suicide rose dramatically after 1975. In 1981 the mortality rate from poisoning reached 31.4 per 100,000 for the general population and more than 130 per 100,000 in those aged 25-34. It declined thereafter, but not to pre-1975 levels (Figure 2).

Although part of this apparent increase in suicide may have been spuriously due to previous under-reporting, there was a clear association with the increasing use of paraquat for suicide (Figure 2).

Recent paraquat poisoning data shows that the peak incidences of paraquat poisoning occurred in 1986-1987 (Table 5). Subsequently, there has been a tendency for a reduction in suicide attempts and paraquat-related deaths, particularly in recent years. The case survival rate ranged from 38-75%.

Figure 2: Suicide and Paraquat-Related Deaths in Western Samoa 1973-1983



Source: Bowles, in Taylor, Tama and Goldstein, 1985.

Table 5: Paraquat Poisoning in Western Samoa, 1982-1992

Year	Paraquat Ingestion	Deaths	Survivors (%)
1982	43	23	20 (46.3)
1983	34	12	22 (64.7)
1984	20	5	15 (75.0)
1985	21	13	8 (38.4)
1986	41	18	23 (56.1)
1987	48	18	30 (62.5)
1988	30	16	14 (46.7)
1989	27	18	9 (33.3)
1990	24	14	10 (41.7)
1991	25	13	12 (48.0)
1992	30	12	18 (60.0)

The relatively high survival rates were attributable to prompt commencement of treatment and because, in some cases, only small doses were taken. In the period 1982-1992, 457 suicide attempts have resulted in 230 deaths of which 162 were associated with paraquat (Davies, 1993).

Occupational Exposure and Poisoning

The effects of occupational exposure to paraquat has been reviewed and summarised (Hart, 1987; IPCS, 1984). Most occupation exposure is dermal.

. Case Reports of Occupational Poisoning Due to Paraquat

Case reports of systemic poisoning from occupational exposure to paraquat have been infrequently reported.

In a review of the literature up to 1988, only 11 fatal and two non-fatal cases of occupational poisoning following dermal absorption of paraquat were identified. Inhalation exposure was not identified as cause of poisoning. Systemic poisoning occurred only following absorption through damaged skin which may have been pre-existing or occurred as a result of prolonged contact with paraquat solution. Four fatal cases followed prolonged contact with dilute working solutions after spillage or leakage from knapsack sprayers. One case also resulted from oral absorption. In one case, the concentration of the working solution reportedly was 0.5%. In view of the corrosive nature of paraquat concentrate and the possibility of prolonged dermal contact or absorption via cuts or abrasions or inflamed skin, it was recommended that paraquat not be applied by knapsack sprayers (Smith, 1988).

The following case reports exemplify the kinds of situations in which fatal paraquat poisoning has resulted from occupational exposure.

Case 1
In Czechoslovakia, an acute percutaneous poisoning occurred as a result of spraying of an improperly diluted paraquat concentrate. A farmer used a leaking knapsack sprayer which delivered the paraquat solution to his head, neck, back and lower body. The skin on his neck and scrotum was heavily corroded; severe systemic poisoning subsequently developed, including liver, kidney and lung toxicity. He died of renal and respiratory insufficiency (Jaros *et al,* 1978).

Case 2
A fatal case of paraquat poisoning following reported dermal exposure only during vineyard spraying in South Africa was reported in 1979. The man had been spraying a 2.8% solution of paraquat in a water and oil base using an ultra-low volume sprayer. About 400 L of the solution was sprayed daily for up to 10 days. No protective clothing was used. On investigation, the applicator was found, to have balanced the tank spray on his shoulder where it had leaked causing local ulceration. There is little doubt that the fatal case reported here was due to the absorption of inadequately diluted paraquat solution, either percutaneously or through the ulceration of the man's shoulder or both. The role of the oil present in the formulation is not known (Levin *et al*, 1979).

Case 3
A fatal case of paraquat poisoning in Greece following percutaneous absorption was described in 1983. A 64 year old sprayer applied a solution of paraquat using an old knapsack sprayer which leaked fluid freely down his back for approximately three and half hours. He did not wash himself until later in the same evening. The

next day he developed a burning feeling in his back where the skin seemed to be irritated. Two days later, medical examination revealed a bluish-red colour of the skin on his back which appeared to be necrotic. The patient also complained of anorexia and weakness. He developed toxic shock with renal and respiratory insufficiency. Paraquat was detected in his blood, urine, liver and kidneys (Athanaselis *et al*, 1983). It was later suggested that the man may have used a spray concentration well in excess of that recommended because adequately diluted paraquat would be unlikely to cause this type of skin damage and give rise to such serious poisoning (Hart, 1984).

Case 4
An unusual case of fatal percutaneous paraquat poisoning associated with cutaneous lesions was that of a 39 year old Canadian woman who worked with paraquat in orchards. She was hospitalised because minor scratches on her arms and legs developed raised lesions. She complained of headache, breathlessness, tightness of the chest, anorexia and loss of weight. There was necrosis of the epidermis and dermis at the affected sites. Her lung function was moderately restricted. Although her condition improved in with treatment in hospital, she was readmitted a few weeks after discharge, following occurrence of further new skin lesions together with shortness of breath, cough, fever, nausea and vomiting. Her skin lesions deteriorated progressively; she developed liver and renal dysfunction and respiratory failure leading to her death. It was considered that the most likely portal of entry of paraquat was through the skin lesions but this was not certain (Newhouse *et al*, 1978).

. Studies of Occupational Exposure to Paraquat

- Paraquat Formulation Workers

Whilst not typical of agricultural users of paraquat, formulation plant workers represent a group of workers relatively heavily exposed to paraquat concentrates for prolonged periods. Thus, their occupational health experience is relevant in any consideration of the adverse effects of paraquat on users.

The exposure of 2 groups of paraquat formulation plant workers have been compared. In England, the workers wore partial protective clothing and were exposed to paraquat dust and liquid formulations during a 37.5 hour working week for a mean period of 5 years. In Malaysia workers worked a 42-hour week with a mean exposure to liquid paraquat concentrate of 2.3 years without gloves, rubber aprons or goggles. They can be considered to have experienced a degree of occupational exposure to paraquat unlikely to be found elsewhere.

Based on clinical examination and medical records reporting acute skin rashes, nail damage, epistaxis, blepharitis and delayed wound healing, 12-66% of cases were consistent with the known adverse dermal effects of paraquat concentrates (Howard, 1979a).

- Paraquat Applicators

Exposure studies of paraquat application under practical field conditions have been conducted in a number of countries and have been summarised (IPCS, 1984).

Oral Exposure
Fatal accidental ingestion of paraquat working dilutions is unlikely because of the dilution factors involved. The lethal amount of diluted paraquat would be in the order of 400 ml-to 2 L at the standard dilution of 0.1-0.5% paraquat cation. This estimate is based upon the presumption that the fatal human dose of paraquat is in the order of 2-3 g.

Ingestion of paraquat is most likely to occur when paraquat concentrate has been improperly decanted into unlabelled containers. Since the great majority of accidental occupational poisonings in the U.K. had previously resulted from such malpractice, the reduction in such cases to only 2 in 1977 indicated a significantly increased awareness of this hazard and/or improved work practice (Howard, 1980).

Significant but unintended oral ingestion of paraquat from diluted solutions can occur from blowing into or sucking from blocked spraying nozzles. Dilute solution blown onto the face may produce local effects, as may smoking when hands are contaminated with paraquat (WHO 1984).

During spraying, oral ingestion may occur as a result of the swallowing the spray impinging upon operator's face when actually working within the spray mist. Whilst this practice is not recommended, it does occur nonetheless. Even so, with spray strengths of not more than 0.5%, it would be impossible to ingest sufficient paraquat in this way to produce severe poisoning. However, local irritant effects from oral contamination by paraquat have been reported when higher concentrations of spray solution have been used under adverse conditions, such as spraying into the wind (Fitzgerald *et al*, 1978).

Dermal and Inhalational Exposure
mixing and loading paraquat
Potential dermal, respiratory and internal exposure to paraquat exposure of applicators mixing and loading paraquat for spraying in vineyards in Arkansas was monitored in 1980-1981. The operators used tractor-mounted low-boom vineyard spray rigs. Persons operating the spray rigs received the highest dermal exposure levels (averaged 0.015 mg paraquat/kg body weight). Exposure of the hands constituted a significant proportion of total dermal exposure: 39% for the spray applicators and 91% for the mixers. Respiratory exposure was minimal. The highest level of potential respiratory exposure obtained averaged 0.008 mg/m^3. This compared favourably with the TLV of 100 μg/m^3 for paraquat. The actually respirable fraction of this exposure would, have been considerably less. Paraquat was not detected in any samples of urine, indicating little systemic exposure (Forbess *et al*, 1982).

paraquat spraying
In field trials conducted to determine the exposure during actual spraying of paraquat, the maximum concentration of paraquat in the air breathed by the sprayers was of the order of 12 μg/m^3. Paraquat was not detected in their urine (Hogarty, 1976).

tractor application
The level of exposure of field workers operating tractor mounted spraying equipment in orchards has been studied. In the United States paraquat was sprayed at a rate of about 1.0 g/L. The exposure of the field workers was found to range from 0.4 mg/h dermally to less than 0.001 mg/h by inhalation. The respiratory values were generally below the limit of analytical detection. Paraquat was not detected in urine samples (Staiff *et al*, 1975).

The pattern of exposure is consistent with that generally found in such studies i.e. inhalational exposure is insignificant and that dermal exposure is modest if proper application procedures and safety precautions are followed.

aerial application
In the United States, occupational exposure to paraquat applied aerially in cotton production has also been studied. Dermal and respiratory exposures of pilots, flaggers and a mixer-loaders were relatively low. The dermal exposures ranged from 0.05 mg/h for pilots and the mixer-loaders to 2.39 mg/h for flaggers. Respirable paraquat was not detected in the breathing zone of any of the workers. Flaggers were exposed to the highest aerial paraquat concentration, 26.3 μg/m^3. The combined dermal and respiratory exposure of the flagger was equivalent to 19.4 mg/working day. These results demonstrated that the hazard to pilots and ground crew during the aerial application of paraquat was low (Chester and Ward, 1984).

In order to provide a relative safety comparison, the levels of inhalational exposure reported in these studies can be compared with the Threshold Limit Value (TLV), 0.1 mg/m^3 (ie 100 μg/m^3) for inhalational exposure to paraquat that is accepted in several countries (IPCS, 1991a). In none of the above cases was the exposure level unacceptable.

Inhalational exposure can be discounted due to the measured low concentrations of paraquat in the breathing zones of spray operators, the low proportion of respirable droplets and the lack of volatility of paraquat (Howard, 1983).

. Comparison of Low and High Concentration Paraquat Application

The introduction of spinning application technology utilising low volume/high concentration spray solutions raised concern about increased operator hazard if paraquat were applied in this way.

A comparative study of the risks of high and low volume spraying paraquat was undertaken over a two week spraying period in Thailand. Paraquat was sprayed at low volume/high concentration (2% paraquat w/v) and at high volume/low concentrations (0.1% w/v). The high volume spraymen (12) wore a shirt and long trousers; 7 were bare-footed except for rubber slippers which gave no protection to the dorsum of the foot whilst the remaining 5 wore plimsolls. Urine samples were analysed for paraquat. Dermal contamination was also measured.

The mean urinary excretion of paraquat of those using the high volume applicator without foot protection differed significantly from those wearing shoes. The degree of skin contamination of the leg and foot by the low volume application was less than that resulting from the high volume application.

Dermal irritation developed in a number of cases. A worker using a high volume knapsack sprayer developed a mild rash on his feet around areas of skin trauma. Three other spraymen developed skin irritation: two were involved in spillages of which one also splashed concentrate into the eye causing a severe conjunctivitis whilst the third, who was soaked with a 2% spray, developed severe groin irritation. All of the skin rashes resolved in about 10-14 days with localised treatment. Final medical examination, one week after the spraying ended, showed no abnormalities.

The degree of dermal exposure which occurred during the low volume/high concentration spraying was significantly higher than the levels of contamination for low volume sprayers and very much higher than that reported by Hogarty (1976) for knapsack sprayers. This accounted for the rising level of paraquat excreted in the urine of those using the low volume sprayers with unprotected feet by the end of the second week. A major contributing factor to this increased absorption of paraquat was the skin damage caused by the 2% paraquat solution.

These findings, from a trial conducted under supervised conditions, indicated that, under the conditions which frequently prevail in developing countries, the problems with low volume spraying of paraquat would be much worse because of prolonged or more intensive spraying. Carelessness, inadequate hygiene, poor protective equipment and other factors would exacerbate this exposure (Howard, 1982). It is for such reasons that application of paraquat at concentrations above 0.5% w/v is contraindicated.

. Studies of Occupational Exposure in Some Countries

- Japan

According to FAO/WHO (1987),

' To evaluate the effects of protective equipment on occupational human exposure to paraquat, a paraquat formulation (240 g/L) diluted 300 times by volume with water was sprayed for 2 hours on weedy ground. During the spraying operations, the concentrations of paraquat aerosol were 11-33 μg/m^3 air. The total dermal exposure was about 0.22 mg. No irritation of the eyes or the skin was reported. The urine of the workers who wore gauze masks contained significant amounts of paraquat 24 hours after spraying. The urine of the workers who had worn a high-performance mask did not contain detectable levels of paraquat. The need for protective equipment to decrease skin contact with paraquat and to avoid aerosol inhalation was recognised (Kawai and Yoshida, 1981).'

- Malaysia

A series of studies of Malaysian agricultural workers occupationally exposed to paraquat under what were relatively extreme exposure conditions has been published. Prolonged herbicide application was required, for up to 10 months of the year, 6 days per week, because of the long tropical growing season. The prevailing oppressive conditions of high temperature and humidity favoured dermal absorption of the herbicides and mitigated against the use of protective clothing. The relatively extreme exposure conditions make these studies worthy of consideration in some detail.

A preliminary study of the plantation workers, who usually experienced high paraquat exposure using knapsack sprayers, was conducted in 1965 to determine the most important route and extent of exposure, under tropical conditions. The high temperature and humidity together with the light clothing of the sprayers increased the potential for dermal exposure. Weekly spraying of about 200-250 gallons of dilute (0.5 g/L) paraquat solution for 12 weeks. Apart from washing before and after spraying, the workers took no additional precautions. Medical examinations, including chest X-ray, were undertaken.

The significant adverse effects attributable to paraquat exposure found were:

- dermatitis of the scrotum and subsequently of the hand and ear in a worker wearing trousers that were continuously soaked by leakage from a faulty sprayer; and
- epistaxis in a worker who prepared the working dilution in a confined space, presumably from inhalation of airborne particles of concentrate and/or dilute solution.

Low urinary concentrations of paraquat (mostly 0.1 mg/L; maximum 0.15-0.32 mg/L) were detected in 78/134 (58.2%) of urine samples. These levels, which tended to increase during the 12 week study period, were undetectable 1-2 weeks after cessation of spraying (Swan, 1969).

In a second, larger study in 1967, combinations of protective apparatus and clothing were evaluated for their effectiveness. Over the 13-14 week trial, there was a considerable reduction in the frequency of urinary paraquat detection (53/394; 13.45% samples) with the highest concentration being 0.15 mg/L. The highest incidence of "positive detections" of paraquat in urine occurred in the group wearing normal clothing (which included canvas shoes) and who sprayed denser weed growth. The wearing of gumboots was the single most important protective measure in reducing measured urinary excretion. The variability of the generally low urinary levels indicated that attention to personal hygiene was probably as important in reduction of exposure as any other factor.

Some other effects of exposure were found. One sprayman who directly inhaled spray mist suffered congestion of the nasal mucosa but not epistaxis. Approximately half of the exposed men had some skin or eye irritation at some stage during the trials. Contamination of eyes by spray mist resolved unremarkably under antibiotic cover. All cases of skin irritation were mild and cleared rapidly with treatment (Swan, 1969).

Table 6: Dermal exposure to paraquat

Occupation	Mean dermal exposure (rate)	Mean total exposure (rate)	Highest individual total exposure (rate)
sprayers	2.2 mg/h (0-12.4 mg/kg/h) (unclothed)	66 mg/h (1.1 mg/kg/h)	169.8 mg/h (2.8 mg/kg/h)
carriers	not recorded	13.6 mg/h (0.3 mg/kg/h)	47.1 mg/h (0.9 mg/kg/h)
tappers	not recorded	7.0 mg/h (0.13 mg/kg/h)	15.5 mg/h (0.3 mg/kg/h)

Quantitative investigations of dermal and respiratory exposure to paraquat was subsequently undertaken. Exposure of knapsack spray operators was compared to that of pesticide formulation workers and rubber tappers (Tables 6 and 7).

Dermal exposure of sprayers was significantly influenced by accidental self-spraying and spillage of the dilute spray. The actual mean leg exposure was measured to be 2.8 mg paraquat/h. Comparison with the calculated leg exposure indicated that only about 5% of the spray penetrated through the operator's clothing. Leg exposure was increased in higher crops and weeds. Overall mean exposure of sprayers hands was 4.2 mg paraquat/h. This related to direct contact with the spray and adjustment of the sprayers. The major source of dermal exposure of carriers was contamination when walking through recently sprayed vegetation and from accidental spillage during carrying and loading. The highest dermal exposure of 12.4 mg/h represented 0.25% of the acute dermal LD50 to male rats of 80 mg/kg bw.

Table 7: Inhalational exposure to paraquat

Occupation	Respiratory exposure
sprayers	0.25 - 0.97 ug/h
carriers	0.24 ug/h
tappers	nil

The highest mean concentration of total airborne paraquat in the breathing zones of spraymen was 0.97 µg/m^3, about 1% of the TLV. The carriers' highest exposure represented 0.24% of the TLV.

The extent of systemic absorption, estimated by measurement of paraquat in urine, was comparable to that found in other studies reported above. Urinary paraquat, detected in 9/19 sprayers and 1/7 carriers, was in the range 0.07-0.35 mg/L but was mostly below the limit of detection (ie <0.05 mg/L). Higher concentrations, 0.69 mg/L and 0.76 mg/L were reported in 2 female spray operators but may have been due to sample contamination. These quantitative results, indicated that the dermal and respiratory exposures to paraquat did not indicate a significant hazard in the normal application of paraquat under tropical conditions (Chester and Woollen, 1981).

A further occupational exposure study was undertaken of 27 Malaysian spraymen who sprayed paraquat (0.1% w/v) for a minimum of 1000 h and with a mean spraying time 5.3 years. Their health was compared with a group of 24 general workers who may have occasionally worked in paraquat treated areas and a group of 23 latex processors who had no exposure to paraquat. The workers did not wear any protective clothing during spraying operations. Spraymen regularly showered after work and changed clothes. However, working clothes were changed infrequently. Minor splashes were not usually washed off and workers seldom washed before eating.

A medical history was taken and full clinical examination performed, including biochemical and haematological investigations. Particular attention was paid to their respiratory status and respiratory function tests, including carbon monoxide diffusion, were performed. The significance of the occupational exposures to paraquat was tested by multiple regression analysis, after allowance for differences in the distributions of race, age, height and smoking history amongst the groups.

According to the authors,

'11/27 (41%) spraymen reported 1 or more incidents of skin irritation or rashes associated with spraying. These were commonest on hands, legs or groin. Groin or buttock rashes were commonly associated with a leaking knapsack sprayer that allowed spray solution to run down the back and between the buttocks. Medical records indicated that all cases cleared rapidly in response to local treatment (usually a steroid cream). Although 12 of the spraymen admitted to spillages or being splashed, only one case of eye injury had been reported, and this responded to treatment without sequelae.'

There were no significant differences between the groups for the respiratory or haematological parameters. However, liver function and renal function of the group of factory workers differed significantly from the other groups.

This comprehensive study demonstrated that the hazard of prolonged spraying of paraquat under tropical conditions can be low with good working practice (Howard *et al*, 1987).

- **Philippines**

In a study of the health of male Philippine banana plantation workers exposed to paraquat, the mean exposure time was 451 days over a three year minimum period. Several of the sprayers, however, had been working as paraquat sprayman over longer periods (up to 18.9 years). Paraquat was applied with a knapsack sprayer normally as a 0.15% spray solution. Mixer-loaders who prepared the working dilution from the 20% concentrate were included in the study.

The health status of the spraymen (43) was compared with other workers (70) not exposed to paraquat but who come from a similar socio-economic background and who were matched in age, physical characteristics and social habits. The health status of the spraymen and the control group was evaluated by means of full medical examination and clinical laboratory investigations, including haematology, blood biochemistry, chest radiography and pulmonary function tests.

There were no clinically significant differences in any of the measurements made between the sprayer and the control groups. Some minor differences in haematology and clinical chemical indices were of no clinical significance. The lung function tests showed no significant difference between the two groups. Fingernail and toenail damage was less in spraymen than the comparison group, indicating good attention to personal hygiene by the spraymen. Conjunctivitis occurred more commonly in spraymen (4) than controls (2). Corneal injury occurred in one of the spraymen. All responded well to treatment (Sabapathy and Tomenson, 1992).

- **Sri Lanka**

A study of exposure to paraquat in tea plantation workers in Sri Lanka has been undertaken. The workers had sprayed a diluted concentrate of about 1:500 daily for a mean of 12 years and a minimum of 5 years. Each sprayman sprayed about eight 15 L tanks of diluted spray solution daily. They were, therefore, each potentially exposed to about 48 g of paraquat/day.

The general health of paraquat spraymen (85) was compared to that of 2 control groups who had no exposure to paraquat: tea factory workers (76) and general estate workers (79).

Each worker underwent a general clinical examination which included examination of his cardiovascular, respiratory and nervous systems and examination of his skin. Routine haematological, renal and hepatic function test were undertaken. Lung function tests recorded ventilatory function and also alveolar function, measured by carbon monoxide diffusion. A chest X-ray was routinely taken.

Paraquat was not detected in the serum or urine of any worker. There was no clinical, radiological or laboratory evidence of lung damage attributed to long-term paraquat exposure. The general health, as well as liver and kidney function of the study group was similar of that to the two control groups. There were no signs of Parkinson's disease on neurological assessment.

The workers exposed to paraquat did have an increased incidence of headache, epistaxis and skin and nail damage. Epistaxis occurred in 3/85 of the study group, none of whom were mixer-loaders and in one of the control group. Some nail damage occurred in 9/85 workers (10.5%) of the study group. Skin damage mainly consisted of cracks on the heels or soles of the feet and may have been due to abrasion rather than paraquat exposure. The overall incidences of skin damage in this study group (23.6%) was lower than previously reported in Malaysian workers (50%).

The relatively low incidence of skin and nail damage in the paraquat-exposed workers in this study is noteworthy. Although the Sri Lankan workers wore little clothing, they washed themselves frequently in running water throughout the working day. In addition, the spray concentration used (0.04% w/v paraquat ion) was relatively dilute. These two factors may explain why paraquat absorption was very low (Gurunathan *et al*, 1990).

- **Trinidad**

A study of Trinidad sugar plantation workers who had been applying paraquat over several years at 1-2 g/L, showed fingernail damage, ranging from local discolouration to nail loss in 18.5% (55/296) of spray operators. The most common lesion was transverse white bands, but loss of nail surface, transverse ridging, gross deformity of the nail plate, and even nail loss, also occurred. Of the affected sprayers, 11 also showed minor nail damage affecting the toes. The index, middle and ring fingers of the right hand were predominantly affected: this was attributed to leakage from the sprayer. There were 2 cases of contact dermatitis of the hands. No cases of eye irritation or epistaxis were reported. The usual clothing of the sprayers consisted of shirt, trousers and gum boots.

These effects were due to negligence on the part of all concerned. Following the uneventful use of paraquat for 2 years, there had been a relaxation of applicator supervision, carelessness in day-to-day application and poor maintenance of equipment. There had also been a failure to ensure adequate hand-washing after work (Hearn and Keir, 1971).

- U.S.S.R.

According to FAO/WHO (1987),

'Similar data were obtained on several groups of workers spraying paraquat as a herbicide and desiccant in cotton fields during the hot season. These workers were exposed to paraquat aerosol concentrations of 0.13-0.55 mg/m^3 air. Dermal exposure was low, not more than 0.05-0.08 mg paraquat on the hands and face. There were no complaints, nor did the clinical and laboratory examinations of the workers demonstrate any significant deviations from the matched control groups' (Makovskii, 1972).

. Retrospective Study of Medical Records

A retrospective survey of the medical records of paraquat spraymen from 29 plantations in Malaysia and 12 plantations in the Philippines analysed injuries attributable to the occupational use of paraquat in the period 1991-1993. The records are maintained for medico-legal reasons.

Exposure to paraquat in Malaysian plantation was relatively high and continuous. The spraymen worked on average 10 months in a year. Each working month consists of 24 days, each comprising about 6 hours of paraquat application. On occasions this may have been extended to 10 hours per day. For the 2,212 workers identified in Malaysia the total number of possible working days over a 3 year period was 1,592,640.

In the Philippines, the use of paraquat is restricted to weed control in banana plantations. This use is seasonal and not as intensive as in Malaysian oil and rubber plantations. Each sprayman had a possible total exposure of 270 days in the 3 year period. For the 137 workers identified in the Philippines, the total number of possible working days over a three year period was 36,990.

The predominant mode of application of paraquat was by knapsack spraying (70%). The remainder (30%) was applied by tractor-mounted pressure-generating application systems. Workers who were exposed to paraquat during mixing/loading were also included in the study.

Paraquat-related injury to the skin was the injury most frequently recorded: 54 cases from 34 estates in Malaysia required medical treatment and accounted for 183 lost employment days over the 3 years (ie 0.01%). About half of the skin injuries were injury to scrotal skin due to leaking knapsack sprayers that trickled spray solution down the back into the gluteal and perineal regions. These injuries responded to local treatment, without other complications. In one case, paraquat concentrate splashed to the groin resulted in hospitalisation for 27 days.

In the Philippines, there were 17 cases of skin injury reported from the 187 spraymen which resulted in 47 days of lost time over the 3-year study period. One of these cases involved injury to scrotal skin caused by an accident with the concentrate. Recovery following treatment was complete. Two spraymen in the injured group of 17 experienced multiple occurrences of minor skin injury. One had 11 incidents of skin lesions whilst the other had 8 such incidents over the 3 year study period. In both cases, all of the injuries healed completely without complications.

Details of the reported injuries were:

Eye injury
In Malaysia, 47 cases of eye injury were reported from 29 plantations, 2 of which accounted for more than 443 sick days. In the other 45 cases chemical conjunctivitis was caused by spraydrift. All cases were treated successfully and recovery was complete. The total number of days lost was 134, averaging 2.9 days per incident.

The Filipino estate workers (137) experienced only 2 cases of eye injury. One was minor but the other was serious and required hospitalisation and work absence for 14 days.

Nail Damage
There were 21 cases of nail damage reported from 8 of the estates in Malaysia and 1 case in the Philippines during the 3 year period. No loss of working days were attributed to these injuries. In Malaysia the nail damage was attributed to handling of the concentrated formulation during mixing operations without the use of protective gloves.

Epistaxis
Some degree of nasal bleeding occurred in 8 of the Malaysian estates studied, involving 23 cases. Most were mild and required no absence from work. Only 7 days of sickness were recorded.

Non-specific
There were 24 complaints from Malaysian workers of non-specific adverse effects, including headaches, giddiness, nausea and vomiting. These were experienced mainly by female workers and could not be unreservedly attributed to spraying or handling of paraquat.

The medical records of spraymen in the Malaysia and the Philippines showed that, from a total workforce of 2349, there were 189 recorded cases of "surface" injury and non-specific effects, from the use of paraquat over a 3 year period. This averaged to about 2.7% of the total workforce in any one year. Not all of the incidences resulted in loss work time, nor could they unambiguously ascribed to paraquat. Apart from 2 ocular and 2 dermal injuries, the other "surface" were minor and responded to treatment (Sabapathy, 1992).

The possible association of the stench in the paraquat with the reported non-specific effects such as headache, nausea and vomiting was not discussed.

. Reported Associations of Paraquat with Some Diseases

- Paraquat, Smoking and Pulmonary Disease

Recently, a possible association between exposure to paraquat, smoking habit and chronic obstructive pulmonary disease has been reported from Colombia. In an agricultural area where the usage of paraquat represented 10% of the Colombian total, a survey of the prevalence of respiratory disease and paraquat exposure, possible and actual, was undertaken during 1986-1987.

A verbally-administered questionnaire identified socio-demographic status, degree of occupational or other exposure to paraquat and general health status, particularly in relation to the respiratory system. Exposed agricultural workers underwent a general medical examination, including measurement of lung function by spirometry. Urinary samples were collected. During actual spraying, air in the breathing zone of 14 workers was sampled for paraquat.

It was found that 11% of the population applied paraquat, predominantly with knapsack sprayers (98.4%). Of these, 71.2% reported that paraquat solution wet their bodies during spraying and the safety instructions provided by the producers or recommended by health agencies were often not being properly followed .

Results of air sampling monitoring showed that concentrations of paraquat were reportedly below the accepted Colombian level of inhalational exposure (0.5 mg/m^3). All samples of blood and urine taken from users of paraquat in this study were negative. About 7% of interviewees complained of respiratory symptoms, mostly of short duration. Of those surveyed, 33.9% of males and 11.4% of females smoked.

On medical examination chronic bronchitis (12.8%), asthma (2.7%) and tuberculosis (0.2%) was diagnosed amongst those examined. Chronic bronchitis occurred in 9/768 (1.2%) of non-users of paraquat and 14/128 (10.9%) of its users. Chronic bronchitis was more prevalent in smokers (paraquat users 13/56 [23.2%]; non-users 7/180 [3.89%]) than non-smokers (users 1/75 [1.3%]; non-users 1/497 [0.2%]). Respiratory function tests, conducted with 486 males, showed both restrictive patterns (users 6/111 [5.4%]; non-users 16/374 [4.3%]) and obstruction (users 12/111 [10.8%]; non-users 14/374 [3.7%]). Respiratory restriction occurred in smokers (users 1/45 [2.2%]; non-users 4/42 [9.5%]) and non-smokers (users 5/52 [9.6%]; non-users 2/43 [4.7%]). Obstruction occurred in smokers (users 7/45 [16.5%]; non-users [0/42]) and non-smokers (users 3/52 [5.8%]; non-users 3/43 [7.0%]).

Paraquat users reportedly suffered from obstructive pulmonary disease more than non-users and that there was an additive relationship between smoking and heavy exposure to paraquat, although the statistical significance was weak (Arroyave, 1990).

Critical epidemiological review of this study shows that respiratory diseases were not classified according to any dose-response or duration of paraquat exposure. While the data do apparently show a difference between users and non-users who smoked or did not, closer analysis shows no statistical significance in the differences between the two groups observed by a test of "significance of difference" and by the "chi-square" test. The exposure differences were largely unknown, since no data for paraquat in either blood or urine were presented. Since the duration of exposure to paraquat was not reported, it is unclear how the exposure score was obtained. Furthermore, respiratory pathology are not shown in relation to the level of exposure, except under the terms "user" and "non-user" groups. Because of these methodological uncertainties, further studies and data would be needed to prove or disprove the hypothesis of this study that chronic lung disease was associated with paraquat exposure in Colombian agricultural paraquat applicators who smoked (Lo, 1993).

- **Parkinson's Disease**

Reports that 1-methyl-4-phenyl-1,2,3- tetrahydropyridine (MPTP) induced Parkinson-like symptoms in man and some animals (Burns *et al*, 1983; Langston *et al*, 1983) gave rise to some concern that other substances, including 4, 4'-bipyidyl derivatives such as paraquat, could act similarly (Snyder and D'Amato,1985; Borccheta and Corsini 1986; Sanchos-Ramos *et al*, 1987). This proposal was challenged (Lewin, 1985; Koller, 1986). Although a correlation between the prevalence of Parkinson's disease and the volume of pesticides sold in Quebec (and also with heavy industry in urban regions) was reported in 1986

(Barbeau *et al*, 1986), a recent case-control study of occupational and environmental risk factors in Parkinson's disease did not find an association with any pesticide exposure (including paraquat and diquat) during handling or spraying (Hertzman *et al*, 1990).

A follow-up study of persons with dermal exposure (3) or who had ingested paraquat (4) found no evidence of Parkinsonism (Zilker *et al*, 1988). Experimental studies designed to produce MPTP-like signs in animals with MPTP analogues, including paraquat and other 4,4'-bipyridilium compounds, were negative and the number of chemical structures which can act like MPTP is limited (Bachurin *et al*, 1991). The suggestion that paraquat would give rise to MPTP-like symptoms in man seems to have little support from experiment or experience in use.

Objective 2

Evaluate the effectiveness of existing programmes aimed at reducing the risks and negative health impacts of paraquat and make recommendations for the future which would improve conditions of use and reduce associated health hazards

General Considerations

From the available information, it is clear that considerable attention has been paid to defining and addressing problems of occupational exposure and amelioration of accidental paraquat poisonings. The vexing problem of the use of paraquat for suicide has been less well defined. This may be because it is inherently more difficult to address and perhaps because it has not been a particular problem in many countries.

The principal strategies adopted to reduce the risks and negative health impact of paraquat, alone or in combination, are:

- modification of formulation packaging and labelling;
- regulatory response;
- improved case identification and analysis;
- study of occupational exposure, definition of working practices and required improvements; and
- education of users, handlers and the public of the hazard and safe use of paraquat.

Available information on these strategies is evaluated in turn.

. Modification of Formulation, Packaging and Labelling

- Formulation

Paraquat has long been available as a 20% liquid concentrate for general agricultural use and in the U.K., at least, in granular form for home garden use.

In response to reports of poisoning with paraquat, a programme of investigation of alternative paraquat formulations has been undertaken.

- Addition of Dye, Stench and Emetic

Since the early l970s numerous avenues have been explored in an attempt to reduce the ingestion hazard of paraquat formulations. An emetic, a stenching agent and a blue dye were added to reduce accidental poisonings where ingestion is usually low but potentially fatal. Whilst of probable benefit in marginal suicide cases, it was recognised from the outset that these measures would not deter a determined suicide attempt.

- **Efficacy of the Emetic**

The efficacy of the emetic in paraquat formulations has been well investigated by the U.K. NPIS. During 1980-1988 some 256 cases who had consumed either the paraquat liquid concentrate or the granular formulation during which did or did not contain the emetic were studied.

Some relevant findings were that:

- those who had ingested the home-garden product containing an emetic were more likely to have vomited than those who had ingested granular paraquat without the emetic;
- there was no difference in the incidence of vomiting in patients taking liquid paraquat concentrate with or without the emetic but the emetic was associated with earlier vomiting; and
- the mortality rate for patients taking the "emeticised" product and vomiting within 0.5 h had a lower mortality rate than those vomiting later than 0.5 h (9.4% compared to 17%).

Unexpectedly, the overall mortality rate for those ingesting the liquid concentrate containing the emetic was slightly greater than the mortality rate for patients taking the product without the emetic (80.6% compared to 70.4%). Patients who vomited within 0.5 h had a lower mortality rate than the group who vomited at any other time.

The presence of the emetic seemed thus to confer only a very small advantage among patients ingesting less than 2 g of paraquat. Patients who had ingested the liquid concentrate tendered to have consumed a greater amount of paraquat, usually more than 5 g. The mortality rate (66%) was correspondingly higher than those who ingested the domestic granular product (11.6%).

In conclusion, the presence of the emetic in paraquat concentrates may have value in preventing serious poisoning, particularly when lesser amounts are taken. As the emetic does not seem to increase the toxicity of paraquat and, as there is no more effective means of preventing paraquat poisoning, it should continue to be used (Volans *et al*, 1993).

- **Dilution**

The possibility of dilution of paraquat concentrate has been investigated extensively. In order to render paraquat solutions relatively safe, if accidentally ingested, it would be necessary to dilute the 20% concentrate formulations to 1-2% w/v. However, this would not address the full range of suicidal ingestion, since several hundred millilitres of the concentrate are often taken in suicide and ingestion of up to a litre has been reported. Experience in Western Samoa has been that working dilutions of 0.5% or less can be taken for suicide, although with a better survival rate than for the concentrate, as would be expected.

Zeneca considered that marketing a paraquat solution, diluted to 1-2%, was impracticable and would so increase transport and handling costs that it would make the product not viable economically.

In 1986, a new formulation with reduced paraquat concentration (4.5%) and added diquat (4.5%) was introduced in Japan in response to a high incidence of paraquat suicide. The effect of this formulation modification of the paraquat-related mortality incidence was subsequently investigated. A series of 174 cases of paraquat/diquat poisoning 1987-1988 were compared with 111 cases of poisoning due to the original paraquat concentrate, containing 20% w/v paraquat.

In both groups, approximately 60% of the patients died from circulatory failure, accompanied by multiple organ failure, within a week of ingestion. Significantly, there was no difference in the overall survival rate of the two groups. There was, however, a noticeable reduction in the late-occurring deaths (6.3%) in the "new" product group compared the mortality (17.3%) of the group who consumed the paraquat concentrate. Accidental ingestion of the new product did not cause death. The dilution and partial replacement of paraquat with diquat improved the survival rate but mostly in cases where relatively small amounts were ingested (Yoshioka *et al*, 1992).

Thus, clinical course of acute poisoning, dilution and partial replacement of paraquat with diquat influenced the pattern of mortality but had little effect on the overall mortality rate. The extent to which the subsequent decline in the incidence of paraquat suicide in Japan after 1986 may be attributable to this formulation change is not clear.

- **Granular Formulation**

Granular formulation of paraquat 2.5% in combination with diquat or another herbicide were developed for home garden use. Even though the granules must be dissolved to be easily swallowed and are packed in sachets containing less than a lethal dose, the granules are still sometimes used for suicide. Nonetheless, the prognosis of taking a solution made from the granules is better than ingestion of the concentrate (Proudfoot *et al*, 1987).

According to Zeneca, the granular formulation is too expensive for general agricultural use.

- **Thixotropic Formulations**

Thixotropic formulations have been investigated but discarded due to technical difficulties in control of quality and undesirable temperature effects.

Particular attention has been given to the formulation partly disclosed in 1987 and said to be a promising advance for the reduction of paraquat poisonings by ingestion (Naito and Yamashita, 1987). It was reportedly a novel non-swallowable formulation of paraquat which had been developed jointly by Tsukuba University and SDS Biotech K.K. The formulation contained a natural thickening agent which reportedly made it difficult to swallow a lethal dose of paraquat solution.

The proposed formulation was investigated by ICI/Zeneca in recognition that if its claimed properties could be reproduced or extended, it could offer improved safety in cases of paraquat ingestion. After considerable evaluation and examination of the commercial aspects it was determined that the product was not viable commercially. Particular problems identified were:

- the dustiness of the formulation;
- the poor sprayability characteristics of the diluted formulation, including aggregation and clogging of spray nozzles;
- the experimentally determined reduction in toxicity of the formulation was less than had been claimed; and
- the questionable benefit of the new formulation as compared to the then newly introduced "Preeglox L" formulation.

- **Emulsions**

Paraquat-containing emulsions have been extensively investigated. Paraquat emulsion yielded only a slight reduction in acute toxicity, however, a formulation with adequate sprayability characteristics could not be obtained. Problems of storage stability were also encountered.

- **Molecular complexes**

Investigation of charge-transfer complexes of paraquat were unrewarding in terms of improved safety.

In Zeneca's view, every possible formulation modification that could reduce the hazard of paraquat by ingestion has been investigated. Accidental poisoning had been largely addressed through the addition of the dye, stench and emetic. The problem of suicide by paraquat ingestion is seen as a social one not easily amenable to control and beyond the reach of the manufacturer.

. Regulatory Response

From a regulatory viewpoint, there is good evidence to show that once an agent has gained notoriety for successful suicide use, restriction of its availability can reduce its use for that purpose. Often quoted examples are the replacement of coal gas by natural gas and the restriction of availability of barbiturates (Lester, 1986).The aetiology of suicide varies between societies for social, cultural and religious reasons at least.The reported effectiveness of measures for reduction of paraquat poisonings taken in western countries, therefore, may not have immediate relevance in developing countries if equally toxic alternatives are readily available. For example, restriction of availability of the insecticide, endrin, which was a favoured agent for suicide in Daspur, West Bengal, did not reduce the local suicide incidence (Nandi *et al*, 1979).

Paraquat formulations are restricted to certain classes of users or for certain applications in some countries. The following indicates the regulatory situation in several countries where paraquat poisoning has been a problem.

- **Republic of Ireland**

In 1968, paraquat, previously on open sale, was scheduled as a poison. It became illegal to sell it except in the manufacturer's original sealed container, which had to be clearly labelled as a poison. Only dealers licensed under the Poison's Act could sell it. Decanting of the liquid became illegal. It remained relatively easy for the general public to buy paraquat from licensed dealers.

As a complimentary measure to restrict the availability of paraquat, the manufacturer reduced the number of retail outlets from 510 to 80 in 1970 and wrote to all farmers in the country stressing the danger of farmers or dealers decanting "Grammoxone" into containers other than the original one.

Despite these measures, poisoning by ingestion of paraquat concentrate from unlabelled containers continued to occur.

In 1975, further regulatory restrictions over the sale of paraquat were introduced. The sale of paraquat was restricted to persons "engaged in trade or business of agriculture, horticulture or forestry" who required the poison "for the purpose of that trade or profession". This restricted public access to paraquat. Furthermore, the product labelling was changed to incorporate specific information about the hazards of paraquat. However, these regulatory restrictions were not applied to paraquat granules which remained on free sale to the public.

Subsequently, there was a real reduction in the number of accidental paraquat poisonings and deaths after 1975 with a lesser reduction in the number of suicides attempts and deaths. The extent to which these reductions resulted from or were co-incident with the regulatory changes was unclear (Fitzgerald *et al*, 1978b).

Subsequent data show that the paraquat poisoning incidence in Eire peaked in 1977 and declined erratically thereafter. It remained significantly higher than the rate for England and Scotland (Onyon and Volans, 1987).

- **United Kingdom**

Similar regulatory measures to restrict the availability of paraquat concentrate to *bona fide* users through control of its sale, supply and use were introduced in the U.K. in response to the increasing incidence of paraquat poisonings that began in the early 1970s.

Some of these cases involved children and, although they were few in number, they attracted considerable publicity. This publicity, in turn, gave paraquat a reputation as '...lethal poison with no known antidote...' and, by so highlighting paraquat's toxicity, encouraged its use for suicidal purposes (Whitehead *et al*, 1984).

Currently, in the U.K., the sale of paraquat is subject to the Poisons Act 1972, the Poisons List Order 1982 and the Poisons Rules 1982. These Rules includes general and specific provisions for the storage and sale and supply of listed non-medicinal poisons.

Paraquat is specified under Part 11 of the Poisons Rules, which restricts its sale to registered retail pharmacists and listed sellers registered with the local authority. There is a specific exemption for pellets containing not more than 5% paraquat ion from the Poisons Rules, which allows for the sale of paraquat (e.g. 'Weedol' granules) to the home and garden market.

Under the Rules, the following regulations must be observed by:

- the name of the final seller and any deputies must be entered with the local authorities, to be included in the list of authorised sellers. The process by which this is achieved is set out in Schedule 8 of the Rules;
- a record of the sale of any listed poison must be kept, as set out in Schedule 11 of the Poisons Rules and entries must be signed by the purchaser;
- the purchaser must be known to the final seller. If the purchaser is not known to the seller then the purchaser must present a certificate, signed by the police, authorising the purchase. The format of the certificate is set out in Schedule 10 of the Rules; and
- the use of the product must accord with the limitations in Schedule 3 ie Agriculture/Horticulture/Forestry sectors.

"Consents", given under the Control of Pesticides Regulations 1986 govern the advertisement, sale, supply, storage and use of pesticides in the U.K. These "consents" apply to all pesticides (ie not just those subject to the Poisons Rules). Consent B requires that no person shall sell, supply or otherwise market to the end-user a pesticide approved for agricultural use unless he has obtained a certificate of competence recognised by the Ministers. Consent C covers the use of pesticides, and requires anyone born after 31 December 1964 to hold a certificate of competence recognised by Ministers, which are available from the National Proficiency Tests Council, when applying agricultural, horticultural or forestry pesticides, unless the application is to his (or his employer's) own land.

The regulatory restrictions taken in the U.K. on the availability of paraquat were complimented by modification of pack sizes and the addition of an stench and blue dye to the concentrate and granular formulation. The emetic was added in 1979 following testing in experimental animals (Whitehead *et al*; 1984).The emetic was added to improve the prognosis in cases of accidental poisoning in which the amount of ingested paraquat was usually significantly less than in cases of suicide. These measures were intended to alert the unwary to the hazard of paraquat ingestion. It was recognised from the outset that they offered little to influence the outcome of determined cases of self-poisoning..

From 1981 onwards there has been a continuing decline in the annual number of paraquat deaths (41 in 1980 to 13 in 1988) with a corresponding decline in the percentage case annual mortality (30% in 1980 to 10% in 1988).The annual number of adult exposures peaked in 1982; the subsequent decrease has been such that the number of reports in 1988 was almost the same as in 1980. The annual number of childhood incidents peaked a year later, in 1983, and also subsequently declined (Northall *et al*, 1993).

Whilst the decline in paraquat poisonings in the U.K. since the early 1980s may be linked to a changed pattern of suicidal poisonings in that country, the regulatory restrictions on the availability of paraquat products, the active interventions by ICI and others to restrain inappropriate media publicity, the increased education about the hazard of paraquat ingestion and the improved training in its safe use, should have all contributed to this welcome decline. It is not possible to gauge the effect of any of these factors in isolation.

- **Japan**

Regulatory measures to restrict the availability of paraquat concentrate to *bona-fide* users through control of its sale, supply and use were introduced in response to the increasing incidence of paraquat poisonings that began in the early 1970s.

Information from the Japanese Ministry of Health and Welfare is that there are two paraquat liquid formulations currently registered in Japan for agriculture use, namely 20% paraquat liquid concentrate and another formulation containing a mixture of 4.5% paraquat with 4.5% diquat.

In November 1985, the Bureau-of Drugs, Ministry of Health and Welfare and the Bureau of Agriculture and Horticulture, Ministry of Agriculture Fisheries and Food, notified pesticide retailers of new regulatory controls over pesticide sales. Increased security against theft of agricultural chemicals was required and that the identity of purchasers of paraquat would be required to be recorded.

A modified herbicide formulation, containing a reduced concentration of paraquat and diquat, was introduced. The agrochemical trade subsequently developed a guideline for the handling and safe use of pesticides.

There was a subsequent decline in the number of incidents involving paraquat poisoning (Matsuda, 1993).

- **Malaysia**

In 1985, the Malaysian Pesticides Board approved the addition of a blue dye and a stench (pyridine derivatives) to paraquat formulations as a warning against accidental ingestion. An emetic could also be added but was not mandatory.

In more recent times, the Pesticides Board has rationalised the number of registered pesticide products. The number of registered concentrations of paraquat that can be present in registered products is being reduced from 18 to 3 (i.e., 200 g/L, 150 g/L and 100 g/L).

Current pack sizes and their distribution are:

- 1 L (6-7%); used by smallholders;
- 4 L (55-60%); used by more general smallholders;
- 20 L (8-10%); used by contractors and larger smallholders; and
- 200 L (15-20%); used by plantations.

The labels of paraquat-containing products had been improved to give clear multilanguage directions, warning statements and colour coding.

Board officials considered that the rationalisation of the available pack sizes of paraquat has decreased the incidence of accidental poisonings arising from the decanting of paraquat into inappropriate containers such as soft drink bottles. Additional restrictions on the availability and use of paraquat under the "Highly Toxic Pesticide Regulations" have been under consideration for some time.

. Improved Case Identification and Analysis

- United Kingdom

The U.K. NPIS has arguably the most comprehensive system for identification, recording, analysis and monitoring of paraquat poisoning data. It has monitored reports the acute toxicity of paraquat since its introduction in the 1960s and, from 1980 onwards, has conducted an toxicovigilance study of paraquat poisonings in collaboration with ICI/Zeneca. A high degree of ascertainment paraquat poisonings has been achieved. This has allowed detailed analysis of poisoning trends and provided the capacity to interpret the outcome of measures taken to ameliorate poisoning by paraquat.

- Malaysia

As previously described, the Ministry of Health has taken steps to improve its data collection on pesticide poisonings in order to formulate appropriate response to issues such as paraquat poisoning. It has also improved the education and training of its personnel engaged in pesticide application in public health programmes.

- Pacific Islands

Paraquat poisoning has been a significant problem in Papua New Guinea and some other South Pacific countries, particularly Fiji and Western Samoa.

In 1986, the South Pacific Commission commissioned a study on paraquat poisoning amongst some of its member countries where self-poisoning with paraquat was a common means of suicide.

In Western Samoa, most of the increase in paraquat poisoning occurred in young adults. In the decade 1975-1985, about 80% of the deaths occurred in the 15-35 year age group. The majority of deaths were clustered in a minority of the villages, with 19 villages accounting for half of the total suicides in the period 1966-1985.

The precipitating event in half of the cases was a scolding or rebuke, often (55%) involving one of the victim's parents. There was a correlation between the number of figures of authority (*"matai"* or *"chiefs"*) in a village and an increased suicide incidence.

The following factors were advanced to explain these observations:

Parent-Child Conflict
According to traditional Samoan values, it is unacceptable for a youth to express anger towards those in authority, including parents. The young Samoan's response is resistance, withdrawal and sullenness which may lead to a suicide attempt in order to influence the parent's attitude. Furthermore, domestic conflict can lead to emotional and impulsive behaviour which, with the ready availability of a lethal agent (paraquat), can also lead to suicide. Many of those poisoned later regretted their action.

Lack of Power or Opportunity
Recent demographic, economic and social changes have frustrated opportunities for upward social mobility amongst the young. Opportunities for emigration have also been curtailed in recent years.

Imitation
The phenomenon of "suicide contagion" has been recognised in western societies. The spread of suicide as an adolescent fad in Western Samoa is suggested by the rapid rise of suicide in an adolescent group and the clustering of suicide cases in a small proportion of villages (99 out of 360 villages).

Culture in Transition
Western Samoan culture is in transition between the traditional Polynesian model and the modernised and urbanised Samoan communities found in New Zealand, American Samoa or the US mainland. This transition imposes additional stressors on the culture and the youth sector (Taylor *et al*, 1985).

It was recommended that data collection on paraquat poisoning be improved, that the actual circumstances of each poisoning be investigated and that the importation, sale, labelling and use of paraquat be controlled.

For suicide prevention purposes, it was recommended that publicity be given to the toxicity of paraquat through a "public awareness campaign". Further, the reporting of suicide incidents in a sensational manner should be discouraged. It was further recommended that, in any cost-benefit analysis of competing herbicides that the human cost of paraquat-associated deaths should be taken into account. Restriction of the use of paraquat and use of alternatives was recommended for those countries where paraquat poisoning was a significant problem (Taylor *et al*, 1985).

As a further response to this problem, the WHO Regional Office for the Western Pacific engaged a consultant psychiatrist to review the prevailing psychosocial-mental health problems of American Samoa, Samoa and the Cook Islands.

The consultant confirmed that in Western Samoa suicide predominated amongst young people aged, 15-24 years and that paraquat poisoning was the predominant means chosen. In some years, more that 90% of deaths were due to paraquat poisoning. The total number of attempted self-poisonings with paraquat in 1973-1990 was 583, with 277 fatalities (47.5%). Both totals were considered likely to be underestimates of the true situation. Whilst these findings were largely in keeping with the known international increase in youth suicide and the use of agricultural chemicals for suicide in developing countries, the relative high incidence rate was remarkable.

An apparent temporal correlation between the availability of paraquat and suicide incidence was identified, with the suicide incidence falling when paraquat was less readily available. Significantly, paraquat spray "residues" (ie the working dilution left over from previous spraying) were identified as being commonly use for suicide.

In summary, the consultant advised that:

- the availability of paraquat concentrate and diluted spray solution to potentially suicidal people should be further restricted;
- consideration be given to the use of less toxic herbicides;
- paraquat should be sold in smaller containers to reduce the availability of unused working dilution;
- the purchaser of paraquat should be required to sign a declaration of responsibility for its safe use and storage;
- the unlocked storage of paraquat "residues" should be discouraged;
- the availability and use of training and materials for the emergency treatment of paraquat poisoning should be maintained; and
- a poisons information centre should be established.

Some of the above measures had already been unilaterally introduced by the marketer of paraquat.

Noting that experience elsewhere had demonstrated that, where a method of suicide or demonstrated self-harm had become frequent and notorious, then useful reductions in total suicide numbers could be made by restriction of that method. In these terms, the consultant advocated restriction of the availability of paraquat in Samoa.

The relatively low mortality rate being encountered in Western Samoa, despite the toxicity of paraquat, was attributed to :

- ambivalence towards the suicide act so that the person spat out the poison or ingested a relatively small amount;
- ingestion of dilute paraquat spray solution; and
- prompt, appropriate and effective first aid and medical management.

The following factors were recognised in relation to the psychosocial aspects of suicide in Western Samoa:

- the restricted "life opportunities" of the youth population;
- work pressure and strong familial expectation of service, devotion, obedience, achievement and restraint of impulses;
- financial difficulties;
- frustration with difficulty in emigrating to another, richer, country. (Significantly, the suicide rate in those Samoans who had emigrated appeared to fall);

- adolescent impulsiveness, a potent shame response to exposed misdemeanour and a need to feel valued and recognised, all of which can provoke a suicidal crisis at times of stress;
- the disinhibiting role of alcohol; and
- the ready availability of a potent and notorious suicide agent, paraquat.

In the shorter term, the consultant recognised the efforts that were aimed at suicide prevention including, exhortation by the media, churches, health educators, schools and suicide study groups. First aid kits containing Fuller's Earth had been widely distributed to district hospitals and villages and training in their use had been given.

For the longer term, the consultant believed that education offered the most effective means to improve the lot of the Samoan people and to address the problem of suicide in the longer term. He recommended:

- that the local "Suicide Awareness Committee" be strengthened;
- collection of reliable poisoning incidence data continue;
- due attention be paid to those at high risk of suicide;
- unused paraquat working dilution "residues" should be safely managed;
- continued availability of complete first aid kits for treatment of paraquat poisoning should be ensured; and
- the introduction of a supplementary herbicide to reduce the frequency of paraquat use.

In more general terms and based on his knowledge of overseas experience, he further advised that:

- media reporting of suicides should be circumspect, factual and avoid sensationalism;
- the community should be encouraged to be aware of and respond to appropriate information about suicide and/or demonstrated self-harm;
- efforts should be made to gather intelligence about suicide and/or demonstrated self-harm elsewhere in the Pacific region;
- communication within family groups should be recognised as an important factor in the generation of interpersonal tensions;
- recognition of warning signs of psychological distress should be encouraged;
- an effort should be made to locate, and study the seriousness of, previous suicide and/or deliberate self harm attempts as these people are at high risk of repeating their suicide attempt; and
- survivors of paraquat poisoning should be examined for abnormal respiratory function and any other sequelae of poisoning (Bowles, 1989; Bowles, 1991).

There is no information presently available to indicate whether or not these proposals have been implemented and/or their degree of success.

- Other Countries

Whilst other national authorities undoubtedly maintain poisons registers, there is little in the open literature to permit assessment of recent trends in paraquat poisoning in individual countries and, more particularly, in those countries where paraquat poisoning has been a particular problem.

The lack of good statistical data on acute pesticide poisoning is a significant problem in developing countries (Jeyaratnam, 1990). This is unfortunate because the collection and maintenance of accurate poisoning statistics can do much to focus attention upon local problem, assist in formulation of an appropriate response provided motivation for its implementation and enable monitoring of the outcome.

. Occupational Exposure and Working Practices

- Occupational Exposure to Paraquat

Studies of occupational exposure to paraquat have been reviewed and summarised in Chapter 1. These studies show that, even under conditions of prolonged exposure under tropical conditions, paraquat working dilutions can be applied safely provided appropriate working practices are followed and due care is paid to personal hygiene. The handling of paraquat concentrate is more hazardous and requires more care, particularly eye protection.

Measures for personal protection and hygiene when handling and using paraquat have been elaborated (IPCS, 1991a). Most of these are common to the handling of most chemicals, but the particular recommendations for paraquat are:

- avoid all contact with skin eyes, nose and mouth when handling concentrated paraquat. Wear PCV-, neoprene- or butyl-rubber gloves (preferably gauntlet form), neoprene apron, rubber boots, and face shield;
- wear a face-shield when handling and applying the diluted formulation; and
- immediately remove heavily contaminated clothing and wash underlying skin.

The procedures for safe handling and application of paraquat solutions are not onerous; that applicators can be instructed and trained in its safe use routinely. Thereafter supervision is required to ensure that proper procedures are followed. Adequate facilities for first-aid and decontamination, particularly clean water, should be provided. All should be made aware of the hazard of paraquat concentrate to the eye and by ingestion and also of the need for prompt attention in such cases. The extent to which proper procedures are actually followed in practice will, of course, vary and so should be reinforced and supervised as far as practicable.

- Surveys of "Smallholder" Exposure to Paraquat

WHO has identified "smallholders" as a group of farmers exposed to "very high doses" of agrochemicals due to their using them "under primitive field conditions with insufficient protective equipment and training" (WHO, 1990). The working practices of independent "smallholders" and their pesticide application practices have not been nearly so well defined as for those employed for herbicide application. Yet, smallholders are assuming an increasing proportion of the farming population of many developing countries.

Since the mid 1980s, ICI/Zeneca has conducted surveys of "smallholder" knowledge, attitude, practice in paraquat use, education and training in Brazil, Colombia, El Salvador, Guatemala, Honduras, Malaysia and Thailand. The principal objective of these surveys was to identify priorities within the range of "smallholder" pesticide use practices that could be improved through education and training. Most aspects of paraquat use were explored, including the incidences of ill-effects associated with its use. In brief, this strategy involves:

- baseline assessment of standards in handling and use of pesticides;
- education and training in safe handling and use, focussing upon identified local needs; and
- monitoring of impact of education and training with adjustment to programmes as required.

This integrated approach is described in detail at Appendix 5.

Brazil
The use of paraquat by Brazilian banana (300) and vegetable smallholders (200) was surveyed during 1988 and 1989 in areas where its usage was high. Most of these banana and vegetable smallholders had been using paraquat for some time, typically 7-9 years.

There was a relatively high awareness of the risks associated with ingestion of small quantities of paraquat concentrate but some 19% of vegetable growers were ignorant of its hazards.The use of personal protective equipment and personal hygiene were generally adequate for the safe use of diluted paraquat but the proportion of smallholders utilising eye protection and gloves during mixing was low. Problems with sprayer maintenance, measurement of paraquat concentrate and disposal of used containers were identified. The procedure for the storage of paraquat concentrate was generally good. The incidence of ill-effects associated with paraquat's use was generally low but was higher amongst banana growers, possibly due to higher weeds and longer continuous working exposure.

The results of this study show the need for education and training of smallholders, even amongst well established users (Whitaker and Ramos, undated).

Central America
In 1987, a survey of the standards applying to the use of paraquat herbicides by small-scale maize farmers in Guatemala, El Salvador and Honduras was conducted. These farmers have incorporated paraquat into their corn farming practice to a high degree. Generally, they did not experience serious problems

from paraquat exposure and were relatively well informed in terms of the conditions for its use. Where ill-effects were experienced they were limited to irritation to the skin, generally the hands and arms. Irritation of the back was also reported in El Salvador and Honduras. The adverse effects of paraquat on fingernails was also evident in each country (Whitaker, 1989).

Dominican Republic

During 1992, the use of paraquat by smallholder farmers producing plantain, rice, potato, coffee beans was surveyed in the Dominican Republic. The smallholders (740) had several years' experience in working with paraquat products which they had fully integrated into their weed control systems. Most smallholders were well aware of the toxicity of paraquat, particularly its hazard if swallowed. They generally exercised adequate standards of care in its mixing and spraying as well as in their personal hygiene afterwards. As found elsewhere, smallholder farmers in the Dominican Republic confused the relative risks of mixing and spraying paraquat. Most wrongly believed that spraying carried greater risk than did mixing and many thought that it was important to minimise contact with the product at either stage. Very few considered that there were no risks with spraying or mixing. Some (11%) considered that, because paraquat "burned" the vegetation to which it was applied it was "more powerful" and hence more hazardous than insecticides. This in turn, encouraged greater care in its application. Others thought it was more dangerous than insecticides for other reasons.

One area of concern was the use of small children to spray dilute pesticides in some cases and their utilisation in spray-support activities, such as transporting water, filling of sprayers and helping to clean them after use as well as the movement of portable sprayers. This work can be contaminating for both the spray operators and their assistants should not be left to untrained operators or to minors.

The incidence of ill-effects attributed by smallholders to the use of paraquat was low in all sectors. In most cases, the paraquat was pre-mixed in large (200 L) drums before application. The survey indicated that contamination most frequently occurred of the hands but also of the eyes as a result. Most smallholders took appropriate action following contamination by washing immediately or as soon as possible. However, there was a minority of farmers who said they would ignore any bodily contamination, particularly if it was on their hands. The need for education in training in sprayer maintenance, pesticide storage and proper disposal of empty containers was apparent from the study (Manon and Whitaker, undated a).

The above study also identified some of the constraints to improvement of the standard of pesticide use in the Dominican Republic. The large smallholder population of the Dominican Republic (over 1 million) is mostly independent of any form of group organisation which would facilitate effective communications about pesticide safety and use. External sources of advice, including the network government and private sector advisers, were limited in their penetration of smallholder communities. Regular sources of information on pesticides do not usually influence smallholders. Government and private extension networks as well as pesticide outlets are useful but other sources of other information on pesticides are of minor importance. Most smallholders place greater reliance on their own experience or the experience of their neighbours rather than external sources of information. Literacy rates were relatively high, despite poor educational levels, being supplemented by family assistance. Comprehension of product labels was low and they were often not read, regardless of the level of literacy and despite recent improvements to label design. Comprehension of pictograms was better in areas where there had been previous education in their use. Despite a long established scheme for colour banding of pesticide containers as an "alerting" mechanism to the degree of hazard, most farmers could only recognise red as denoting the most toxic pesticides. The media, radio and TV, had only a limited role in communicating pesticide safety information. The authors identified Government extension officers and pesticide retailers, and an extensive network of rural teachers, paramedics and, to a lesser extent, doctors as a resource of people who had the potential to communicate safety information (Manon and Whitaker, undated b).

Ecuador

An independent study, conducted in 1984, of 238 Ecuadorean farmers, farm workers, store owners, medical personnel and students, including a subset of 111 regular pesticide users, reached similar conclusions about the need for improved education and training. Some 23 different pesticides, ranging from DDT to paraquat to methyl parathion were identified and were applied mostly by backpack sprayers (91%), although some were applied by hand. Few farmers owned protective equipment and most did not use available equipment for reasons of cost, unfamiliarity and/or impractibility in tropical conditions.

Questioning of the pesticide users showed that whilst nearly 59% (59/105) claimed to recognise symptoms of pesticide poisoning, 43% were unable to identify any correctly and 52% could only correctly identify 1 to 3 symptoms of poisoning. In general, 1 in 5 were unsure if they had experienced any common symptoms of pesticide poisoning. Nearly 70% believed that pesticides could make them ill but that they themselves were not in any danger. With regard to modes of poisoning, all recognised that they could be poisoned by ingestion, 81% believed they could be poisoned by inhalation ("smelling") the pesticide but only 64% believed they could be poisoned by dermal exposure ("touching") a pesticide.

The ready, unregulated availability of pesticides, the lack of safety equipment and ignorance of basic facts on pesticide use and safety all created conducive conditions for poisoning. Regulatory control, safer alternatives and the education of all handling pesticides in their safe use was called for (Grieshop and Winter, 1989).

Malaysia

In 1987, a survey of paraquat use by smallholders in Peninsular Malaysian rubber and oil palm producers was undertaken. The sample population of over 400 smallholders, both rubber and oil palm farmers was in proportion to their relative numbers in States where use of paraquat was widespread, namely Johore, Perak, Kelantan and Pahang.

The rubber and oil palm smallholders were found to have considerable experience in the use of paraquat, having applied it, on average, for over ten years. They were well aware of the potentially fatal consequences of swallowing small quantities of paraquat. However, many smallholders even held the popular but mistaken belief that spraying dilute paraquat was of equal or greater hazard than handling and mixing the concentrate.

Most smallholders were aware of the need to wash concentrated paraquat from the skin should spillage occur. Most claimed to wash their hands following the mixing of paraquat, whether or not any spillage had been noticed. Whilst this finding suggests that adequate hygiene practices were generally being followed, results from the survey show that few smallholders wore protective gloves or eye protection when handling the concentrate, mostly because they could not see the need and thought the use of protective equipment during dilution of paraquat inconvenient and uncomfortable.

The survey found that the clothing usually worn during the application of diluted paraquat, typically consisting of long-sleeved shirts, long trousers and rubber boots or shoes was adequate for the purpose. There appeared to be widespread recognition of the need to wash both spray clothing and the body after each day's spraying.

Most smallholders surveyed had not experienced ill-effects that they associated with the use of paraquat. Those ill-effects that had occurred were mostly rashes on the hands and feet.

The survey results demonstrated the relatively low frequency and intensity with which Malaysian smallholders use paraquat. This, together with the general adequacy of their hygiene practices, contribute to the relatively low incidence of ill-effects associated with its use across all locations and racial groups.

Nonetheless, the storage of paraquat, was found to be largely improvised as was the disposal of used pesticide containers. This left much scope for improvement as did the handling of the concentrate. These findings and the occurrence of even mild skin injury and the potential hazard of improper container disposal supports the need for continuing education and training programmes in the safe use of paraquat and other pesticides (Whitaker, 1989).

Thailand

A survey was conducted by questionnaire of 732 Thai smallholders in the lowland areas of Eastern, Western, and Southern Thailand where there is extensive use of paraquat in a wide range of annual and perennial crops, particularly maize, cassava, fruit and rubber. Most of the smallholders have used paraquat for several years and successfully integrated it into their weed control practices for different crops. In all crop sectors, most farmers (98%), were quite aware of the fatal consequence of the ingestion of even a small amount of paraquat. Most farmers believed that it was equally important to avoid contact with both paraquat concentrate and its dilution. However, a higher proportion of smallholders wrongly believed it was more important to avoid contact with the diluted product during spraying than to avoid contact with the concentrate.

Most Thai smallholders made 1 to 2 applications of paraquat in each crop cycle. In the maize and cassava sectors, average annual use was approximately double those in fruit and rubber.

There were differences in the manner of preparing paraquat for spraying. Some smallholders premixed the paraquat in large (mostly 200 L) drums before transferring the diluted solution to knapsack sprayers, thus predisposing to greater dermal contamination. Others, particularly the cassava, fruit and rubbers growers, tended to dilute the concentrate in the sprayer apparatus.

Reported levels of skin irritation were higher among maize growers than in other sectors. This was attributable to higher levels of contamination and lower levels or personal hygiene. Problems of sprayer maintenance were identified, particularly amongst maize and cassava producers. Lower standards of personal hygiene in these producers were also apparent. Encouragingly, most smallholders recognised the danger of clearing blocked sprayer nozzles by blowing from the mouth and tendered to use a wire or needle.

Most farmers (66%) had not experienced any problem that they associated with using paraquat. The most frequent complaint of ill effect attributable to the use of paraquat was that of nausea "from the smell" of the stench in the concentrate. In maize growers, relatively high levels of skin irritation also occurred. Some 30% of farmers had noticed adverse effects that were not thought serious enough to warrant medical consultation. Two people in the maize and 1 person in the cassava sector said they had been hospitalised due to paraquat poisoning. While ill effects cause few people to seek medical attention, in some cases (16%) they cause respondents to stop work, mostly for one to two days. Measures for the reduction of dermal contamination, particularly in maize farmers, with paraquat warrant investigation.

Problems were identified with disposal of empty paraquat containers, as farmers tendered not to destroy them by burning or burying them as recommended. There was a high degree of container recycling, particularly amongst maize producers but also amongst cassava and fruit growers, although the great majority of the smallholders recognised that this was poor practice. In most cases it did not involve the storage of food or water.

There is considerable room for improvement in the storage of paraquat on Thai smallholdings. While most farmers recognised the importance of keeping children and, to a lesser extent, foodstuffs, away from pesticides, their storage methods were usually improvised. Although most tended to purchase paraquat and other pesticides as required and did not regularly store them around their home, sizeable minorities did so. Places chosen for such storage were often inside houses at floor level, although the maize, cassava, fruit and rubber farmers tendered to store pesticides outside under or away from their homes. The principle consideration in selection of a storage site was to keep the pesticides away from children but in relatively few cases were the storage sites locked. Separation from farm or domestic animals, food and drinking water were secondary considerations.

This information again justifies measures to improve storage on smallholdings through education and training (Whitaker *et al*, 1993).

As the adverse effects and practices described in these surveys are based upon self-reporting rather independent investigation, they are prone to the respondent bias usually expected in surveys studies and also from a lack of a comparative control group responses. They do, nevertheless, illustrate contemporary agricultural practices and help to identify those most in need of correction.

. Education of users, handlers and the public on the safe use of paraquat

Available information consistently points to the need for education and training of all of those who handle, store and use paraquat about its hazards and how it can be used safely. To be effective, such education should address the local problems and conditions and be expressed in a manner compatible with local customs and agricultural practice. Studies of smallholder practices, attitudes and needs have already identified some of the practices requiring improvement in particular countries.

Although education and training programmes are continually being undertaken around the world, little seems to be known about the degree of success they achieve or otherwise. The following information indicates the nature of programmes undertaken in 2 countries with particular reference to paraquat.

- Malaysia

The Malaysian Agrochemicals Association, in collaboration with its membership, has introduced a 3 year modular education programme to improve the general awareness and knowledge of Malaysian agricultural workers in safe use of pesticides. Efforts are being made to promote common messages across the industry so that farmers and users do not become confused by inconsistency. The first step, a "train-the-trainers" programme is nearing completion. Secondary training of farmers and other pesticide users will then begin. Funding is being sought from Government and international aid organisations to extend the programme increasingly to all pesticide users.

Semigovernmental agencies such as the Malaysian Agricultural Research Institute, the Rubber Research Institute of Malaysia, FELDA, and FELCRA have also organised short training courses on the safe use of pesticides.

In 1985 ICI Agrochemicals Malaysia introduced a product stewardship programme for the responsible and ethical management of its products with education and training as its principal features. A primary objective has been the education of management, supervisors and workers on rubber and palm oil estates about the hazards of paraquat and its safe use. A company medical officer has made some 1200 visits to Malaysian estates for this purpose since 1985. Direct safety education of farmers has been introduced as part of normal sales promotion. Education of technical and advisory staff has been introduced at agricultural colleges, training schools and in the Department of Agriculture. An increased acceptance of the use of protective clothing designed for tropical use during mixing (e.g. Tyvac aprons) was being seen as a direct result of this type of education.

A training programme on management of paraquat poisoning introduced for doctors, paramedics in hospitals and for medical assistants employed on the Malaysian estates has been introduced. Based on experience gained, the programme has since been modified and improved. Thus, in 1993, the following additional measures were introduced to increase awareness of paraquat's hazard potential:

- pictograms on labels;
- leaflets attached to packs;
- a poster campaign at distribution points;
- a campaign in print, radio and electronic media;
- an "incentivised" motivation scheme to educate users and their families;
- a media campaign.

The degree of penetration of the agricultural community and the resultant impact that these measures will have on improving the safe handling and use of all agricultural chemicals, not just paraquat, is yet to be determined.

- **Japan**

In response to the increasing incidence of paraquat suicides in Japan in the 1980s, a "Paraquat Safety Committee", comprising the principal paraquat marketers in Japan, including ICI, was established in 1986 to coordinate, *inter alia*, education of paraquat distributors, farmers, the public and medical organisations about the toxicity and hazards of paraquat in that country. Initiatives undertaken included:

- a request to regulatory authorities to curtail the then widespread sale of unregistered paraquat products;
- control of the volume of paraquat products supplied so that there was only a sufficient supply to meet market need;
- gathering of accurate statistical data on the incidence of poisoning by pesticides and paraquat in particular;
- dissemination of information about the safe storage, handling, use and disposal of paraquat;
- development of a "Safe Handling Manual" for suppliers and users of paraquat;
- media campaigns to promote public awareness of the issues;
- distribution of safety posters to retailers (12,000), leaflets to farmers (30,000 in 1989 alone) and polythene bags (3,330,000 in total) with printed safety slogans for distribution of paraquat products; and
- advice to medical organisations and poison centres on the management of paraquat poisoning.

The combination of the above measures and the regulatory measures previously described, together with the introduction of the modified "Preeglox L" formulation, seem to have been effective in reducing the incidence of paraquat poisoning, because by 1988 the number of paraquat poisonings had fallen markedly. There were also fewer requests for information on paraquat. The number of requests for analysis of biological samples had declined by 1989 to less than a quarter of that in 1986. There were also significantly fewer press reports of paraquat poisoning.

Objective 3

Undertake a comparative evaluation (opposite paraquat) of positive or negative environmental and health impacts of accepted alternative chemical herbicides

Introduction

There is no immediately available alternative herbicide to replace all uses of paraquat since some of its herbicidal properties are apparently unique. It was recognised from the outset of this review that there is now a wide range of herbicides with differing spectra of biological activity which could serve this purpose but that it would not be possible to consider each alone or in combination for all conditions of use. Consequently, it was agreed to focus upon the major non-selective herbicides which are mostly used for the control of grasses in tropical plantation crops which are most relevant to the interests of projects sponsored by the World Bank.

Alternative Herbicides

Information initially provided to the consultant suggested that possible economic alternatives to the use of paraquat for non-selective weed control in tropical agriculture include diquat, glyphosate, sodium arsenite and perhaps sodium chlorate (Diatloff, 1993).

Glyphosate was chosen for particular consideration because it, together with paraquat, now is the major non-selective herbicides used for about 80% of the weed control in tropical plantations. Furthermore, recent reductions in the cost of glyphosate have led to its increased competitiveness and expansion of its use. Glufosinate-ammonium was later suggested as another possible alternative to paraquat.

. Sodium Arsenite

Although an effective, non-selective herbicide, sodium arsenite has high acute toxicity and has been associated with a disproportionate number of poisonings when used as a pesticide (Clarkson, 1991). Since arsenic is an established human carcinogen, the use of sodium arsenite as an alternative to paraquat is not considered further.

. Sodium Chlorate

Sodium chlorate has long been used as a herbicide. It uses have largely been supplemented by more modern herbicides. It has moderate acute toxic and may cause irritation of the skin, eyes or upper respiratory tract (Clarkson, 1991). There is otherwise inadequate information to evaluate its acceptability as an alternative herbicide from a public health view point. It is not considered further.

Diquat

. Introduction

Diquat is a non-selective contact bipyridinium herbicide and desiccant. It is the 1,1'-ethylene-2,2'-bipyridinium dication, a derivative of 2,2'-bipyridyl which, like paraquat, has the capacity to undergo redox cycling, forming a radical cation but at a higher electronic potential. Like paraquat, only the cation has herbicidal properties and its reduction is reversed by oxygen.

The physical and chemical properties of diquat are similar to those of paraquat. It is highly soluble in water, slightly soluble in alcohol and practically insoluble in other solvents. Diquat is stable in neutral or acidic conditions but is hydrolysed by alkaline conditions. Like paraquat, it is inactivated by clay and anionic surfactants.

. Diquat Formulation

Diquat is generally marketed at a 20% aqueous solution of the dibromide salt (200 g (cation)/L). Water soluble granules containing 2.5% diquat and 2.5% paraquat are available for use in home gardens in the U.K. Working dilutions vary between 1 g/L and 5 g/L in water. Diquat is also marketed in various combinations with other herbicides (IPCS, 1984).

. Agricultural Use of Diquat

Diquat is used in more than 100 countries around the world, mostly as a desiccant but also as a contact herbicide. It is used to control broad-leaf weeds in crops and aquatic vegetation, both submerged and floating, for destruction of potato haulm and for desiccation of seed crops.

Diquat is applied at a rate of 0.4-2 kg/ha. After dilution, it is generally applied by ground sprayers at 200-500 L/ha or sometimes by air at 40-50 L/ha.

Diquat and paraquat have similar herbicidal action except that diquat is not as effective against grass weeds as paraquat (Sagar, 1987).

. Toxicology of Diquat

The animal toxicology of diquat has been reviewed and summarised (FAO/WHO, 1984; Stevens and Sumner, 1991; Summers, 1980; IPCS, 1984). The toxicity profile of diquat and paraquat in animals is similar. However, diquat is less acutely toxic and does not produced the peculiar pulmonary toxicity that characterises paraquat.

The primary toxic effect of diquat in animals is gastrointestinal damage resulting in diarrhoea with subsequent dehydration. After repeated dosing or following dosing with high doses of diquat, toxicity occurs in the liver, kidney, and the nervous and endocrine systems. High concentrations of diquat are irritating to the skin, although less so than paraquat. Development of cataracts has been reported in rats and dogs following long-term treatment with diquat. This observation has not been reported in man. Diquat is embryotoxic at high doses but it has not been found to be teratogenic in rats and mice or carcinogenic in long-term feeding studies on rats given diquat at levels up to 720 mg/kg diet. *In vitro* mutagenicity studies have been inconclusive, although generally suggesting weak activity, while the results of *in vivo* studies have been negative. Thus, the results of animal studies suggest that low-level exposure to diquat is unlikely to induce toxic effects in man. The no-observed-effect level in rats has been estimated at 0.75 mg diquat dibromide/kg bw/day and the acceptable daily intake for man is 0-0.008 mg/kg bw (FAO/WHO,1978).

There is less information about the toxicity of diquat to humans than for paraquat. There have been fewer reports of human poisonings with diquat, the lethal human dose being estimated to be 6-12 g of diquat dibromide. The treatment of poisoning by diquat is the same as treatment of paraquat (Stevens and Sumner, 1991).

Prolonged exposure of the base of the fingernail to a 20% diquat solution results in nail growth disturbances: spots, white bands and even shedding of the nail. Like paraquat, the nail regrows after cessation of exposure to diquat.

Concentrated diquat solutions have also been reported to delay the healing of superficial cuts on the hands of spray operators. Inflammation of the nasal mucosa during agricultural application or mixing of diquat has been attributed to the inhalation of droplets or splashes of liquid concentrate (IPCS, 1984).

The commonly accepted TLV for diquat, 0.5 mg/m^3, (IPCS, 1991b) may be used for comparative purposes.

. Accidental and Suicidal Exposure to Diquat

Accidental diquat poisoning has been reported (IPCS, 1984). As for paraquat, the outcome is generally more favourable with accidental rather than for suicidal ingestion.

Like paraquat, diquat has been used for suicidal purposes. Ingestion of large amounts of diquat can be rapidly fatal. The initial symptoms resemble those typical of paraquat poisoning: gastrointestinal irritation, ulceration of the mucous membranes, acute renal failure, liver toxicity and respiratory difficulty. Central nervous system effects may occur.

The following reports of individual cases indicate various conditions under which diquat poisoning has occurred.

- **Case Reports of Accidental and Suicidal Exposure**

A series of 11 cases of poisoning by aqueous concentrate and soluble granules of diquat has been reviewed. Vomiting, abdominal cramping, diarrhoea and erosion of the gastrointestinal mucosa occurred quite soon after ingestion. Gastrointestinal complications, consisting of ulceration of the oral mucosa, paralytic ileus and diarrhoea, predominated. Anuria occurred in 4 fatal cases whilst 2 milder cases developed only a degree of renal failure. Coma marked all fatal cases, often preceding circulatory shock. Severe neurological complications due to a lesion of the brainstem also occurred in at least 2 patients. Pulmonary fibrosis was not a feature (Vanholder *et al*, 1981).

Case 1

Accidental ingestion of a mouthful of diquat of unstated concentration by a 53 year old man caused nausea, vomiting and diarrhoea. Absorbents were administered soon after ingestion. Despite forced fluid therapy, he developed renal failure and required dialysis for 6-7 days but eventually made a good recovery (Fel *et al*, 1976; cited by Stevens and Sumner, 1991).

Case 2

A 23 year old man who ingested 300 ml of diquat concentrate vomited 5-10 minutes thereafter. He subsequently developed signs of gross central nervous system toxicity. Prompt aggressive therapy, including gastric lavage and haemoperfusion, were unsuccessful. Cardiovascular collapse and death occurred 14 hours after admission. Autopsy findings revealed oesophagitis, tracheitis, gastritis and ileitis. The renal, gastrointestinal and central nervous system complications proceeded cardiovascular collapse (McCarthy and Speth, 1983).

. Occupational Exposure to Working Dilutions of Diquat

Fewer quantitative studies of worker exposure to concentrates and working dilutions of diquat have been published than for paraquat.

Wojeck *et al* (1983) studied the exposure of workers applying 1.76% w/v diquat by hand operated spray or using direct injection of 4.41% w/v spray mixtures into water for hydrilla control. The spray crews applied the diquat solution 2-5 hours daily for 4 days per week.

Inhalational exposure was found to be less than 0.01 mg/h. The dermal exposure was estimated at 0.20-1.82 mg diquat/h during the treatment of water hyacinths and 0.17-0.47 mg/h during the treatment of water hydrilla. Urinary analyses were negative for diquat.

The dermal exposure to diquat was closely related to the concentrations used in the working solutions. It was considered that the use of disposable coveralls and regularly washed impermeable gloves would further reduce potential exposure to nearly undetectable levels. As for paraquat, respiratory exposure was consistently a small proportion of the total body exposure.

- **Case Reports of Exposure to Working Dilutions of Diquat**

Case 1
A case of full thickness skin burns due to exposure to working dilutions of diquat has been reported. A herbicide applicator in California applying diquat to grasses used a hand-pumped backpack sprayer which leaked. The man's jacket, pants were saturated and diquat accumulated in his rubber boots, the only protective clothing he was using, for hours. He developed painful feet on the first day and so wore two pairs of socks on the second day. He later presented with burns to the soles of both feet. The burns were full thickness, particularly on the plantar surface of the right foot. After unsuccessful conservative treatment, skin grafting was required. Whilst his wounds healed, he continued to complain of pain on the plantar surfaces of both feet and had difficulty in walking.

The lack of adequate protective clothing and malfunctioning equipment allowed this unusual situation to develop. The prolonged contact in an occlusive situation resulted in the full thickness burn. No symptoms of systemic poisoning were observed (Manoguerra, 1990).

Case 2
Diquat has been reported to cause upper gastrointestinal injury following minimal exposure. A chemical factory worker who had used a diquat dilution in his garden claimed to have accidentally consumed spray solution by "licking his lips" after he had rubbed them with a rubber glove he was wearing. He developed mild continuous vomiting, diffuse abdominal pain and diarrhoea. On investigation, he was found to have mild renal impairment with proteinuria. Endoscopy showed oesophageal inflammation and localised erosion of the stomach. His tongue subsequently sloughed a large zone of its mucosa. After treatment, these lesions healed within a month.

Case 3
An association between direct exposure to diquat and Parkinson's disease has been claimed. A 72 year old farmer developed Parkinson's disease some 10 days after he had worked with diquat. His exposure was to an aqueous solution of 10% diquat dibromide to his hands for about 10 minutes. He developed erythema of the skin with hyperkeratosis together with conjunctivitis. The irritation cleared up after four days. He subsequently developed severe Parkinson's disease.

The authors considered that there was a probable cause-and-effect relationship between the exposure to diquat and the development of Parkinson's disease. They noted that the patient had suffered a mild stroke two years earlier which may have facilitated entry of diquat into brain tissue. They also noted that old age may have played a role in the neurotoxicity of diquat (Sechi *et al*, 1992).

Whilst the association between Parkinson's disease and exposure to diquat reported here is not certain, the modest dermal and ocular effects do not suggest significant exposure. Parkinson's disease is associated with advanced age.

Environmental Fate Of Paraquat And Diquat

Because of their similar chemical nature, herbicidal activities and toxicological properties, the environmental fate and impact of the bipyridinium herbicides, paraquat and diquat, are considered together. Their environmental fate has previously been reviewed in detail (Summers, 1980; IPCS, 1984).

. Fate of Diquat and Paraquat in Plants

- Photodegradation

Diquat and paraquat undergo rapid photochemical degradation on plant surfaces or when in solution. Diquat, in solution, readily decomposes in sunlight. However, paraquat in solution is stable to sunlight but does photodegrade on plant surfaces. The main photochemical degradation product of paraquat is 1-methyl-4-carboxypyridinium chloride which further degrades to methylamine.

According to WHO (1984), the rate of decomposition of paraquat on plant surfaces relates to the intensity of UV irradiation; in strong sunlight, about 2/3 of the applied paraquat decomposed within 3 weeks. The residue of 4-carboxyl-1-methyl pyridinium salt was about 7% of that paraquat applied directly (1.12 kg/ha) at intervals of up to 4 months.

- Metabolism

Diquat and paraquat are not metabolised to any significant extent by plants.

. Fate of Paraquat and Diquat in Soil

- General Considerations

Some general consideration of herbicide-soil interaction are useful in the understanding of the fate of herbicides in soil.

Following post-emergent treatment with a herbicide, a large proportion of the amount applied reaches the soil. On entering the soil, herbicides may be bound in different ways to soil constituents. They may be transported from the target area and they will be subject to degradation by different mechanisms. In the soil, herbicides are bound through adsorption to clay minerals, organic materials, metallic oxides or to humic substances. Within the soil, herbicides may be transported by diffusion or mass transport. Movement by water depends upon the aqueous solubility. The soil adsorption characteristics of a herbicide are of great importance in determining its rate of transport.

Decomposition of herbicides occurs through photochemical, chemical and biological processes. Ultraviolet light may decompose herbicides on leaf and soil surfaces. Chemical reactions in the soil include hydrolysis and oxidative processes. However, biological decomposition by soil microorganisms is generally the most important means of herbicide decay. Some microorganisms utilise herbicides as a substrate for their growth.

The rate of decomposition of herbicides in soil is influenced by the properties of the herbicide, the climate, the soil type and the mode of cultivation. The chemical structure of the herbicide as well as its physical properties (solubility, affinity or adsorption) can directly or indirectly influence the rate of decomposition. Soil properties such as content of organic matter and clay, pH, are both directly and indirectly involved in regulating the activity of soil microorganisims. Thus, persistence is not a fixed property of a herbicide but is influenced by all the above factors. These vary from site to site and from time to time (Tortensson, 1985).

One of the most important properties of the bipyridinium herbicide is their ability to strongly adsorb to soil constituents so that they become biologically unavailable. Many of their applications in agriculture depend upon this phenomenon.

According to Summers (1980), soils and their minerals differ markedly in their ability to absorb diquat and paraquat. A typical soil adsorbs 0.3 mg/g of paraquat whereas the clay minerals, kaolinite (a typical non-expanding clay) and montmorillonite (a common expanding lattice clay), adsorbed 2.5-3 mg/g and 75-85 mg/g respectively. Although paraquat binds more strongly, diquat also binds readily to clay particles in soil. The absorption capacity of kaolinite for diquat is about 2 g/kg and that of bentonite 80-100 g/kg. Sandy soils have a small capacity to strongly adsorb paraquat and diquat. These herbicides bind to the organic matter of soil to an even lesser degree.

- **Soil Mobility**

The mobility of diquat and paraquat in mineral soils has been studied in relation to environmental contamination. They are essentially immobile. In one case limited movement of paraquat occurred when the dominant clay minerals were vermiculite and kaolinite and when the solvent was strong sodium chloride solutions. These atypical indications suggest some ion exchange from weak absorption sites onto the minerals. Movement of the herbicide also occurred at very high application rates once the adsorption capacity of the soil had been exceeded (Summers, 1980).

Concern has been raised that the degradation product of paraquat, 4-carboxy-1-methylpyridylium ion could contaminate groundwater. The 4-carboxy-1-methylpyridinium salt is only slightly adsorbed to organic and loam soils and so is available for microbial degradation. In one study it remained in the top one inch of soil and the residual amount decreased with time (Baldwin, 1966). The residues reportedly dissipated within one week (Calderbank, 1966). There was no evidence of ^{14}C-4-carboxy-1-methylpyridinium moving down the soil profile after soil application (Baldwin and Griggs, 1970). As a consequence, the degradation product would be unlikely to leach into groundwater.

Degradation in Soil

In a long term trial on a loamy soil, paraquat was applied at 0,90,198 and 720 kg/ha to a depth of 15 cm. Over seven years paraquat residues declined by 5% a year at 90 kg/ha and by 7% per year at the higher application rates. In another trial, at 4.4 kg/ha the rate of loss of paraquat residues was about 10% per year. The soil residues tended to plateau as the rate of application equalled the rate of degradation. Data over a further 4 years confirmed and extended earlier results.

Non-Microbial Degradation

Diquat and paraquat are not lost from soil by volatilisation. Both are resistant to chemical degradation in soil but are degraded photochemically. In surface soils, paraquat loss through photodecomposition was 20-50% in 3 weeks (Eisler, 1990).

Microbial Degradation

In solution, paraquat is rapidly degraded by some soil microorganisms but its degradation rate is greatly reduced when it is strongly adsorbed to soil particles.

Both diquat and paraquat are susceptible to slow degradation and metabolism by soil microorganisms. Some bacteria and actinomycetes tend to increase in number in the presence of paraquat.

According to Summers (1980), paraquat produced some effects on soil microorganisms when applied at very high rates but there was no effect when applied at normal application rates.

Many soil microorganisms can grow freely in paraquat-containing media but only a few are capable of degrading it. These include: *Corynebacterium fascians, Clostridium pasteurianum, Pseudomonas fluorescens, Rhizobacter* sp., *Aerobacter aerogenes, Agrobacterium tumefaciens* and *Bacillus cereus.* Soil actinomycetes, including *Streptomyces* sp. and *Nocardia* sp. can degrade paraquat, as do soil fungi such as *Pencillium cyaneum* and *Aspergillus aculeatus.* The fungus, *Neocosmopara vasinfecta*, can reduce paraquat to its radical ion. The bacteria *Pseudomonas fluorescens, Rhizobacter* sp. and *Aerobacter aerogenes* can all decompose diquat.

Field studies, have produced variable results. Paraquat, at concentrations of 10, 100, 500, and 1,000 ppm had very little effect on the microflora of a sandy loam soil. At 10,000 ppm, the number of fungi was reduced by about 20% whereas the number of bacteria and actinomycetes increased to about 150%. Other reports have shown that the bipyridinium herbicides have little effect on the total microbial populations in soils. Observed differences between various studies reflect differences in the microbial species involved and the possible utilisation of the herbicide as a substrate. When comparisons are made between microbial soil populations in paraquat-treated field plots and untreated control plots there was often some reduction in the microbial population of the treated plots. This is due largely to denudation of the vegetative cover rather than a direct antimicrobial effect of the herbicide.

. Residual Phytotoxicity

The residual phytotoxicity of a herbicide in soil can be determined as its "Strong Adsorption Capacity". This is defined as that concentrations of paraquat in the soil which gives, when the soil is equilibrated with water, a concentration in the water which is sufficient to cause a 50% inhibition of root elongation of wheat seedlings grown in that water. For paraquat, this concentration is about 0.01 µg/ml.

The herbicidal activity of residual paraquat in soils is deactivated in soil up to a level of addition that depends upon the nature of the soil. The absorption capacity of even the top 2.5 cm of soil usually far exceeds the normal rates of application of paraquat. Since the absorption capacity of soil relates to the clay mineral content, the capacity for absorption of paraquat extends throughout the depth of the soil. Transfer to the clay fraction of any paraquat remaining in killed herbage occurs, for as the herbage decomposes, any remaining paraquat will be incorporated into the soil. Provided equilibrium is attained, a large adsorption reservoir remains in the soil. Thus, it is unlikely that paraquat from normal agricultural use will accumulate in sufficient quantities in soil to damage crops.

This is particularly so in medium and heavy soils with a relatively high clay mineral content. Long-term studies of the residual activity of diquat and paraquat in such soils have shown that up to 50% of the applied paraquat was still present 15 months after application. In an orchard treated with paraquat, 25 kg/ha four times a year for 8 years, residues of 4-6 ppm were found in the in the upper 5 cm of soil. However, these levels were not phytotoxic.

Continuous application of paraquat on different soil types has shown that strongly bound paraquat residues were degraded in soil by microbial activity at a rate of 5-10% per annum. A correlation was reported between the level of paraquat residues, the number of treatments, application rate and depth of soil planting.

High application rate trials have been conducted in order to assess the level of residual paraquat required to elicit phytotoxicity. At 112 kg/ha, phytotoxicity occurred at 4 typical agricultural test sites. On undisturbed plots of mineral soils, seedlings did not appear for several months and on organic soils the time lag was even longer. Phytoxicity disappeared on cultivation. In another trial, a total of 565 kg/ha paraquat was applied in 5 doses over 4.5 years. Phytotoxicity was confined to the surface layers of the soil. Free paraquat was detectable in the top 2.5 cm only. Again, residual phytotoxicity disappeared when the soil was more deeply cultivated.

Diquat and paraquat, however, are more likely to be bioavailable in sandy soil. There have been occasional reports of phytotoxicity in crops grown in sandy soil several days after application of bipyridinium herbicide and in soils with a high organic content such as peats. Some studies have shown that the adsorption capacity of peat soils for paraquat is such that the application of paraquat to these soils is safe only if it is well incorporated to a depth of 6-10 cm. As the alkalinity of the organic soil increases, diquat and paraquat become less available to plants.

Studies of Residual Phytoxicity in some Countries

ICI/Zeneca has conducted an extensive series of studies of the dissipation and residual phytotoxicity of paraquat in soils has been undertaken in a number of countries.

Cameroon

In 1990-1991 a study of soils on which paraquat had been used in the normal agricultural production of the banana, sugar cane and oil palm plantations and from maize fields where paraquat had been used repeatedly. It was found that the paraquat residues within the top 20 cm of the soil were low (mean 1.6 mg/kg) and represented less than 5% of the Strong Absorption Capacity of the soils. It was concluded that the use of paraquat for arable crops on plantations was without risk of the development of phototoxic soil residues (Stevens, 1991).

Central America

A study of soil residues of paraquat arising from normal agricultural use and the soil deactivation capacities was undertaken in 1985-1987 in Honduras, Costa Rica and El Salvador. The principal crops grown were banana, coffee and maize respectively. Where possible, crop samples were taken for paraquat residue determination. Samples were taken from 60 soils from banana and coffee plantations and maize fields. The soil contained paraquat residues ranging from 0.16-11 mg/kg. To estimate the degree of saturation for each soil's deactivating capacity, the paraquat residues in each soil was compared with the corresponding SAC values. For 51 of the soils the percentage saturation was less than 1% and for the remaining 9 soils the saturation ranged from 1.3 to 6.2% .

No detectable residues were found in any crop samples, the limits of determination being 0.02 mg/kg for maize, coffee bean samples and banana peel samples and 0.01 mg/kg for banana flesh (Stevens and Dyson, 1993).

Costa Rica

The paraquat deactivation capacity of soils from 20 coffee plantations in Costa Rica were found to generally range from 100-500 mg paraquat/kg soil. Even when paraquat had been applied at up to twice a year (1.2 kg/ha) for 20 years, soil residues were less than 10% of the soils deactivating capacity and in the majority of cases were less than 1%. Paraquat was tightly bound to the soil and was not desorbed by saturated ammonium chloride solution. Residues of paraquat in coffee, berries and beans were at or below the limit of determination (0.02 mg/kg). Strongly adsorbed paraquat residues in the soils were not absorbed by crops and there was no translocation of residues into the crop (Constenla *et al*, 1990).

Kenya

The soil residues of paraquat in 8 Kenyan coffee plantations were shown to be well below the capacities of the soil to absorb and completely deactivate the compound. They were considerably less than the theoretical maximum paraquat residual levels rising from repeated paraquat application over many years (Stevens and Bewick, 1989).

Malaysia
A survey of soils from 11 rubber plantations and 14 oil palm plantations on which paraquat had been used extensively was undertaken in 1985-1986. The measured paraquat residues in the soil were low, ranging from 0.22-5.3 mg/kg and corresponding to an average of less than 14% of what had been applied.

. Fate of Diquat and Paraquat in Water

Diquat and paraquat are used extensively in the control of aquatic weeds. Both herbicides quickly dissipate from natural water systems, largely due to their adsorption by sediment and suspended material and through absorption and uptake by aquatic plants and algae. They tend to accumulate on sediment surfaces, either directly or after absorption by aquatic plants and animals. They are then released on decay of the living tissue but then become bound by the sediment. The nature of the sediment determines how closely bound the herbicides will be and, ultimately, their biodegradation by microoganisms.

According to Summers, 1980, paraquat disappears from water to about half the initial concentration (1 mg/L) within 36 hours and after two weeks the concentration was below 0.01 mg/L. Four days after application, weeds had accumulated approximately 25 mg/kg paraquat, indicating that absorption by weeds was largely responsible for its removal from the water body. Analysis of mud 5.5 months after treatment showed that about 36% of the applied paraquat remained in the mud, mostly in the top 2.5 cm. Paraquat absorbed to the mineral content and was biologically unavailable.

Diquat behaves similarly to paraquat in water. In addition to uptake by weeds, its disappearance from treated water is due to photodegradation at the water surface and adsorption by bottom mud. Trials in ponds with an initial concentration of diquat of 2 mg/L, residues of diquat were not detectable after 8 days. When pond water was treated with diquat at 2.5 mg/L, residues of 0.01-0.08 mg/L were found 7-9 days after application but were not detected after 14-30 days. Studies from ponds, large and small lakes, canals and reservoirs similarly demonstrated the fast disappearance of diquat from treated water. Absorption by aquatic weed is again a feature. Decomposition of the dead weeds occurs rapidly but diquat is retained in the bottom mud and not released back into the water.

It is therefore not surprising that the presence of soil considerably reduced the persistence of both bypyridinium herbicides in water. For example, an initial concentration of 0.5 mg/L diquat declined to nil in 9-10 weeks in water alone; in 2-3 weeks in water containing soil and in 1-2 weeks in water containing soil and plants. The corresponding figures for paraquat were 35, 6-8 and 3-4 weeks respectively. This rapid dissipation is attributed to absorption by algae and degradation by sunlight, particularly for diquat. In many natural aquatic environments, residues of diquat and paraquat have been found to dissipate even more rapidly.

After application for aquatic weed control, subsequent decomposition of the plant tissue can lead to depletion of the concentration of the dissolved oxygen in the water. Since this can kill fish, application of herbicide for aquatic weed control should be staggered in time and place.

Diquat and paraquat are not readily desorbed from the mud. Therefore they are generally unavailable for microbial degradation.

Run-off from fields treated with paraquat has been shown to contain negligible amounts of the herbicide. Furthermore, water that does contain small amounts of paraquat loses it rapidly on contact with soil. Thus, water that has been treated with paraquat can quite safely be used for channel irrigation if an interval of about 10 days is observed between treatment of the water and its use (IPCS, 1984).

. Ecotoxicity of Diquat and Paraquat

The hazards of paraquat to fish, wildlife and invertebrates has been reviewed recently (Eisler, 1990).

- Aquatic Organisms

– The use of diquat and paraquat in aquatic weed control as well their use in agriculture, has prompted extensive investigations into the toxicity of diquat and paraquat to fresh water fish and other aquatic fauna.

The toxicity of paraquat for fish varies with the species, the size of the fish, and the softness or hardness of the water. Many species have shown complete survival at 96 mg/L over 96 hours, although the decreased oxygen concentration following decay of weeds may be dangerous in some situations. Rainbow trout tolerated 1 mg paraquat/L in a prolonged toxicity test; 30% mortality occurred after 16 days of repeated exposure. Carp fingerlings exposed to paraquat in the presence of weeds were more susceptible than those in a weed-free environment owing to the reduced oxygen content of the water (Summers, 1980).

Toxicity to fertilised fish eggs and fry has also been studied. The highest concentration of diquat that did not cause death to small fry during 12 days exposure was 10 mg/L. The recommended rate of application of diquat for aquatic weed control (0.5-1 mg/L) should not greatly effect the survival of fish eggs and fry.

The toxicity of the bipyridinium herbicides to other aquatic fauna has also been studied. Natural waters treated with these herbicides to control vegetation tend to show a decrease in the number of herbivorous invertebrates and an increase in numbers of detritus feeders. This corresponded to the destruction of vegetation and accumulation of decaying matter. The most likely cause of decreased number of herbivores was direct starvation. It was concluded that diquat at 1 ppm tendered to be harmless to aquatic fauna despite marked changes in the numbers of arthropods and molluscs by destruction of their habitats and an increase in aquatic earthworms and detritus-feeders increased in number due to the greater amount of decomposing plant matter. However, it has been shown that diquat at 1 mg/L could well cause direct adverse effect on certain fish food organisms such as *Hyallella.*

Paraquat is toxic to *Paracalliope fluviatis* at 0.05 mg/L. The smaller arthropods are more susceptible. Although most species of crustaceans and all other species of invertebrates were relatively unaffected at paraquat concentrations below 1 mg/L, early developmental stages of certain species of crustacea are quite sensitive. Larvae of the estuarine crab, *Rhithropanopeus harrisii* have been shown to be particularly sensitive to paraquat (Eisler, 1990).

Diquat, at 1 mg/L, had no detrimental effect on tadpoles of the frog, *Rana temporaria* or the toad, *Bufo bufo*. However, at a concentration of 1-2 mg/L, diquat was toxic to embryos of the toad, *Xenopus laevis*. Paraquat caused mortality of *Rana temporia* tadpoles at 1 mg/L after 6.5 days. Tadpoles of *Rana pipien* were sensitive at 0.5 mg/L (Summers, 1980). Paraquat was teratogenic to both species and caused growth retardation in *R. pipiens* at 0.1 mg/L (Linder *et al*, 1989). It has been subsequently shown that formulated paraquat is more toxic than paraquat itself to this species.

- **Soil Organisms**

The effect of bipyridinium herbicides on soil fauna has been studied extensively.

The numbers of soil invertebrates in diquat and paraquat-treated soil is sometimes less than in untreated plots, presumably because the vegetation on which they thrive has been killed off. In one case, the use of paraquat combined with the herbicide linuron has been effective in retarding increases of the root lesion nematode, *Pratylenchus penetratans* in peach orchards in Canada.

A long term study of the effect of paraquat and cultivation on soil invertebrates showed earthworm populations were often more numerous in paraquat-treated plots than in cultivated plots. Overall, paraquat appeared to have no deleterious effect on soil fauna. High concentrations of paraquat in soil can reduce the number of worms and microarthropods. This may be due to either reduced plant cover or direct paraquat toxicity. Paraquat bound to soil has been shown not to be absorbed by earthworms and is considered to have no substantial effect on soil microarthropods (Summers, 1980).

- **Other Mammals**

Studies of the toxicity of the bipyridinium herbicides to animals in the wild have been reported.

Application of paraquat to spruce plantations for grass control had no effect on the spatial distribution and population of small mammals such as field mice *Microtus arvalis* and voles, *M. agrestis* but shrews *(Sorex sp.)* migrated from treated to untreated areas (Summers, 1980).

The effect of feeding treated lucerne to rabbits immediately after spraying at a concentration 211 mg diquat/kg dry weight has been studied. No signs of poisoning or gastro-intestinal damage were found. However, the hare, *Lepus europaeus*, has been reported to be quite susceptible to paraquat. A 50% mortality occurred in 5 days in 8 wild hares released onto plots of alfalfa that had just been sprayed with paraquat at the normal usage rates. Subsequently routine monitoring of wildlife incidents in the U.K. by the Ministry of Agriculture, Fisheries and Food and Office National de la Chasse in France has not revealed a significant number of wildlife including hare deaths due to paraquat (Barnes and Tapper, 1983; Anon 1989).

- **Birds**

Paraquat is generally less toxic for birds than for mammals. The lowest doses of paraquat that produced harmful effects in sensitive birds were 20 mg cation/kg in nestings of the American kestrel, 20 mg cation/kg in the diet of northern bobwhites and 40 mg cation/kg in the drinking water of domestic chickens (Eisler, 1990). Dietary EC_{50} values have been established in bobwhite quail, Japanese quail, ring-necked pheasant and mallard at 710, 703, 1063 and 2931 mg/kg respectively (Hill *et al.*, 1975).

Paraquat is embryotoxic to some species of birds. Aqueous paraquat solution (0.56 kg cation/ha) applied to the surface of mallard eggs inhibited embryonic development. These rates are less than the recommended field application rate of 1 kg cation/ha (Eisler, 1990). However, when paraquat was sprayed directly onto pheasant eggs at up to 2 kg cation/ha before incubation, there was no effect on the hatchability of the eggs. Monitoring of bird populations in U.K. where paraquat has been widely used, revealed no adverse effects (IPCS, 1984).

Comparison of Diquat with Paraquat

Diquat and paraquat share similar physico-chemical properties and biological activities. Diquat is less effective as a grass herbicide than paraquat but does have some particularly useful applications. Both are useful aquatic herbicides. From a strictly toxicological viewpoint, diquat is 2-3 fold less acutely toxic than paraquat. Diquat has not gained the notoriety of paraquat as an agent for suicide. Accidental and occupational poisoning by diquat is less common and usually less severe. Systemic poisoning from dermal absorption of diquat has not been reported.

From an environmental viewpoint, there is little to choose between diquat and paraquat, although diquat has been studied less extensively. Both bind strongly to soil after application and are degraded microbially thereafter. Normal soil residues of each are herbicidally inactive. Neither migrates through soil and water. Paraquat is more toxic to some crustaceans and should be used cautiously in estuarine areas. Otherwise these bipyridinium herbicides seem to have little or no effect on wildlife. Their common properties of fixation, inactivation and show degradation in soil favours their use in some environments.

Paraquat has particular physical, chemical and biological properties as a herbicide. Its capacity for binding to soil after herbicidal application first introduced the prospect of minimal-, or even, no-tillage agriculture. Its rapid penetration into plant matter makes it "rain-fast", a feature which is of particular value in tropical agriculture where sudden precipitation commonly occurs. Diquat shares some of these properties but is less active against grassy weeds and is somewhat less rainfast.

Gyphosate

. Introduction

Glyphosate, N-(phosphonomethyl) glycine, is a broad spectrum, non-selective, post-emergent systemic herbicide. It was introduced as a herbicide in 1971 and is now registered on over 50 crops in more than 100 countries around the world. The chemistry, agricultural use, mode of action, toxicology and environmental fate of glyphosate have been reviewed (FAO/WHO 1987; Duke, 1988; Grosshard and Atkinson, 1985; Malik *et al* 1989; Smith and Oeheme, 1992).

Glyphosate has low solubility in water (12 g/L at 25 ^{0}C) and is insoluble in organic solvents. It has a negligible vapour pressure. It is not liable to significant photo-decomposition or volatilisation. It is a relatively strong acid able to form a variety of salts.

Glyphosate affects photosynthesis, plant respiration and synthesis of plant nucleic acids. However, the primary mode of herbicidal activity of glyphosate results from inhibition of the shikimic acid pathway of aromatic amino acids in plants (Duke, 1988; Smith and Oeheme, 1992). The absence of this metabolic pathway in mammals may be an important factor in the low mammalian toxicity of glyphosate.

. Glyphosate Formulation

The most common formulation of glyphosate, "Roundup" is formulated as an aqueous concentrate of the isopropylamine salt (41%, containing 360 g/L glyphosate acid equivalent) with an polyethoxylated amine surfactant at relatively high concentrations of up to 15-17%.The surfactant enhances phytotoxicity through the wetting of plant surfaces and a solvent action or micelle formation (Turner, 1985). Other salts of glyphosate such as the trimethylsulfonium (trimesium) are also marketed as herbicides.

. Agricultural Use of Glyphosate

The agricultural use of glyphosate, its fate in the environment and toxicology have been reviewed (FAO/WHO, 1987b; Grosshard and Atkinson, 1985; Malik *et al*, 1989).

Unlike diquat and paraquat which are contact herbicides, glyphosate is translocated following its application to foliage. The unique mobility of glyphosate within plants and its extreme effectiveness at sites of action in buds gives it unprecedented ability to control perennial weeds. It is very effective on deep-rooted perennial weeds and on annual and biennial species of grasses, sedges and broad-leafed weeds (Holly, 1985).

As well as its use in broadacre agriculture, glyphosate is used in fruit plantations, forestry, viticulture and for aquatic weed control. It is used for weed control in the tropics and sub-tropics, for pasture renovation and for general weed control in non-crop situations (Grosshard and Atkinson, 1985).

The rate of application of glyphosate depends on the type and size of weeds and the degree of control required. It is generally in the range 1-5 kg/ha. Gyphosate may be applied by high volume applications in water as well as low volume and ultra-low volume methods.

. Toxicology of Glyphosate

The toxicology of glyphosate in has been reviewed and summarised (Atkinson, 1985; FAO/WHO, 1987b; Stevens and Sumner, 1991; Smith and Oehme, 1992.)

- Experimental Animals

Glyphosate and its salts have low mammalian toxicity. Its oral LD50 and dermal LD50 in rats are >5,000 mg/kg and >17,600 mg/kg respectively. The inhalational LD50 is 3.18 mg/L (4 h). It is poorly absorbed by rats following oral administration and thence is largely excreted in the urine. Absorption through the skin of monkeys is also low.

Chronic dietary administration of glyphosate to mice and rats was unremarkable, as was shorter-term administration. Glyphosate was not toxic to rabbits on dermal exposure or to rats by inhalation. Dogs were unaffected by dietary exposure to 500 mg/kg bw daily for 1 year. Glyphosate was not mutagenic in a range of *in vitro* and *in vivo* assays. There was no evidence of carcinogenicity. It did not affect the reproduction of rats and was not teratogenic in rats or rabbits.

The Acceptable Daily Intake for Man is 0.3 mg glyphosate/kg, based upon a chronic dietary study in rats (FAO/WHO, 1987b).

Commercial glyphosate formulation may be more toxic in animals than glyphosate itself. Similarly, whereas glyphosate is only slightly irritant to the eye and skin, the commercial formulation is moderately irritating. This difference can be attributed to formulants and adjuvants (Atkinson, 1985).

- Dermal Toxicity

The irritation, sensitisation, photoirritation and photosensitisation potential of glyphosate has been studied in 346 volunteers. A formulation that contained 41% glyphosate as the isopropylamine salt was applied at either full strength or as a 10% dilution to intact or abraded skin. Unabraded skin showed no greater irritancy potential than a dishwashing detergent. When tested on abraded skin, glyphosate resulted in slightly greater incidence of erythema at 24 h. However, at 48 h the irritancy was similar to dishwashing liquid. After 21 days of accumulative irritancy testing, glyphosate was slightly irritating but less irritant than the dishwashing liquid or an all-purpose cleaner. Glyphosate demonstrated no potential for skin sensitisation photoirritation or photosensitisation (Maibach, 1986).

The degree to which glyphosate could be washed off, bind to or penetrate human skin and become systemically available has been investigated. Glyphosate, administered as the "Roundup" formulation, undiluted and diluted with water (1:20 and 1:32), barely partitioned into the human stratum corneum (<1%). *In vitro* absorption of glyphosate was no more than 2%. Percutaneous absorption of ^{14}C-glyphosate in rhesus monkeys, *in vivo*, was 1-2%. Washing of the application site with soap and water removed 90±4% of the applied dose, whilst washing with water alone removed 84±3%. About 50% of the initially applied dose was recovered after 24 h. These results are consistent with the low dermal binding and absorption characteristics of glyphosate and its ready removal from skin by washing with water and/or water and soap (Wester *et al*, 1991).

If glyphosate is splashed in the eyes, a conjunctival irritation can occur which usually clears in 48 hours. Severe conjunctivitis can sometimes occur (Mack, 1993).

Accidental and Suicidal Glyphosate Poisoning

The mechanism of glyphosate toxicity in humans has not been established, although uncoupling of mitochondrial oxidative phosphorylation may be implicated. No specific treatment is available for ingestion of a significant volume of concentrated glyphosate other than to provide intensive supportive care. The outcome of poisoning depends upon the amount ingested, the clinical situation and its management (Tominack *et al*, 1989; Talbot *et al*, 1991).

Published reports demonstrate that glyphosate concentrate can be used for suicide. A series of 56 cases of toxicity due to glyphosate concentrate formulations were reported in Japan between June 1984 and March 1986; 48 cases were attempted suicides and there were 3 accidents (all in infants). The mean amount of concentrate ingested was about 120 ml. The signs and symptoms included sore throat, gastrointestinal irritation, including abdominal pain and vomiting, in almost all cases. Erosion of the pharynx, oesophagus and stomach was found in 7 cases. Haematemesis and melaena sometimes occurred. Post mortem of those who died within 48 hours of ingestion revealed erosion, necrosis and haemorrhage of the jejunum and ileum with a large area of oedematous mucous membrane. Pulmonary oedema occurred in 3 cases and severe pneumonia in 2 cases. There was moderate clouding of consciences in two cases. The clinical picture of acute glyphosate concentrate poisoning was one of hypovolaemic shock. Renal failure (oliguria and uraemia) and hypotension occurred in all fatal cases and transiently in survivors. Maintenance of blood pressure required massive infusions of fluid.

It was suggested that the polyoxyethyleneamine surface-active agent (POEA), present in the glyphosate formulation, contributed to the acute toxicity of the formulation. The surfactant is more acutely toxic than glyphosate. Such surface active agents have been reported to cause gastrointestinal and central nervous system symptoms and haemolysis (Sawada *et al*, 1988).

Another series of 93 cases of acute poisoning in the Republic of China with a glyphosate-surfactant herbicide was published in 1991. Over the period 1980-1989 there was a temporal increase annual in reports of poisoning, rising from 1 to 30 per annum (Talbot *et al*, 1991).
Severe symptoms only occurred after ingestion of at least 85 ml of concentrate. In some cases ingestion of estimated volumes of concentrate up to 500 ml did not cause severe poisoning.

There were seven deaths and the average time of death after ingestion was very short (4.7 h). Two of the deaths involved ingestion of multiple agricultural agents. Of the 86 survivors, 5 had taken glyphosate concentrate while drinking alcohol and two had mixed it with fruit juice. All other intentional ingestions were of the undiluted 41% concentrate. Intentional ingestion (80 cases) resulted in erosion of the gastrointestinal tract seen as sore throat (43%), dysphagia (31%) and gastrointestinal haemorrhage (8%). Other organs affected less often were haematopoietic (non-specific leucocytosis) (65%), lung (23%), liver (19%), cardiovascular (18%), kidney (14%) and central nervous system (12%).

The deaths following ingestion of the concentrate alone were due to a syndrome that involved hypotension unresponsive to intravenous fluids or vasopressor drugs and sometimes pulmonary oedema in the presence of normal central venous pressure. Those over 40 years of age who ingested more than 100 ml of the concentrate were at the highest risk of a fatal outcome (Talbot *et al*, 1991).

The severity of acute oral poisoning partly correlated with the estimated amount of glyphosate concentrate ingested:

- asymptomatic cases who ingested 5-50 ml and exhibited no signs or symptoms;
- mild poisoning (5-150 ml), mainly git symptoms (nausea, vomiting, diarrhoea, abdominal pain, mouth and throat pain) that resolved within 24 h. Vital signs were stable and there was no renal, pulmonary or cardiovascular involvement;
- moderate poisoning 920-500 ml) gastrointestinal symptoms lasting longer than 24 h, gastrointestinal tract haemorrhage with oesophagitis or gastritis, oral ulcerations, hypotension responsive to intravenous therapy, pulmonary dysfunction not requiring intubation, acid base disturbance, evidence of transient hepatic or renal toxicity or temporary oliguria; and
- severe poisoning (85-200 ml): pulmonary dysfunction requiring intubation, renal failure requiring dialysis; hypotension requiring treatment with vasopressor agents; cardiac arrest; coma, repeated seizures or death.

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A similar series has been reported from the Taiwan National Poisons Centre for the period January 1986 to September 1988. There were 97 cases of ingestion of glyphosate-surfactant herbicide concentrate of which 11 were fatal; all fatalities occurred amongst those attempting suicide. Of the 88 ingestions, 5 were accidental and the intention was unknown in 4 cases. The average amount ingested by survivors was 120±112 ml and by non-survivors 263±100 ml. Exposures by other than the oral route were not recorded. Ingestions in those who intended suicide but survived, averaged 13l±114 ml. Accidental ingestions averaged only 25±22 ml. The minimum lethal dose that was recorded was 150 ml. Of the 97 cases reported,10 involved ingestion of another substance in addition to glyphosate; alcohol in 8 cases, unidentified tablets in two cases and an organic arsenic compound in 1 case. The clinical course was similar to that reported previously (Tominack *et al*, 1991).

In the manufacturer's experience, deaths due to glyphosate poisoning are often associated with ingestion of other substances, including alcohol (Jackson, 1988).

Cases of intentional self-poisoning with glyphosate formulation have also been reported from New Zealand. As above, pronounced gastrointestinal irritancy occurred, leading to massive fluid and electrolyte loss and renal failure in 2 of 4 cases.

The human and experimental experience of surfactant toxicity includes vomiting and diarrhoea at high doses, hypovolaemia, haemolysis, pulmonary oedema and impaired consciousness. On the other hand, extreme diarrhoea and hypovolaemia was not observed in animals treated with the surfactants. They also noted that the concentration of glyphosate in the glyphosate- surfactant concentrate is more than 3 times the concentration of the surfactant and also, despite its relatively poorly absorption, some systemic signs are observed with glyphosate poisoning. It was thus considered unlikely that the toxicity of glyphosate-surfactant formulation could be ascribed solely to the surfactant (Menkes *et al*, 1991).

This discrepancy between the low acute toxicity of glyphosate and the clinical features of poisoning by ingestion of its formulation containing POEA surfactant may be due to the combination of ingredients in the formulation. Some of the clinical manifestations may be due to complications of aspiration (Martinez *et al*, 1990).

Incidental effects of accidental exposure to glyphosate concentrate have been reported to resolve with little sequelae. For example, a worker, who accidentally rubbed glyphosate concentrate in his left eye, developed gross periorbital oedema and chemosis of the eye which was associated with a tachycardia, palpitations and elevated blood pressure. He also had a headache and slight nausea. His symptoms settled with modest management and he resumed work the next day (Temple, 1992).

- Toxicity of Glyphosate Surfactant

Polyethoxylated amine surfactants are widely used in industry (textile manufacturing, leather and fur processing, metal finishing, paints and resins), agricultural chemicals (spreading and wetting agents) and household products (Sherex Chemicals, undated; Zerkle *et al*, 1987).

The polyethoxylated alkyl amine (POEA) surfactant used in Monsanto's "Roundup" formulation is moderately toxic in rats after ingestion (LD50 approx. 1,200 mg/kg) or in rabbits after skin application (LD50 > 1,260 mg/kg). The surfactant is severely irritating to corrosive to the rabbit's eye and can be irritating to rabbit skin (Monsanto, 1989).

"Roundup", containing 15-17% v/v of surfactant, is significantly less toxic to animals; its corresponding oral and dermal toxicities are about 5,000 mg/kg.

Studies in experimental animals have shown that these surfactants can, at high intravenous doses, can induce cardiac depression in dogs (Tai *et al*, 1990) and central nervous system depression in rats when given parenterally or by gavage (Zerkle *et al*, 1987).

A comparative study of the intra-pulmonary and intragastric toxicity of POEA and glyphosate in rats indicated that the pulmonary toxicity of "Roundup" was mainly due to POEA but that the surfactant was not responsible for the oral toxicity of "Roundup" (Sonsoni and Martinez, 1991).

It is unclear that the acute human toxicity of glyphosate-surfactant formulations can be ascribed solely to any single component of the "Roundup" formulation, although the POEA surfactant is clearly significant.

- Exposure to Working Dilutions of Glyphosate

There have been relatively few reports of adverse effects due to exposure dilutions of glyphosate. However, according to Moses (1989).

'Glyphosate-related illness was third on a list of skin illnesses reported to the Californian Department of Food and Agriculture from 1983 through 1986.'

Talbot *et al* (1991) reported 13 cases of accidental exposure to diluted spray. The cases of dermal contact were asymptomatic while only mild oral discomfort occurred after accidental ingestion.

In New Zealand, the majority of incidents reported have involved accidental exposures, mostly while spraying. In general, these cases exhibited minor local irritancy which responded to symptomatic and supportive care. Thus, a male adult spraying a double-strength solution contaminated his hand with a solution due to a faulty hand piece on the spray unit. He wiped his face with his hand and subsequently developed a swollen face and paraesthesia which settled over 48 hours and required no specific treatment. In another case, a male worker was accidentally drenched by a horticultural spray developed generalised pompholyx (inflammation and itching of the skin), most marked on his arms and hands which required parenteral steroid therapy (Temple, 1992).

A study of the exposure of Finnish forestry workers to glyphosate during silviculture clearing with brush saws equipped with pressurised herbicide sprayers was reported in 1991. The study group (5) and the control group (5) were medically examined prior to and after their one week working period. Glyphosate exposure was measured in the workers' breathing zones and by urinalysis during the period of application and again, 3 weeks later.

Exposure of the workers through the breathing zone was low, the highest atmospheric concentration being only 15.7 $\mu g/m^3$. Urinary concentrations were less than the limit of detection (<0.1 $\mu g/\mu L$). There were no differences in the results of the medical or laboratory examination of exposed and control groups (Jauhiainen *et al*, 1991).

The exposure to glyphosate of conifer nursery workers has been studied in Arkansas. Some of the workers commonly spent 7-10 months each year in situations potentially exposed to glyphosate. The degree of total exposures were found to be low from urinalysis conducted over 12 weeks. There was no indication of a human health hazard from glyphosate exposure when use in normal nursery practice (Lavy *et al*, 1992).

Environmental Impact Of Glyphosate

. Introduction

The environmental fate and biological activity of glyphosate has been reviewed (Duke, 1988; Grosshard and Atkinson, 1985; Malik *et al*, 1989, Smith and Oehme, 1992). Glyphosate has a favourable combination of physical and chemical properties which cause little environmental impact.

. Degradation in Plants

Glyphosate is poorly degraded in plants. Undegraded glyphosate has been reported to be exuded by the roots of plants following its application to the foliage. A number of studies have shown little metabolism by plants.

. Fate in Soil

Like diquat and paraquat, glyphosate is rapidly adsorbed onto soil. Its degree of adsorption correlates with the available phosphate absorption capacity of the soil. The content of organic matter and soil pH have little effect on its adsorption but free organic phosphate generally decreases its adsorption. Once adsorbed, glyphosate is practically immobile in soil.

The main route of glyphosate degradation in soil is microbial, in both aerobic and anaerobic conditions. The principal degradation product of glyphosate in soil is aminomethyl-phosphonic acid which itself is further degraded biologically. The rate of glyphosate degradation in soil varies considerably between different soil types. Half lives ranging from a few days to several months or years have been reported (Tortensson, 1985).

Persistence of glyphosate in soil does not seem to be a problem, although it has not been well studied (Duke, 1988).

. Soil Mobility

Glyphosate has very low mobility in soil. However, like diquat and paraquat, the major factor influencing the mobility of glyphosate in soil is its very tight binding. The adsorption of glyphosate to a soil is related to soil type, the clay content, the mineral structure,cation exchange and organic phosphate fixation capacity. Glyphosate is poorly bound to soil organic matter.

Soil leaching studies indicate that glyphosate has little propensity for leaching, even on the least adsorptive soil types. Run-off from treated soil is very low (Malik *et al*, 1989). Its mobility is slightly increased at high pH and by high levels of inorganic phosphate in the soil (Tortensson, 1985).

. Fate of Glyphosate in Water

The fate and biological effect of glyphosate in the aquatic environment has been studied. Glyphosate is extremely effective against emergent and bank-side weeds. It can also be applied to control emergent vegetation in water courses and for control of water lilies.

Glyphosate is quite stable at acidic pH. However, in natural waters, it is degraded by microbial action, photolysis and adsorption to sediments.

In an experimental pond at low temperature (4-9°C), the glyphosate content fell to about 30% of its theoretical initial value of 200 ppm after 50 days. Over-winter storage at 4°C further reduced the glyphosate aqueous concentration to less that 3% of that present 1 year before. Analysis of the sediment showed that more than 50% of the glyphosate was extractable in an unchanged form from the clay-like material.

Field studies have shown fairly rapid loss of glyphosate from water: following applications at 3.6 kg/ha to a water body 30 cm deep, the half life was 12 h; the aqueous concentration declined to the limit of determination after 8 days. The metabolite, aminomethylphosphic acid, was detectable.

As for paraquat, these results reflect the influence of suspended solids in an adsorbing and removing glyphosate residues from water (Tooby, 1985). However, glyphosate can move considerable distances in canal or stream water, despite its absorption to suspended matter. Most of the glyphosate entering the streams of a forest ecosystem was due to direct contamination from spraying (Duke, 1988).

. Ecotoxicity of Glyphosate

- Soil Organisms

The response of soil microbes to glyphosate can provide information on its effect on soil fertility. Soil microbes degrade glyphosate in soil and also in water. Glyphosate may inhibit or stimulate the growth and activity of these microorganisms. In particular, glyphosate is used in cereals both pre- and post-harvest, so that residues, retained in the straw may influence the interaction between soil microbes in the degradation of straw.

Degradation of glyphosate by soil microorganisms is the main route of its dissipation from the environment (Duke, 1992).

Many microbial species are inhibited by glyphosate in pure culture; this inhibition is selective, variable in magnitude and is frequently dose-related. In terms of agricultural practice, inhibitory effects, especially on the cellulolytic fungi, occur at concentrations well above those normally used in agriculture and which exceed the resultant soil concentration. As glyphosate is adsorbed and degraded in the soil this level falls accordingly. In some instances, glyphosate delayed decomposition of straw but the degree was too small to be of practical significance. Glyphosate does not curtail soil nitrification.

Laboratory experiments suggest that glyphosate is potentially toxic to some invertebrate plant-inhabiting fauna. However, under semi-field conditions (experimental ponds) no severe effects were observed. No significant effects have been observed in limited tests in soil. Thus, glyphosate at 1,10, and 100 mg/g did not significantly effect the mortality or growth of juvenile earth worms, *Allolobophora calinosa*. No deleterious effects on the mite, *Pergalunma* sp., exposed for 12 days to 0.336 g/m^2 were observed. However, the isopod, *Porcellio formosus*, suffered increased mortality. The overall adverse effects of glyphosate on soil fauna were considered to be small or absent (Eijsackers, 1985).

- Aquatic organisms

The effect of glyphosate on aquatic organisms has also been studied after application at 2.2 kg/ha to each of two streams and a pond. It was found that the diatom population, notably *Tabellaria* spp., *Navicula* spp. and *Cybella* spp., increased in the sediment, probably due to the change in habitat following the eradication of emergent vegetation and the consequent change in nutrient status, incident light and temperature.

Glyphosate and its commercial formulation have caused acute toxicity in a number of fish and invertebrate species. The estimated safety factor for rainbow trout, based on the 96 hour LC50 and the predicted maximum environmental concentration of glyphosate, was 14. The early life stages of fish species, the yolk-sac and "early swim-up fry" were the most sensitive whilst eggs were less sensitive. Rainbow trout showed no adverse effect upon reproduction, when exposed to 0.02, 0.2 and 2.0 mg/L glyphosate for a period of 12 hours. Rainbow trout did, however, tend to show a preference to avoid concentrations of glyphosate above 10 mg/L (Bronstad and Friestad, 1985).

In general, the toxicity of glyphosate to fish and aquatic invertebrates is low, although fish feeding may be interrupted due to alteration of environmental habitat an increase in open water area and predation (Smith and Oeheme, 1992).

- **Birds**

Through alteration of vegetation, glyphosate can modify the density, habitat use, and foraging behaviour of nesting birds. Preliminary studies suggested that at least four bird species were unable to maintain pre-spray density, even with shifts in habitat. Most alien species returned to pre-spray foraging behaviour 2 years after treatment. At this time, the vegetation was similar to the conditions existing prior to glyphosate application (Sullivan, 1985).

- **Mammals**

Glyphosate has little environmental impact on mammals. It did not show any adverse effect on the distribution of small mammal population, at least during the first year after application. It had no apparent adverse effect on the reproduction, growth and survival of field population of deer mice one year after treatment. Studies of food preference and habitat of black-tailed deer indicated that these animals did not discriminate between glyphosate-treated and untreated foliage (Sullivan, 1985; Smith and Oeheme, 1992).

Glyphosate, as used in forestry in British Colombia, had no discernible effect on the distribution and abundance of deer mice, shrews, Oregon voles, or Townsend chipmunks in the year following application. Over several years there was migration of some of the animals in treated areas to adjacent untreated areas where the food supply was more abundant (Malik *et al*, 1989).

The use of glyphosate in zero-tillage farming should not adversely affect the hatchability of upland nesting birds (Smith and Oeheme, 1992).

Comparison of Glyphosate to Paraquat

The acute oral toxicity of glyphosate concentrate to skin, eye and mucous membrane is low. It has little dermal irritancy and is not corrosive, unlike paraquat concentrate.

Nonetheless, its concentrate formulation can represent a significant hazard when ingested. This may be attributed to the relatively high concentration of the polyethoxylated surfactant used in the glyphosate concentrate which is more toxic than glyphosate itself. Consequently glyphosate concentrate is only about an order of magnitude less acutely toxic than paraquat concentrate.

In recent times, glyphosate concentrate has found increasing use as a suicide agent in some countries. No explanation for its selection for this purpose has been identified.

The signs and symptoms following significant ingestion of a significant volume of glyphosate concentrate may be severe enough to resemble that of acute paraquat or diquat poisoning. Localised oral irritation, erosion of the mouth and upper gastrointestinal tract, severe irritation of the gastrointestinal tract and hypotension can occur. In severe cases glyphosate poisoning is refractory to treatment.

As with many agricultural chemicals, there is no specific antidote for acute poisoning by glyphosate concentrate, management depends upon the clinical situation.

Once diluted to appropriate working dilutions, glyphosate does not seem to cause a significant incidence of adverse effects, although there have been few case reports or field studies from which to judge. A few cases of allergic response to glyphosate working dilution have been reported.

Glyphosate and paraquat are both herbicides with little selectivity. Both are inactivated after reaching the soil and degraded thereafter. Paraquat is firmly adsorbed to soil and is biologically unavailable. It is only slowly degraded by microbial activity. Adsorbed paraquat is immobilised in soil and not subject to leaching.

Like paraquat, the herbicidal activity of glyphosate disappears after it reaches soil. This is due to a number of factors, including binding to soil components. In the soil, the rate of microbial degradation of glyphosate primarily depends on the degree of microbial activity. It is often slow. The low motility of glyphosate within soil makes it unlikely that it would enter water bodies through run-off or by leaching.

When used as aquatic herbicides, glyphosate and paraquat both adsorb to particulate matter so that their concentrations fall rapidly. Paraquat is particularly toxic to some crustacea and so should be used with caution in estuarine areas.

Like paraquat, glyphosate has shown no propensity for bio-accumulation. Studies with exposed food animals and fish have shown similar results i.e. only concentrations of these herbicides are retained in tissues.

The inactivation of the paraquat, diquat and glyphosate in soil is a major consideration in their use. Their behaviour and degradation in soil and water does not suggest that the herbicide would cause unexpected damage after application to soil or elsewhere in the environment.

Glyphosate has not been found to show significant adverse effects on soil microorganisms or invertebrates. It does not seem to affect small mammals, although the nesting and foraging of birds may be influenced after its application, as with other herbicides probably from habitat disturbance.

Whilst there is some concern about adverse environmental effects of these herbicides on the environment, their use can have favourable impact on the environment through reducing excessive soil cultivation and ensuing erosion.

These herbicides have little direct effect on wildlife. However, they do impact on wildlife through changes in habitat. Management of the habitat is the key to maintaining a good, diverse wildlife population and if this is carried out the impact of these herbicides can be reduced further.

Glufosinate-ammonium

. Introduction

Glufosinate ammonium, ammonium 4-[hydroxy (methyl) phosphinyl]-DL-homoalanine, is a phosphinic acid derivative of glutamic acid. It was first introduced in 1984 and is now registered as a herbicide and non-selective desiccant in many countries.

The herbicidal action of glufosinate-ammonium is related to the inhibition of glutamine synthetase, the enzyme which plays an important role in ammonia detoxification and amino acid metabolism in plants.

Glufosinate-ammonium has low vapour pressure but is quite soluble in water (1370 g/L at 20°C).

. Glufosinate-ammonium Formulation

Glufosinate-ammonium is formulated as a water-soluble concentrate containing 60-200 g/L glufosinate-ammonium and an alkyl ether/sulphate wetting agent, propylene glycol ether as a solvent as well as a defoaming agent and a blue dye. A ready-to-use liquid (0.2 g ai /L) and a water-based aerosol are also available.

. Agricultural use of Glufosinate

Glufosinate-ammonium is a non-selective herbicide and contact and systemic action that is used for the control of annual and perennial mono-and dicotyledenous weeds in fruit crops and vineyards, in tree nurseries, under ornamental shrubs and on noncrop land. The application rates, depending upon weed cover, are 5-7.5 L/ha, corresponding to an active ingredient application rates of 1-1.5 kg/ha. In vineyards and on stone crops, the rate is up to 2 kg/ha (FAO/WHO,1991).

. Toxicology of Glufosinate-ammonium

The animal toxicology and biological activity of glufosinate-ammonium has been reviewed (Beuter and Leist,1987; FAO/WHO,1991; Ebert and Leist,1989; Ebert, Leist and Mayer,1990).

Glufosinate-ammonium has been found to be rapidly excreted by all of the mammalian species tested. About 80-90% of an oral dose remained unabsorbed and was eliminated unchanged in the faeces over 48 hours with about 10-15% being eliminated in the urine.

Glufosinate-ammonium itself has low-moderate acute oral toxicity; the mouse (LD_{50} about 450 mg/kg bw) is more sensitive than the rat (LD_{50} >2,000 mg/kg bw) whilst the dog more sensitive (LD_{50} 200-400 mg/kg bw). The acute dermal toxicities (LD_{50}) in rats and rabbits are also low, being >4,000 mg/kg and 2,000 mg/kg respectively. The acute inhalational toxicity (LC_{50}) to rats is >0.621 mg/L for an aerosol and 1.26 mg/l for a dust respectively. Lethally intoxicated rats and mice exhibited neurological signs such as "tonoclonic" spasms, jumping and rolling spasms as well as lacrimation and salivation (Ebert and Leist, 1989; Ebert and Leist, 1990).

The acute oral toxicity of the 200 g/L glufosinate-ammonium liquid concentrate is low, being about 1500 mg/kg bw in the mouse and in the rat. The dermal toxicity of the undiluted water-soluble concentrate formulation is about 1400 mg/kg bw whilst the inhalational toxicity again ranged from 3.22 mg/kg bw (males) to 4.31 mg/kg bw (females). Poisoned animals exhibited central nervous system signs: changes in spontaneous activity, narrowing or widening of the palpebral fissures and increased lacrimation(Ebert and Leist, 1988).

Glufosinate-ammonium is not irritant to the skin and eyes of rabbits. The formulation was slightly irritant to the skin and moderately irritant to the eyes, an effect attributable to the formulating agents. Neither glufosinate-ammonium nor its formulation was sensitising to the skin of guinea pigs.

Glufosinate-ammonium did not effect the reproduction of rats fed the equivalent of 6 mg/kg bw/day. It was not found to be teratogenic in rats or rabbits.

Glufosinate-ammonium was not genotoxic in *in vitro* and *in vivo.* It was not carcinogenic in long term studies in rats and mice. There was no indication that glufosinate-ammonium produced acute delayed neurotoxicity in hens.

The Acceptable Daily Intake for is 0.02 mg/kg bw, based upon the results of a long-term feeding study in rats (FAO/WHO, 1991)

- Mode of Action

Studies in laboratory animal show that glufosinate-ammonium competitively inhibits glutamine synthetase in different tissues but that tissue glutamate and ammonia concentrations are only increased at high doses.The inhibition of glutamine-synthetase was largely reversed in mammals after 7 days and completely after 28 days. After 28-days, feeding of glufosinate-ammonium in the diet of dogs had no effect on glutathione and carbohydrate metabolism or on the biosynthesis of non-essential amino acids in rats and dogs. CNS stimulation was only produced in test animals at high doses and could not be explained by changes in the cerebral levels of neurotransmitters. Glufosinate-ammonium did not affect the binding of various neurotransmitter receptors *in vitro* nor the concentration of catecholamine neurotransmitters *in vivo* . It is likely that glufosinate-ammonium interferes with the neurotransmitter function of glutamate when it achieves a sufficiently high cerebral concentration (Beuter and Leist, 1987; Hack, Ehling and Leist, undated).

. Accidental and Suicidal Poisoning with Glufosinate-ammonium

Although glufosinate-ammonium is registered worldwide, the only reported cases of suicide have occurred in Japan. Between November 1985 and 1990, a total of 39 cases of formulated glufosinate-ammonium ("Basta" or "Ignite") ingestion were recorded. Seven cases accidentally took 5-20 ml, 24 cases drank 50-200 ml and 7 cases ingested 250-500 ml. One took an unknown amount.

Ten adults died: five of these had also had taken paraquat and one had taken an organophosphate; another had taken an unknown combinations of agents. Most of the others taken alcohol prior to suicide. Ingestion of 100 ml of the 200 g/L formulation would give an effective dose of about 400 mg/kg bw. Only slight intoxications occurred at these doses. However, lethal amounts would require ingestion of 250-500 ml of the concentrate("Basta") , corresponding to 1,000-2,000 mg glufosinate-ammonium /kg bw (Leist, 1991).

. Occupational Exposure to a Working Dilution of Glufosinate-ammonium

In an exposure experimental study, a hand-held spray gun connected to a tractor mounted tank resulted in an exposure to glufosinate-ammonium of 0.6 mg/person/day. Using a model of exposure, the exposure from a tractor mounted boom sprayer was estimated at 40.4 mg/person/day, with a calculated dermal exposure of 15.9 mg/person/day and a calculated inhalational exposure of 0.075 mg/person/day. Full details are not available for evaluation.

These exposure estimates can be compared with "tolerable exposures" during mixing/loading and application of 280 mg/person/day (dermal) and 9 mg/kg person/day (inhalational), based on the experimentally determined no-effect levels and using a 100-fold safety margin (Leist, 1991).

Environmental Fate of Glufosinate-ammonium

. Introduction

The environmental degradation and fate of glufosinate-ammonium has been reviewed and summarised (Dorn *et al*, undated; FAO/WHO, 1991).

. Degradation in Plants

Metabolic studies in several types of plants with radiolabelled glufosinate-ammonium have shown that deamination to an alpha-keto acid was followed by oxidation to the main metabolite, 3-methylphosphinico-propionic acid. Further metabolism mainly led to complete degradation and incorporation into natural plant components. No other plant metabolites were identifiable.

. Fate in Soil

Since glufosinate-ammonium is the monoammonium salt of DL homoalanin-4-yl methylphosphinic acid, it is assumed that only the phosphinic acid anion is present at normal environmental conditions (pH).

The degradation of glufosinate-ammonium in soil, water and sediment all follow the same pathway, leading to the main metabolite, 3-methylphosphinico-propionic acid,but occur but at rates different to the same metabolic transformation in plants and animals.

Glufosinate-ammonium does not accumulate in soil; it is decarboxylated to 3-methylphosphinico-propionic acid. Further degradation to 2-methylphosphinico-acetic acid or by beta-oxidation to the corresponding keto compound, 3-methylphosphinico-3-oxo-propionic acid occurs up to about 5%. This degradation product has also been identified as a metabolite in mammals. No other metabolites are found. Thus, the major metabolites of glufosinate-ammonium in soil are the methylphosphinico-acetic or the corresponding propionic acid derivatives.

The ultimate microbial degradation products of glufosinate-ammonium are carbon dioxide and initially soil-bound residues which are then subsequently mineralised. In a sandy loam soil, laboratory tests indicate that the residence time of the residues from the top 0-20 cm soil is sufficient to enable complete degradation before they can be leached to deeper layers.

. Soil Mobility

Lysimeter studies, conducted over a period of three years, during which glufosinate-ammonium was applied twice in spring and a third time in autumn, showed that the total leachate amounted to about 0.1% in sand and 0.5% in loam soils. Most of the leachate was present as carbonate and none of the known degradation products of glufosinate-ammonium were found, indicating that soil microorganisms had utilised the metabolites in biosynthesis. After two years, the top 0-10 cm layer contained 24-40% of the radioactivity and the 10-20 cm layer contained 4.9-9.1%, with only 0.5-1.6% in the 20-30 cm layer. Amounts present in lower layers were below 1%. Less than 2% of the applied radioactivity was present in all layers below 60 cm.

The leaching behaviour of glufosinate-ammonium in soil depends to a large extent on the adsorptive properties of the soil and, at the same time, rapid degradation. Due to its high polarity, little is adsorbed to organic matter. Moderate soil absorption does occur, depending upon the amount and type of clay minerals in the soil, such as levels of iron oxides and soil pH.

Crop plants accumulate only the 3-methylphosphinico-propionic acid is in trace amounts. The maximum levels of radioactivity in the following crops were: spinach 0.04 mg/kg; radishes 0.08 mg/kg; carrots 0.04 mg/kg, dry wheat straw 0.25 mg/kg and wheat grain 0.5 mg/kg. A significant proportion of the residues was bound into natural plant components such as cellulose and starch.

. Fate in Water

The degradation of glufosinate-ammonium in water/sediment systems has been found to be qualitatively the same path as that occurs in soil. Glufosinate-ammonium is not photodegraded in water.

. Ecotoxicity of Glufosinate-ammonium

The toxicity of the active ingredient, the "Basta" formulation and the main metabolite 3-methylphosphinico-propionic acid has been determined using a variety of typical non-target organisms. The maximum environmental concentrations under unfavourable conditions were estimated at 0.05 mg a.i./L or 0.25 mg formulation/L in static water and 4 mg a.i./kg in soils.

- Aquatic Organisms

The growth of two species of green algae were significantly affected at active ingredient concentrations above 2.5 mg a.i./L and above 10 mg/L for the formulation.

The concentration of glufosinate-ammonium that immobilised 50% of Daphnia water fleas (EC50) was in the range of 500->l,000 mg/L. The LC_{50} in a 48 h static acute test was 15-78.4 mg/L.The formulation was more toxic with EC50 values between 15 and 78 mg/L. The no-observed-effect concentrations in reproduction tests with Daphnia magna after 21 days were 32 mg a.i./L with the active ingredient and 1.8 mg/L for the formulation.

Studies with fish showed low acute toxicity. The lowest 21 day LC_{50} was for trout (7.1 mg/L). The lowest no observed effect concentration was for blue-gill sunfish, *Lepomis macrochius* (1.8 mg/L). The formulation was more toxic for fish, the LC50 values being between 14-56 mg formulation/L and the no-observed effect concentrations ranged from 7-56 mg formulation/L. This greater toxicity was ascribed to formulation components in separate testing. Prolongation of exposure period did not significantly increase toxicity.

In a flow-through study at a concentration of 0.1 mg/L with *Lepomis macrochius*, measurable concentrations of up to 0.03 mg/kg were found in the inedible parts of the fish whilst in the edible portions the concentration was 0.01 mg/kg after 28 days.

The main 3-methyl phosphinico-propionic acid metabolite did not inhibit algal growth or immobilise water fleas or cause mortality or intoxication of fish.

Assuming worse case maximal environmental contamination levels of 0.05 mg a.i./L and 0.25 mg formulation/L, it can be seen that the lowest no-observed effect concentrations obtained in a long term study is lower by a factor of some 640 for the active ingredient and twice as much for the formulation. These results, obtained under laboratory conditions are unlikely to be encountered in field use and where the exposures are likely to be transient (Dorn *et al*, undated; Fisher, 1989).

- Soil organisms

The effects of formulation on soil microorganisms following single and repeated (5-10 times) application at high doses were measured via oxygen consumption in the soil, ammonification and nitrification.

Earth worms were unaffected by formulation concentrations above 1,000 mg/kg.

- **Birds**

The acute toxicity of glufosinate-ammonium following single oral administration to adult Japanese quail, bobwhites, Mallard ducks and partridges in each case was greater than 2,000 mg/kg bw. Signs of intoxication were only observed as slight mortality and symptoms observed at 2,000 mg/kg with Japanese quail and partridges. In 8-day feeding studies in Japanese quails, bobwhites and Mallard ducks, the LC_{50} values were 1250 mg/kg bw, 1,000 mg/kg bw and <1,000 mg/kg bw respectively. In reproduction studies in bobwhites, quails and mallard ducks over 24 and 22 weeks respectively, threshold concentration of glufosinate-ammonium for adverse effects of reproduction was greater than 40 mg/kg bw in the bobwhite, quail and 60 mg/kg bw in the Mallard duck.

The acute toxicity of the formulated herbicide containing 200 g/L glufosinate-ammonium was greater than 2,000 mg/kg bw in each case.

Since the formulated herbicide is applied at application rate of up to 7.5 kg/ha, equivalent to l.5 kg ai/ha, repeated exposure of birds is possible by the ingestion of contaminated vegetable and animal (invertebrate) resultant estimated maximal food sources. Nonetheless, consideration of the result of residue trials and of the largely dietary exposure of birds to glufosinate-ammonium up to 13 mg/kg bw/day, indicates a considerable margin of safety (Ebert and Leist, 1990)

- **Other animals**

Caged honey bees were not affected by application of 15.0 L/ha of the formulation in field cages. On soil without vegetative cover, the formulation caused some mortality of spiders but not when vegetation was present.

Comparison or Glufosinate-ammonium with Paraquat

Unlike paraquat, the toxicity of glufosinate-ammonium is low. It has little or no irritancy to skin and eye or by ingestion.

Some cases of human poisoning with glufosinate-ammonium have been reported from Japan. The extent to which these are associated with self-poisoning is uncertain. As fatal ingestion seems to require ingestion of the order of 250-500 ml of the 20% concentrate, accidental poisoning should not be a real problem. The clinical effects of human poisoning are not described.There is also little available information on the effects of occupational exposure of glufosinate-ammonium, although the results of the animal toxicity studies do not indicate that it would present a hazard in normal use.

Unlike paraquat, glufosinate-ammonium is mobile in soils which it reaches after application. It thus has the capacity to migrate through soil and into watercourses.

However, it can be considered to be labile in the environment because it is rapidly degraded microbially, both in soil and in water sediments. The presence of glufosinate-ammonium in water is unlikely to present problems because of its low inherent toxicity and its degradation in sediments. Its toxicity to soil and aqueous organisms, furthermore, is relatively low.

In applications where it is agronomically efficacious, glufosinate-ammonium may be a suitable alternative to paraquat. It seems to present little problem from a public health viewpoint.

Objective 4

Recommend future research or other action that the public and private sector agencies involved in the development, registration, manufacturing and distribution of paraquat-based products should undertake to increase dissemination of safety information and provide demonstrable results in safety.

Conclusions and Recommendations

Paraquat has relatively high toxicity but this has not precluded its use in agriculture. However, its toxicity has unusual aspects. It is irritant and corrosive to skin, eye and mucous membrane and, if swallowed, the gastrointestinal tract. Once absorbed, it is also toxic to internal organs (e.g. liver, kidney, adrenals). It is selectively accumulated by the lung. Those who survive its immediate toxicity can later succumb to the unique pulmonary fibrosis it can cause. The fatal human dose is estimated at 3-5 g.

Considerable effort has been devoted to identification of the negative health impacts of paraquat. These divide into problems of accidental exposure, intentional self-exposure and occupational exposure. The effectiveness of the responses to these problems has varied.

The following recommendations are aimed at "public sector agencies", although "private sector agencies" are often well, or even better, placed to contribute to this process by virtue of their research capability, expertise and experience and their local sales and distribution networks.

. Accidental Poisoning

Given its hazards and widespread use around the world, it is not surprising that there have been numerous reports of accidental, suicidal or other poisoning by ingestion of paraquat.

The principal hazard of paraquat, by far, arises from ingestion of 20% concentrate. Accidental poisonings due to its ingestion have most often been reported following wrongful decanting into other containers. A stench and a distinctive dye added to the paraquat concentrate seem to act as a deterrent to accidental ingestion and perhaps may deter some self poisonings. It should be appreciated that alternative paraquat concentrate formulations are available that do not contain a stench and/or dye. These additives should be required by registration where it exists and actively encouraged elsewhere. Although it now seems established that inclusion of the emetic is only useful in marginal poisoning cases, its inclusion in the concentrate should also be encouraged to improve their prognosis.

The incidence of accidental poisoning due to decanting of paraquat seems to have declined, possibly due to the availability of smaller packs or increased hazard awareness.

Accidental paraquat poisoning may also occur due to poor spraying practice. This aspect is reviewed as part of the consideration of occupational poisoning.

> **Recommendation 1:** All formulations of paraquat concentrate should contain a distinctive dye, stench and, where possible, an effective emetic.

. Labelling and Packaging

The label of a pesticide product such as paraquat is the primary source of accurate information on its hazards and safe use. Significant attention is paid to devising labels that are meaningful to the user and which convey information on measures for safe handling and use. Significant improvements to label design have been made in recent times through the use of colours and design. Yet, the label information should not be too sophisticated to be meaningful. The combined use of colour banding, prominent warnings and symbols on the Malaysian paraquat label illustrates what can be achieved.

Paraquat labels should identify the particular hazard of ingestion and skin and eye contamination and provide directions for safe use and first aid measures. There should be a warning against decanting.

Paraquat containers should be of a volume appropriate for the intended use and appropriately packed and labelled. Appropriate restrictions on pack size can reduce the practice of decanting into inappropriate containers which may not be adequately labelled and also reduce the need to store unused concentrate or working dilution.

These measures should be controlled through registration where that is possible and strongly encouraged elsewhere.

> **Recommendation 2:** The labelling of paraquat products should contain appropriate safety information and hazard warnings and also comply with relevant national requirements, or where the latter are not available, relevant FAO standards.

. Occupational Poisoning

The 20% paraquat concentrate is corrosive to eyes, skin and mucous membranes. Untreated eye contamination can have serious consequences. Paraquat presents a major hazard on ingestion, whether accidental or otherwise. For these reasons, those handling the concentrate should be fully aware of its hazards and take appropriate precautions. Eye protection, gloves and an impervious apron should be used.

Paraquat is poorly absorbed through normal skin. Dermal irritation can occur from prolonged contact with the working dilution and dermal exposure can become a significant hazard in situations of prolonged and/or excessive exposure. Dermal poisonings usually have followed exposure situations in which the integrity of the dermis was broached, either by some previous injury or from the paraquat solution. There have been relatively few reports of systemic poisoning from dermal exposure and these have mostly been due to inadequate dilution and/or improper use.

Paraquat should not be applied at higher concentrations (ie not exceeding 0.5% w/v) lest the protective dermal barrier be broached. Paraquat working dilutions should therefore be adequately diluted in order to avoid possible dermal injury and/or absorption. A supply of clean water is required for proper dilution and also for washing and decontamination in case of accident.

The use of traditional protective clothing and apparatus is impractical in tropical climates. A series of well documented exposure studies show that it is largely unnecessary for paraquat application. Inexpensive, lightweight personal protective equipment, such as face shields and aprons suitable for tropical use, is becoming increasingly available. Its use should be encouraged. It should be available wherever paraquat is sold or supplied and used.

Inhalational exposure to paraquat has been shown not to be hazardous provided appropriate application equipment is used. Paraquat itself is not volatile; absorption via the lung requires penetration of paraquat mist particles to the lower airways which is unlikely to occur because of their particle size. Inhalation of a spray mist or transfer of paraquat to the nose from contaminated hands can result in local irritation of the mucosa of the oro-naso-pharanyx, leading to a serosanguinous discharge or even frank epistaxis. These can both serve as a useful warning of poor working practice.

The use of appropriate spray equipment and nozzles that produce only coarse droplets is in itself an important precaution against paraquat inhalation. Inappropriate application equipment such as mist blowers or ultra low volume applicators which can produce very fine particles should not be used.

Sufficient dilute solution to cause serious poisoning is unlikely to be swallowed accidentally, even after such ill-advised action decanting into unlabelled drink containers or from sucking from spray nozzles

The volume of the concentrate made available to the workplace should be controlled so that the amount of surplus concentrate and/or working dilution is minimal and pilferage is not encouraged. If the concentrate is to be available to the individual farmers, a clear case can be made for limitation of the volume of the container so that unnecessary amounts are not stored at home or available for accidental or deliberate poisoning.

> **Recommendation 3:** All persons handling and applying paraquat should be made aware, through appropriate education and training, of its hazards by dermal, ocular and oral exposure. They also should be educated in the necessary precautions in the handling of the concentrate and safe application of the working dilution, including the need for avoidance of decanting and for secure storage of paraquat concentrate and surplus working dilutions.

. Guidelines for Safe Use of Paraquat

Public sector agencies sponsor agricultural projects of two distinct types; large scale projects such as the FELCRA project in Malaysia which are centrally co-ordinated and other projects which may also be large and involve numerous smallholder farmers.

Large-scale projects offer an opportunity for co-ordination of the procurement, storage, distribution, handling and use of pesticides for which specific controls and conditions may be applied. These conditions can be drawn together as guidelines, as has been done in the Malaysian estate sector. Projects that involve small-scale farmers present different challenges in terms of needs for education, training and responsible safe use. Greater emphasis should be placed upon control of the distribution and use of paraquat products. For example, there should be emphasis on appropriate pack sizes and proper packaging and labelling. Again, guidelines suited to the specific local needs should be developed and implemented. Where registration applies, these guidelines should complement the registered label.

It is understood that guidelines for procurement of pesticides for use by some public sector agencies are in preparation: Consideration should be given in the proposed guidelines to the adequacy of local control of pesticide use as well as the usual regulatory requirements.

Private sector agencies also often have useful information that is locally relevant which should be, taken into account. In the interests of public and occupational health and safety, suppliers of paraquat should be able to provide locally relevant information and education in its storage, handling and safe use and disposal.

The "Paraquat: Health and Safety Guide " of the International Programme on Chemical Safety (IPCS, 1991a) could be used for this purpose.

> **Recommendation 4:** Appropriate guidelines for the safe handling, use, storage and disposal of paraquat should be introduced in public sector projects. They should be relevant to the type of project and local conditions. Private sector agencies should contribute to this process.

. Paraquat Suicide

During the 1970s paraquat began to develop an unenviable reputation as an effective suicidal poison that was increasingly manifested into the early 1980s. The unusual feature was that this phenomenon developed in some countries but not in others. To what extent the subsequent decline in paraquat suicide incidence in most of the countries from where relevant data is available was due to other factors such as altered community attitudes to self-poisoning and/or increased awareness of the hazard of paraquat ingestion we are, as yet, poorly informed. The socio-cultural factors associated with this phenomenon are complex and include a mixture of age, sex, race, religion and social class. The complexity of the psycho-social aspects of paraquat suicide is demonstrated by the studies undertaken in Ireland, Fiji, Malaysia, Sri Lanka and Western Samoa.

Efforts to reduce the hazard of ingested paraquat have not been successful. Addition of the colour and stench has probably reduced the incidence of accidental ingestion but does little to deter those determined on suicide. The emetic is probably only of benefit when a small amount of paraquat is swallowed. Despite its corrosivity, foul taste and the added dye and stench, several hundred millilitres of the 20% paraquat concentrate are commonly taken for suicide; in some reported suicides up to 1 L, at least 50 times the lethal amount, has been swallowed.

The outcome of paraquat ingestion is ultimately determined by the amount of paraquat ingested rather than the concentration of its solution. The obvious step of dilution of the concentrate is unlikely to prevent suicide. Whilst dilution should improve the prognosis in some accidental poisoning and suicide attempts, the degree of dilution that would be required to prevent suicide is indeterminable because the amount ingested will vary according to the determination of the person swallowing it. Dilution and partial replacement of paraquat with diquat did not prevent self-poisoning in Japan, although the paraquat suicide incidence has subsequently declined, probably as a result of the combination of measures taken in that country. Even the working dilution (0.5% or less) has been used for suicide in Western Samoa when it was readily available.

Pesticides are more commonly used for attempted or completed suicide in developing countries than in the developed countries where drugs are usually the preferred agent. Since pesticides are usually more toxic than drugs, the result is a higher fatality rate, even if completed suicide was not the initial intent. The high mortality incidence of paraquat poisoning reported from countries such as Fiji, Malaysia, Sri Lanka, Western Samoa and Surinam may indicate strong suicidal intent, ignorance of the high hazard of paraquat ingestion or both.

Appropriate regulations to restrict the availability of paraquat products are in place in many countries, as they are for other similarly hazardous poisons. The extent to which the restriction of the availability of paraquat taken in the U.K. and other countries has directly contributed to the decline in paraquat poisonings is uncertain. Again, the reduction is probably due to the combination of all of the regulatory and other measures taken and, perhaps, also to altered public perception and behaviour.

In general, the available data show that suicidal ingestion of the concentrate is almost always complete whilst the probability of survival of accidental poisoning is higher. For this reason, there have been calls from public health professionals for restriction of the availability of paraquat in countries where paraquat suicide is a problem.

The complete banning of paraquat has been proposed as a means of eliminating paraquat poisoning. This is unrealistic. Measures have been taken against accidental ingestion and should be supported by increasing public awareness of the hazards of paraquat and other pesticides. Elimination of suicide is an altogether different and far more complex matter.

Nonetheless, the free availability of paraquat formulations in countries where little or no pesticide regulation applies is a cause for concern, particularly if paraquat poisoning is a problem.

The availability of dangerous poisons may be restricted to particular uses or class of users so that they are not available to the general public. The International Programme on Chemical Safety recommended such restriction in 1984 (WHO,1984). This recommendation still remains appropriate.

> **Recommendation 5:** Where practical and reasonable, the availability and use of the 20% paraquat product should be limited to *bona fide* agriculturalists, horticulturalists and professional users, who work with trained personnel, properly maintained equipment and adequate supervision

. Consideration of Alternatives

Whilst public health experience shows that the restriction of a notorious suicide agent can reduce its use for this purpose, this has usually been in circumstances where an alternative such as another hazardous poison was not readily available. The situations in Malaysia and Surinam, reviewed in Objective 1 provide good evidence that the determined suicide finds an alternative, if other dangerous poisons are readily available. Nonetheless withdrawal and replacement of paraquat by a less hazardous alternative herbicide becomes appropriate if its safe use is unlikely or where paraquat poisoning has achieved notoriety. Introducing an alternative should then assume priority over agricultural needs.

The private sector can contribute to this process by developing and alternative uses of existing herbicides or introducing new products.

> **Recommendation 6:** Consideration of alternative herbicides to paraquat, should be undertaken wherever paraquat poisoning is a problem or where appropriate training and safety measures are unlikely to be used. The potential hazards of alternatives to paraquat should be assessed before their use is supported by public sector agencies.

. Reducing the Notoriety of Paraquat

It is unfortunate that the notoriety of parquat as a poison for suicide has not also engendered an appreciation of the pain and misery suffered by those ingesting it. Yet the claim that paraquat should be afforded special status as a poison because an antidote is not available is not only specious but counter-productive in public health terms. It has probably even contributed to the notoriety of paraquat as an agent for suicide. The reality is that few poisons have a specific antidote and, even where one is available, its utility is usually determined by the circumstances of acute poisoning and the clinical situation. Those who have advanced this proposition, like those who have sensationalised paraquat poisonings in other ways, must bear some of the responsibility for some deaths so caused.

As there is some indication that reduced publicity to paraquat poisonings has contributed to the decline in self-poisonings seen in the UK and Japan, every effort should be taken to reduce the notoriety of paraquat. Public sector agencies, especially Government authorities, who may be seen as impartial in these matters, should exercise due influence to draw to the attention of the media the negative impact of sensationalising of paraquat poisoning.

Private sector agencies can contribute to this process through dissemination of accurate information on paraquat poisoning and eschewing its notoriety.

> **Recommendation 7:** Every effort should be made to discourage the notoriety of paraquat as a means of suicide and to encourage responsible reporting of paraquat poisoning cases by the media.

. Management of Paraquat Poisoning

First aid measures such as removal of contaminated clothing and washing of contaminated skin or flushing of eyes contaminated by paraquat should be undertaken promptly. In cases of ingestion, vomiting should be induced if it has not already occurred and the patient taken to the nearest hospital or treatment centre. These measures can best be undertaken by someone trained for the purpose.

Prompt initiation of therapy can improve the prognosis of paraquat poisoning, especially where the amount ingested is low. Measures to delay or prevent its absorption have been used in management of poisoning but should be commenced as quickly as possible after ingestion if they are to have the best chance of success. Clinical assessment of the severity of the poisoning should be undertaken so that the need for necessary treatment is not underestimated. ICI/Zeneca have distributed a guide for doctors "The Treatment of Paraquat Poisoning" which outlines the first-aid, diagnosis and treatment of paraquat poisoning. This should continue.

> **Recommendation 8:** Paramedical and medical personnel in regions where paraquat is used should be specifically informed of the seriousness of paraquat poisoning, its diagnosis and current management.

. Improved Poisoning Incidence Data Collection and Analysis

Accurate data on poisonings is fundamental to development of effective poisons control strategies. The incidence and outcome of cases of paraquat poisonings should be monitored and collated so that changes in poisoning trends can be discerned and acted upon. This is difficult enough in developed countries and is even more so in developing countries where the need is greatest. Indeed, the lack of adequate data on the incidence of pesticide poisonings in developing countries is a well recognised problem that hampers efforts to define and address it.

ICI/Zeneca has collated much of the data available on paraquat poisonings from local records and has made them freely available for the present study. However, the value of these data, like the available published data, can only reflect the thoroughness with which they were initially collected.

The most meaningful incidence data on paraquat poisoning and its outcome comes from the U.K., a country where paraquat where paraquat poisoning has been a problem but also one with an excellent poisoning data collection and analysis system.

True comparison of the available poisoning data from different countries is difficult because of differing data collection methods and variable data quality.

Retrospective analysis of hospital admission data have been the most useful source of information in most countries. However, these records may be incomplete or reflect only a proportion of the actual number of paraquat poisonings.

Retrospective analysis of accident reports maintained for medico-legal reasons in Malaysia and the Philippines, has yielded valuable longitudinal data on the incidence of workplace accidents and injuries in these over time. They indicate that the occupational risk from paraquat use is low.

The poisoning incidence reported in relatively small populations should be interpreted cautiously since small variations in the number of poisonings can distort the true situation either way.

For these reasons, every effort should be made to collect full and accurate data that is appropriate for analysis of poisoning incidences and outcomes. This should be done in a consistent manner so that results can be compared over time and from place to place, enabling problems to be identified and redressed.

Public sector agencies should obtain data on the incidence of paraquat poisonings in projects they sponsor. These data should be analysed as part of the oversight of such projects and the findings incorporated in their progress reports.

ICI/Zeneca has been collating paraquat poisoning data for many years. Its experience would greatly contribute to the overall process and should not be overlooked.

> **Recommendation 9:** Data on the incidence of human poisonings, accidental or otherwise, associated with the use of paraquat should be collected in a standardised manner, analysed thereafter and reported as part of the ongoing management of publicly sponsored projects. Paraquat distributors should participate in this process.

. Procurement of Paraquat

Public sector agencies should only support the use of pesticides in projects with which they may be associated that are nationally registered for that use. In countries where there is no established registration mechanism, governments or public sector agencies should seek the advice of FAO on agricultural matters or the IPCS for public health or environmental advice related to the proposed use.

Private sector agencies should strive to compliance with local regulatory controls and apply the same standards in regions where a formal registration process does not yet exist.

Recommendation 10: As far as practicable, only those pesticides registered for the proposed use in the country of the project should be supported by public sector authorities. In situations where no national pesticide registration scheme applies, public sector authorities should seek the views of relevant international agencies on the appropriateness of the proposed use.

. Increasing Awareness, Education and Training

The need to improve the conditions for storage,handling,use and disposal of pesticides, including paraquat, has been repeatedly identified as necessary to addressing the of problems of pesticide poisoning. Clearly, improvement of standards of the use of pesticides cannot be achieved by mere reliance upon the self-motivation of poorly educated farmers who often may lack basic knowledge of pesticide safety and/or the appropriate safety equipment. It requires proper education and training.

Targeted assistance for enhancing education and training in pesticide safety should be developed and applied by public and private sector agencies, taking into account the relevant local socio-cultural considerations and contemporary agricultural practices.

The level of training will vary according to the background and education of the participants. Courses in the safe use of pesticides should emphasise the need to reduce exposure and outline the basic concepts that underlie practical recommendations of safe use (WHO, 1991c).

A substantial programme of increasing the awareness of paraquat distributors, retailers farmers their families of the hazards of paraquat and the measures for their control was undertaken in Japan in the mid-1980s. The effectiveness of this programme by itself is difficult to evaluate because of the other measure taken at the time. Nonetheless, there was a subsequent decline in the poisoning incidence.

In Malaysia, a structured programme for increasing awareness of pesticide hazards and training in their safe storage, handling and use is being undertaken. ICI Malaysia is conducting an extensive programme focussed on prevention of poisoning and safe use of paraquat. As this programme is still in its early stages, it is not possible to estimate its effectiveness. Some objective measure of its effect upon improving farmer awareness of pesticide hazards and pesticide safety should be applied and made known so that the degree of resulting benefit can be assessed.

The work of Whitaker and his co-workers, reviewed in Objective 2, is providing almost unique baseline data and identifying deficiencies in pesticide handling, storage, application and disposal practices that can be remedied through education and training. This pioneering work should be duly recognised, developed further and acted upon by public and private sector agencies.

Appendix 5 outlines a rational strategy for education and training of farmers in the safe use of pesticides that integrates communication, education and training modalities. This strategy should be applied more widely and its effectiveness assessed and made known.

Recommendation 11: Public sector agencies should support education and training in the safe use of paraquat of all of those engaged in its supply, storage, handling and use as a component of its support of projects in which paraquat may be used. The private sector should continue to contribute to this process.The effectiveness of such programmes should be evaluated and reported.

. General Considerations

The World Health Organisation has recognised the extent of the problem of suicide by pesticide poisoning in developing countries. WHO has recommended the urgent introduction of intervention programmes to prevent acute pesticide poisoning. It sees the need for a collaborative approach to this problem, involving Governments, the agrochemical industry, the community, scientists and international agencies (WHO, 1991).

The problem of paraquat poisoning should be addressed in this context.

The International Programme on Chemical Safety, based at WHO, is developing INTOX, an international collaborative programme for the collection and analysis of poisoning incidence data and for dissemination of information to poisons control centres around the world.

The experience and expertise of this programme should be utilised in collection of standardised date on paraquat poisoning and its analysis.

Recommendation 12: Public sector agencies should collaborate with the International Programme on Chemical Safety on issues related to pesticide poisoning.

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Appendix 1: Exposure To Herbicides

General aspects common to studies of all pesticides and their use are considered. These include the terminology, the effect of application equipment on exposure and the dermal and respiratory factors that can influence the degree of toxicity a person can experience.

Application Method

The method of preparation and application of pesticides, including herbicides, can greatly influence the degree of contamination to which a worker is exposed.

A study comparing the relative dermal and inhalation exposures to a herbicide during preparation and spraying from various types of modern agricultural application equipment was conducted in the United Kingdom.

The study compared exposures arising from the use of:

- tractor-drawn hydraulic sprayer with a tank capacity of 1600 L;
- tractor-mounted hydraulic sprayer with the tank capacity of 925 L;
- tractor-mounted controlled droplet applicator with a tank capacity of 400 L hand-pumped knapsack with a tank capacity of 20 L, fitted with a 1 m boom and four nozzles; and
- hand-pumped knapsack sprayer with a tank capacity of 20 L fitted with a single lance and a cone nozzle.

Inhalation exposure was monitored by the use of a personal monitoring pump worn by each operator during spraying applications, but not during mixing and loading. Dermal exposure was assessed using the WHO standard protocol (WHO,1982).

Pouring the concentrate into the tanks of the tractor powered sprayers resulted in higher exposure by an order of magnitude compared with that incurred by filling the knapsack sprayers with diluted pesticides. During mixing and loading, the potential average exposure from the hydraulic sprayers was 102.1-244 mg/operation, the controlled droplet applicators averaged 121.8 mg/operation whilst for the knapsack sprayers the average was 11.0 -13.2 mg/operation.

Mixing and loading of the pesticide concentrate into tractor-powered sprayers was more contaminating to the operator than the subsequent spraying of the diluted materials. During spraying, the potential dermal exposure of the tractor powered sprayers averaged 40.3-42.7 mg/h, the controlled droplet applicators averaged 96.4 mg/h and the knapsack sprayers received the highest averaged dermal exposure of 89.0 -159.1 mg/h, as might be expected.

The distribution of pesticide contamination over the body during filling was consistent between all types of sprayers. However during spraying, the hands were usually the most heavily contaminated part of the body and the lower legs could be contaminated during knapsack spraying.

Overall, the total potential dermal exposure related to the type of sprayer used. Thus, relative exposure potentials were: hydraulic sprayers 2.8 -3.3 μg/g, controlled droplet applicators 7.5 μg/g and knapsack sprayers 221-247 μg/g of herbicide applied.

For each of the 5 types of sprayers studied, the potential inhalational exposure was substantially lower than the potential dermal exposure. This was attributed to the downward direction of the spraying and to the relatively large droplet size, generally >150 microns (Abbott *et al*, 1983).

The relative patterns of exposure reported in this comparative study can be expected to be applicable to any pesticide use in other agricultural conditions, although the actual degree of exposure may vary.

Routes of Exposure

. Dermal exposure

Mammalian skin is complex in structure and can act as a relatively impermeable barrier to absorption of xenobiotics. Factors determining absorption of xenobiotics, including pesticides through mammalian skin, have been reviewed (Dugard and Scott, 1984; Wester and Maibach, 1985). These factors include:

- physical chemical properties of the substance;
- degree of hydration of the stratum corneum;
- ambient temperature;
- age;
- sex;
- race;
- variations within the region of the body;
- influence of solvents and surfactants; and
- increased permeability of damaged and or diseased skin.

Age, sex and race are probably less important than two additional factors, surface area of contaminated skin and duration of exposure. These additional determinants are taken into account in the following considerations.

. Inhalation Exposure

Inhaled aerosols are deposited along the entire upper respiratory tract. However, the depth of penetration of the respiratory tree decreases as particle size increases. Larger particles, 5-10 μm and above, are deposited mainly in the upper respiratory tract, including the nasal cavity and are swallowed, expectorated or else exhaled.

Only particles in the 1-2 µm range are deposited in the lower respiratory tract (WHO, 1978).

The distribution of the size of the particles in the droplets produced by spraying nozzles in normal agricultural application has been studied and analysed. With conventional spraying equipment very few particles of diameter <16 µm were produced. Only 0.001% of the particles produced by these nozzles were of respirable size (5-7 µm in diameter).

The operators of knapsack sprayers were unlikely to inhale paraquat concentrations exceeding 50 mg/m^3. An average inhalation exposure was likely to be about 10 µg/m^3. The respirable fraction of particles inhaled by knapsack sprayers was approximately 50%.

This relatively high figure was due to the retention of the smaller and lighter droplets in, or their migration towards, the breathing zone of the spray operator whilst the larger and heavier droplets were projected towards the ground. Nonetheless, the total number of droplets reaching the breathing zone of the sprayer represented only a very small proportion of the original spray mist. However, if a spray operator were to work within his/her own spray mist, he/she could inhale concentrations of paraquat of the order of 10,000 µg/m^3 which would be extremely high in comparison to the level of exposure expected with proper field use, 10 µg/m^3 (Hogarty, 1976). It is for this reason that spraying into the wind is contraindicated.

Appendix 2: Discussions with Knowledgable Persons

As required by the Terms of the Consultancy, the consultant visited the United Kingdom for discussions with Zeneca Agrochemicals, the principal manufacturer of paraquat, in September and October 1993. He also visited the Director of the Medical Research Council's Toxicology Unit at Leicester for discussion of paraquat toxicology and poisoning. In addition, the consultant sought the views of the Director of the National Poisons Information Service who has a special interest in paraquat poisoning.

Zeneca Agrochemicals

Paraquat and diquat were originally developed and commercialised by ICI Agrochemicals plc. Recently, Zeneca Agrochemicals has acquired ownership of ICI agrochemicals, thus assuming responsibility for paraquat and diquat.

Separate visits were made to Zeneca facilities at Fernhurst, Central Toxicology Laboratory and Jealott's Hill Research Station. Discussions encompassed regulatory aspects of paraquat, its toxicity and its formulation toxicology, studies of occupational exposure and safety, user education and training and environmental fate and effects.

. ICI/Zeneca Response to Paraquat Poisonings

The principal problem with paraquat is that of acute poisoning. The history of poisoning by paraquat which has perhaps best been documented in the U.K. shows that early poisoning cases were largely a result of accidental ingestion. Beginning in the 1970's there was an increasing incidence of reports of deliberate self poisoning. Paraquat poisoning cases received increasing media attention which, in turn, promoted public awareness of the acute toxicity of paraquat and its potential as an agent for suicide.

Suicide with paraquat or any other agent was seen as a complex issue, reflecting social and other problems. Whilst the registrant was powerless to prevent such misuse, ICI/Zeneca was disturbed at this development and so had initiated an extensive research programme aimed at reducing the hazard of paraquat ingestion. ICI had also adopted a policy of actively informing the media of the implications of excessive publicity to cases of paraquat poisoning for inducing imitation and had cautiously advocated that responsible restraint be exercised in the public interest. There has been a noticeable decline in media reporting of such cases in recent years.

The regulatory actions taken in the U.K. to restrict the availability of paraquat were accompanied by modification of pack sizes and the addition of an emetic, stench and blue dye to the concentrate and granular formulation. These measures were introduced with the aim of alerting the unwary to the hazard of unintentional paraquat ingestion. Addition of the emetic was intended to improve the prognosis in cases of accidental poisoning in which the amount of ingested paraquat was usually significantly less than in cases of suicide. It was recognised that these measures offered little to influence the outcome of determined cases of self-poisoning.

U.K. Poisoning statistics show that there has been a progressive decline in both accidental and suicidal paraquat poisoning; the last accidental fatality with paraquat in the U.K. was recorded in 1982. Prior to that time there had been some 6-8 accidental paraquat deaths per year.

The experience in the U.K. had been reflected in a number of other countries. It is hoped that the recent experience in the U.K. where paraquat suicides were receiving less media attention and the rate of paraquat suicide was declining would similarly be reflected elsewhere.

An extensive series of studies of occupational exposure and monitoring for adverse health effects, leading to the definition of safe working practices, has been undertaken and published. The mode of paraquat toxicity in mammals has been elucidated. Procedures for the treatment and management of poisoned persons have developed and disseminated worldwide. Supplies of Fuller's Earth for use in management of cases of paraquat poisoning as well as a guide for doctors,"The Treatment of Paraquat Poisoning", have been widely distributed. Clinical and epidemiological studies have been supported and their results published. Detailed toxicological data and information on paraquat (and diquat) have been provided to regulatory authorities worldwide and submitted for international peer review, most notably for the IPCS in Environmental Health Criteria No 39' and the JMPR in 1986 (paraquat) and 1993(diquat). The 1984 recommendations of the IPCS are fully supported by Zeneca.

Since the early 1970s numerous avenues have been explored in an attempt to reduce the hazard of paraquat formulations. The introduction of an emetic, stenching agent and a blue dye were considered to have been particularly important in reducing accidental poisonings and probably beneficial in marginal cases.

. Occupational Hazards of Paraquat

Studies of occupational exposure to paraquat have been conducted in several countries under a wide range of conditions, including manufacture, formulation and use. The degree of exposure encountered in some of these studies far exceeded the degree of exposure that would be anticipated under normal conditions of use. The consistent results of these studies do not indicate significant hazards associated with the degree of exposure that should be encountered during normal usage. Reports of adverse effects such as dermal irritation, nail damage or epistaxis do occur and can provide a useful warning of poor working practice. These are remediable through improved education and training of workers and their supervisors of the potential hazards and how they can be avoided.

Localised toxicity following dermal exposure is the greater occupational hazard likely to be encountered with paraquat. Human volunteer studies had convincingly shown that paraquat was poorly absorbed dermally. These studies have been supported by numerous studies of field exposure and occupational epidemiology. Nonetheless, it is known that significant paraquat absorption can occur through abraded or otherwise damaged skin and that fatalities have occurred in some such cases. These have sometimes been complicated by the inadequate dilution of paraquat concentrate or poorly maintained spraying equipment. Again, such situations can be avoided through proper user education and training in the safe preparation and use of paraquat spray solutions.

. Problems Encountered in Particular Countries

Zeneca is continuing to conduct field surveys and compile baseline information on paraquat usage and associated problems in many countries around the world.

- Costa Rica

A recently published study on pesticide poisoning in Costa Rica (Wesseling *et al*, 1993) has recently raised concern about the high incidence of occupational poisoning by paraquat in that country. Zeneca has commissioned a collaborative retrospective study of pesticide poisonings in 1990-1993 to identify factors contributing to the reported poisonings.

- Japan

Paraquat, in various formulations, has been registered in Japan since the 1960s. In the early to mid-1980s there was a disturbing increase in cases of suicide with paraquat, rising to well over 1,000 paraquat suicides per year. This represented about 5% of the total number of suicides that occur annually in Japan.

In response to this high incidence of paraquat poisoning and the concern of the Japanese authorities, a number of initiatives were undertaken.

A new formulation containing 4.5% paraquat and 4.5% diquat as well as the dye, stench and emetic were introduced to Japan in 1986. In addition, a bittering agent, sodium detoniate, "Bitrex" was added to counteract the use of paraquat by "urban guerrillas" to deliberately contaminate consumer products such as soft drinks. In view of the considerable media attention that had been given to paraquat suicides, the new product was deliberately named "Preeglox L" in order to detract from its paraquat content.

ICI actively participated in the activities of the "Paraquat Safety Committee" which developed and organised strategies for countering the disturbing incidence of paraquat poisonings. The subsequent decline in the incidence of paraquat poisoning was not only pleasing, but also encouraging for future efforts to address the problem of paraquat suicide in other countries.

Zeneca felt that these responses had been appropriate for the particular situation in Japan but that the "Preeglox L" formulation would not be as efficacious in tropical agriculture as the 20% concentrate.The 20% paraquat concentrate still remains registered in Japan.

- **Pacific Islands**

The Pacific Islands have produced a disturbing incidence of paraquat poisoning. In Zenica's view, these have often been accompanied by intemperate media attention which has aggravated the situation. The same principles of product stewardship have been applied in these countries as elsewhere and there has been a subsequent reduction in accidental paraquat poisonings. Suicide by paraquat poisoning, however, remains a serious problem, probably for complex socio-cultural reasons.

. Education and Training of Farmers

The FAO International Code of Conduct on the Distribution and Use of Pesticides highlights the joint responsibility of the public and private sectors for improving education and training in the use of agricultural chemicals. Zeneca is pledged to support the FAO Code.

Education and training in the proper use of agrochemicals clearly has an important role to play in improving the lot of smallholders in developing countries. It is an important challenge for the 1990s in which Zeneca has a significant interest.

Zeneca is concerned about the appropriateness of providing potentially hazardous products such as paraquat to smallholder farmers, many of whom are illiterate and often have limited access to technical information on pesticides and advice on their safe use. Zeneca also recognised that to deny smallholders the benefits of use of such modern agricultural tools would be to their disadvantage. Ultimately, the risk and benefit of such usage should be the responsibility of the national registration authority.

Zeneca believes that, if significant advances are to be made in improving crop production yields, the quantity and quality of international and national resources devoted to agrochemical education and training must be increased during the 1990s in both the public and private sectors. Any such increased investment in agricultural education and training should properly reflect the actual needs of individual smallholders rather than transposed priorities. Consequently, Zeneca has initiated base-line surveys of agricultural chemical application practices in a number of countries and is integrating the results of these surveys into its training programmes to improve the standards for use of its products. Such surveys, initially focussing upon paraquat, have been conducted in South East Asia, Central America, and South America; their results have been summarised and reviewed elsewhere in this report.

Zeneca further believes that application of such techniques has important implications not only for the improved safety and use of agricultural chemicals but also in the future development of integrated pest management (IPM). If IPM is to be realised, it will require appropriate safe and effective use of pesticide at a higher standard than is currently achieved in many areas. Its successful application will thus require substantial education and training of farmers in its techniques as well as the proper use of pesticides. This represents a significant challenge for farmers in tropical agriculture who often are amongst the least educated but are the most numerous. As yet, there is little clear idea on the resource requirements for this considerable undertaking. An outline of the challenge of pesticide education and training for tropical smallholders and its relevance to IPM has been published (Whitaker, 1993).

. Paraquat Soil Residues

Concerns are raised from time to time over the possible contamination of soil by paraquat, leading to its subsequent unsuitability for crop production.

Since the 1960s, paraquat has been used in more than one hundred countries. According to Zeneca's records, although long term field trials have shown that soil-bound paraquat residues can have the half life of the order of ten years, there has not been a single case of the paraquat deactivation capacity of a soil being saturated with normal paraquat use.

In addition to studies previously described, an active programme of investigations, particularly in tropical countries in areas where paraquat is heavily used, is being undertaken. Results thus far are generally encouraging and continue to show that paraquat soil concentrations do not achieve significance or present a hazard to future crops.

. Soil Microorganisms

The possibility of adverse effects of paraquat on soil microorganisms sometimes raises concern, Published studies in this area often tend to utilise higher concentrations of paraquat *in vitro* which could never be achieved under field conditions. A recently published study (Sahid *et al*, 1992) of the effects of paraquat and alachlor on soil microorganisms in a peat soil was cited as an example. In this study, an effect of both paraquat and alachlor on soil microbial concentrations was demonstrated. The experimental paraquat concentrations used, namely 0, 100 and 250 ppm, were 200-500 fold more that recommended for agricultural use. This was recognised by the authors, who concluded that the low concentration of paraquat or alachlor characterise normal field application, would be unlikely to be economically important. They did, however, point out that localised high concentrations of herbicide could occur in soil.

Any reasonable interpretation of the significance of data generated under such excessive exposure conditions is most difficult.

. Wildlife

Concerns have been raised that paraquat may be responsible for the decline in the number of hares in rural England particularly in southern, central and eastern counties of England during the 1960s. Thereafter the hare population continued to decline but more slowly.

It was pointed out that paraquat had not been available for agricultural use in the U.K., during the early l960s the period when the hare population declined most rapidly.

Some factors linked to this decline include weather pattern and predation, especially by foxes and loss of farm and crop diversity (Barnes and Tapper, 1983).

Research by the Game Conservancy has indicated that the decline in hare numbers is due mainly to changes in the agricultural landscape with increased field size and the use of blocks of fields in the same rotational phase and less grass ley in the agricultural rotation.

In autumn 1984, there was a large number of hare deaths. 100-150 dead animals were necropsied and their tissues examined for pesticide contamination . In no case was a pesticide detected and paraquat was not implicated (Edwards, 1986).

Similar investigation has been conducted in France. Animals found dead there were subject to autopsy in an attempt to establish the cause of death. In 1988, 1,722 animals were necropsied, including 1,525 hares, 63 rabbits and various small animals and birds. The causes of deaths varied, ranging from pseudo-tuberculosis to trauma and septicemia. Toxicological investigations showed that the highest number of poisonings occurred in hares (178), wild boars (25), ducks (18), and rabbits (15). Pesticides that were identified in these investigations included the anticoagulant rodenticides, chlorophacione, coumafen and difenacoum. Paraquat was identified in two cases (Anon, 1989).

. Agronomic Aspects of Non-selective Herbicides

In addition to paraquat and diquat, Zeneca also markets other herbicides, including glyphosate (as its trimesium salt,"Sulfosate") and so considers it is in a position to comment upon the use and relative benefits of all 3 herbicides.

- Bioefficacy

According to Zeneca, paraquat has a wide spectrum of activity. It will "burn" any green plant tissue above the ground but does not kill perennial weeds for which glyphosate is superior.

Paraquat is more effective against grasses than diquat.

Both diquat and paraquat exert their herbicidal activity within one to two days, whereas glyphosate can take up to four to five weeks. The speed of action of paraquat (and diquat) can be of particular advantage for the tropical farmer who can see effects from the application up to as little as three hours under tropical conditions. Furthermore, crop sowing or replanting can be undertaken as little as four hours after application. In addition, paraquat does not penetrate brown bark, enabling its use against weeds growing close to crop stems and trunks without crop damage.

These features can greatly help the small farmer come to understand the concept and benefits of chemical weed control. It has been found in some countries (eg Nigeria) that paraquat was well accepted by smallholder farmers enabling them to adopt chemical weed control practices. Glyphosate, which requires more skill in use, came to be accepted thereafter.

Glyphosate is slower in action but has the advantage that, when retreatment of perennial weeds is necessary, a longer interval between treatments is possible than with paraquat.

Glyphosate needs a larger weed surface for its absorption and so it is sprayed later in the season when the weeds are bigger.

- **Rainfastness**

Rainfastness is an important property for herbicide effectiveness, particularly in tropical regions where precipitation is often frequent. For example in the Ivory Coast, during the rainy season, there is often only six hours available for spraying during the day between the dew drying and rainfall.

Paraquat is rainfast within 15 minutes after application and diquat is rainfast within 15-30 minutes.This property provides greater flexibility for their use, maximises the number of spraying hours per day and minimises the need to respray after rain. It therefore improves the efficiency of spraying teams and contractors.

Glyphosate is generally less rainfast, with the period of application before rainfall ranging from 1-6 h, according to the formulation.

- **Translocation**

Neither diquat or paraquat are translocated within the plant and so leave the root and rhizome system intact beneath the soil. This has both advantages and disadvantages.

Glyphosate is translocated within the plant, destroying the roots and rhizomes and so gives long term control of perennial weeds.This permits a longer spray interval between spray rounds and gives flexibility both in the stage of application and the volume of application.

The lack of translocation of diquat and paraquat means that less expertise is required with their application techniques to limit the potential damage to non-target plants from overspray or drift e.g. it allows spraying right up to mature stems and bark. Paraquat is usually superior to diquat in such circumstances. Any accidental foliar damage will be restricted to the point of contact. This makes use of paraquat practicable for post emergent use in field crops such as maize, cotton and vegetables as well as in young plantation crops such as oil palm, rubber and bananas. The lack of translocation supports the benefits of mulching, retention of soil moisture and reduction of light reflection. In addition, preservation of the root system of weeds can help to maintain the soil structure and so reduce erosion.

- **Soil Inactivation**

Minimum and zero tillage agriculture have the advantages of reduced costs of crop establishment in time, labour and energy; timely planting; preservation of soil structure, moisture and nutrients; facilitation of double cropping and reduction of soil compaction.

Inactivation on contact with the soil is the major feature of each of the herbicides, glyphosate, diquat and paraquat that has made their use minimal or no tillage agriculture possible.

The inactivation of these herbicides by soil means that they can be misapplied or applied at excessive rates, without adversely affecting land and that they do not leach into water. It allows sowing immediately after spraying. It also permits intercropping, with one crop growing between the rows of another.

- **Other Features**

Other attributes of paraquat include:

- the long half life of the concentrate ("Gramoxone") formulation, particularly in tropical countries;
- paraquat mixes easily with other herbicides so that such mixtures can be employed to achieve both emergent and pre-emergent weeds; and
- paraquat was cost competitive with hand or mechanical weeding, particularly when initial weed growth has been controlled.

In summary, both paraquat and glyphosate can control virtually all weeds. Over application will not effect nearby plants or following crops. Any crop can be planted after treatment with minimum or no tillage. They do not leach from soil to contaminate groundwater.

Paraquat can be used between rows of field crops and vegetables and, with care, in young plantations. Its effects can be quickly seen and any crop damage is limited to the area of contact. Its use reduces the risk of soil erosion and it is rainfast within 15-30 minutes.

Glyphosate provides long term control of perennial weeds and offers flexibility in dilution rates and stage of application.

Zeneca sees paraquat and glyphosate as complimentary herbicidal products. In its experience, rotation of these non-selective herbicides is commonly practiced to take advantage of their complimentary properties.

National Poisons Information Service, London

The Director, Dr Glyn Volans, has an international reputation for poisons control strategies and has a long standing interest in paraquat poisoning. He was a convenor of the Second European Symposium on Paraquat Poisoning, 1986.

In Dr Volans' experience, the incidence of serious paraquat poisoning has fallen noticeably in the U.K. to less than 50 cases per annum. There seem to be fewer suicidal gestures.

Regulatory restriction of the availability of "Grammoxone" to professional users has had a marked effect on the incidence of suicide. However, in his opinion the most important measure in reducing paraquat self-poisoning was breaking the cycle of the notoriety of paraquat as a poison being fulfilled by sensationalist media reporting of individual cases. Avoidance of negative media publicity was essential.

Dr Volans generously provided the unpublished results of research conducted by the NPIS which are reviewed in Objective 3.

MRC Toxicology Unit, Leicester

Dr Lewis Smith, Director, has a long-standing interest in paraquat, its mode of action and investigation of measures to overcome its acute toxicity on ingestion. This stems from the time when he was at ICI's former Central Toxicology Laboratory.

The principal hazard of paraquat is that of ingestion. There is ample information to show that, once properly diluted, paraquat may be used safely under a wide diversity of conditions.

The minimum lethal ingested dose of the 20% paraquat concentrate for an adult was about 15-25 ml i.e. 3-5 g of paraquat. Suicides by ingestion of 1 litre or more of paraquat concentrate are known.

Suicide with paraquat encompassed a spectrum of human behaviour. This ranged from the cases of parasuicide, the so called "soft suicides" which may or may not prove fatal and the so called "hard suicides" where ingestion of a large volume of paraquat was virtually a form of self mutilation.

A fatal amount of paraquat concentrate is relatively easy to ingest if one considers that a mouthful can easily range from 25-45 ml. It was not uncommon for larger amounts to be taken for suicide .

Modification of the formulation by addition of a distinctive blue dye, a stench and the emetic as well as the introduction of the product stewardship programme in the 1980s had done a lot to reduce cases of accidental paraquat poisoning. The aim of these measures was to eliminate inadvertent poisonings as well as to assist in case of parasuicide. It was always recognised that little could be done about persons deliberately intent upon suicide.

It has been shown in experimental animals that the toxicity of aqueous solutions of paraquat was proportional to the concentration of paraquat. Yet the obvious measure of dilution of the concentrate, was, in Dr Smith's opinion, unlikely to be very rewarding for prevention of suicide. Since many suicide cases ingest 100-200 ml, dilution would need to be of the order of at least 4-5 fold to begin to have effect. Yet the minimum lethal dose of a 5% paraquat solution would still be of the order of 50-100 ml, barely more than two mouthfuls. Further dilution to say, a 1% solution, would be proportionately less toxic but the diluted solution would be correspondingly more difficult and expensive to transport and distribute. Not only would this render the product economically unviable but it would not eliminate the suicide problem, since a determined person could still ingest enough of the diluted product, or any other available poison to be fatal.

Dilution of the paraquat concentrate could reduce inadvertent poisoning and help in cases of parasuicide. This had been born out with experience with the home garden product "Weedol" which contained 2.5% paraquat and 2.5% diquat. "Weedol" was marketed in the UK in sachets each containing less than a lethal dose. Accidental deaths with "Weedol" were virtually unknown and yet some suicides continued to occur, indicating that a person intent upon suicide would readily consume more than one sachet.

Experience in Japan also supported this view. Suicide by paraquat had become a "vogue" in the 1980s, although other methods such as hanging were still far more common. Modification of the paraquat formulation, adjustment of the pack size, amendment to the label, including a change of name to "Preeglox L" and a public education campaign had virtually eliminated accidents, had reduced the incidence of parasuicides but, perversely, had not changed the rate of completed suicide.

In Dr Smith's opinion, the change of name had been the single most important factor in reducing the number of poisoning cases in Japan. Yet, as the new formulation came to be recognised as an alternative source of paraquat, cases of suicide with the new formulation began to appear so that the overall suicide mortality rate remained unchanged.

Appendix 3: Observations from a Visit to Malaysia

The consultant visited Malaysia during the week of September 6-11, 1993 to gather information about the current use of paraquat in that country. Arrangements for this visit were facilitated by the Malaysian Ministry of Health.

Dr Ashok Seth of the World Bank, Washington, joined in discussions held over the period September 6-9 with Government officials, agricultural producers and agricultural chemical marketers and their Associations. Discussions were later held with representatives of public interest groups and some faculty members of the Department of Community Medicine, Faculty of Medicine, Universiti Kebangsaan Malaysia.

The consultant later visited an oil palm estate to observe the application of herbicides under current Malaysian practices.

Use of Agrochemicals in Malaysia

Agricultural chemicals are widely used in Malaysia in the production not on only of major plantation crops but also in the production of crops such as vegetables, rice, fruit and tobacco.

Herbicides account for about 80% of the total use of pesticides in Malaysia followed by insecticides (15%) and other pesticides (5%; e.g. rodenticides, nematicides). Herbicides are used mainly on plantation crops, such as rubber, oil palm and cocoa. Those most commonly used are paraquat, glyphosate, 2,4-D, diuron, MSMA (methylarsonic acid), picloram and dalapon. Insecticides may find use on rubber plantations whilst both insecticides and fungicides are often used on cocoa (Lum *et al*, 1993).

The pattern of usage of agrochemicals in Malaysia has altered considerably in recent years with the relative growth of the small farmer sector ("smallholders"). According to Whitaker (1989), there are over 715,000 rubber and oil palm smallholder families in Peninsular Malaysia, farming some 1.5 million hectares of rubber, 0.6 million hectares of oil palm, and supporting almost 4.3 million people - 75% of the rural population. This population is divided into those grouped into settlement schemes, managed by two Government affiliated organisations, FELDA (Federal Land Development Agency), and FELCRA (Federal Land Consolidation and Rehabilitation Authority), and those which are "independent". Development of the "independent" non-Government sector is co-ordinated by other organisations such as the Rubber Industry Smallholder Development Authority (RISDA).

Malaysian farmers, in general, reportedly pay little attention to the safe use of pesticides (Lum *et al*, 1993). According to Lee (1993), six independent surveys of plantation workers and farmers conducted between 1987-1990 in Malaysia have shown that a considerable percentage of farmers complained of some symptom(s) of pesticide exposure. The surveys covered sprayer operators in rubber, oil palm, cocoa, rice, fruit, ornamental crops and vegetables, coconut and mixed crops. Five of the surveys were conducted in West Malaysia while the sixth covered Sarawak.

The percentage of spray operators reporting to have some symptom of pesticide poisoning reportedly ranged from 32-72%. The majority of poisoning cases were associated with the handling of unspecified herbicides and insecticides and, to a lesser extent, fungicides and other agrochemicals. Dermal reactions, including contact dermatitis, with blistering, erythema and cracking and fissuring of the skin were reported. Fuller details were not given.

Inappropriate clothing and faulty equipment were the most common cause of these symptoms. Poor hygiene (e.g. not washing of the hands before eating or smoking) was also a significant contributing factor. Safety measures, such as the wearing of protective gloves and facial shields and the proper maintenance of equipment were often disregarded. Some 58% of estate workers who handled pesticides daily were considered at high risk (Lee, 1993).

. Regulation of Pesticides in Malaysia

- Pesticides Board, Ministry of Agriculture

The various legislative requirements for the regulation of pesticides in Malaysia are administered by the Pesticides Board, Ministry of Agriculture. These are the:

- Pesticides Act (1974);
- Pesticides (Labelling) Regulations(1984);
- Pesticides (Importation for Education or Research Purposes) Rules 1976;
- Pesticides (Licensing for Sale and Storage for Sale) Rules 1988.

The Pesticide Board registers pesticide products for a renewable 3 year period in accordance with the relevant Act, Rules and Regulations. All premises that store pesticides for sale and/or sell pesticides are required to be licensed and inspected. Advertising of pesticides in the electronic media is also regulated by the Board.

The Malaysian Ministry of Health is not directly involved in pesticide regulation, apart from representation on the Pesticides Board. Through its Occupational Health Section, the Ministry is involved in the occupational aspects of pesticide use and with pesticide poisonings, occupational, accidental or otherwise, through the public hospital system.

. Use of Paraquat and Glyphosate in Malaysia

- Manufacturer's Viewpoint

Paraquat
According to its principle manufacturer and supplier, ICI Agrochemicals (Malaysia), paraquat, marketed in Malaysia since the 1960, has made a significant contribution to Malaysia's economy, particularly through its extensive use in the two major

agricultural industries, rubber and palm oil production. It also finds increasing use in field crops, vegetables and rice.

Paraquat is said to have particular advantages for weed control in Malaysia. It is relatively inexpensive, easy to use and does not alter the vegetation spectrum significantly because it kills only the above-ground portion of the weed, thereby retaining the integrity the subsurface soil structure and not encouraging overgrowth by other weeds. Significantly, paraquat does not adversely affect crops such as oil palm, bananas and pineapple which are often sensitive to other herbicides. Above all, it is highly rainfast, so that tropical precipitation falling soon after application does not affect its efficacy.

Due to changes in the profile of Malaysian agriculture,plantation usage of paraquat has declined whilst usage of paraquat by "smallholder" farmers has increased correspondingly. Most smallholders apply paraquat themselves, using high volume application (400 L/ha) of dilute spray, about 2-3 times per year.

- **Glyphosate**

Monsanto Malaysia considered that glyphosate is now well established in Malaysia as a cost effective alternative to paraquat in plantation crops. It is finding increasing acceptance in non-plantation agriculture. Recent price reductions and the introduction of new formulations and admixtures were said to have resulted in an expansion in its use from perennial weed control to the control of annual weeds and for general weed control. It has also come to dominate certain specific applications such as the control of "Lalang" weed.

The introduction of controlled droplet applicator technology to large plantations and by government land schemes had increased labour efficiency and reduced application costs. New nozzle technology resulting in low spray drift has enabled the use of glyphosate formulations in very young oil palm trees and in orchards where it could not be previously used.

Monsanto is undertaking continuing effort to introduce new technologies and to educate smallholders and estate workers in the proper use of glyphosate products.

- **Agricultural Producers' Viewpoint**

Producers' representatives from the Malaysian Rubber Producers' Council, United Plantation Association of Malaysia, and the FELDA, FELCRA and RISDA projects, consider that herbicides, including paraquat, are essential to modern, efficient agricultural production in Malaysia.

Plantation workers have been, and are being, educated about pesticide hazards and their safe use, including proper maintenance of application equipment. General "Guidelines for the Safe and Effective Use of Pesticides", have been developed and are being applied.

The United Planting Association of Malaysia indicated that paraquat is now being kept in locked stores on plantations and records of its use are also being kept to reduce pilferage and misuse.

The National Smallholders' Association of Malaysia represented Malaysian smallholders mostly (80%) owning 3 ha or less. On average they would apply 1.5 L of paraquat concentrate 2-3 times per year. The smallholder sector saw paraquat as cheap and effective herbicide useful under diverse tropical conditions. Storage is not seen as a problem as most smallholders purchase their paraquat concentrate only when needed. The Smallholders' Association provides advice to its members on safe use and handling of pesticides. Some smallholder co-operatives sell and distribute diluted paraquat solutions despite increased container and transport costs. It was claimed, however, that the sale of diluted paraquat gave rise to problems of "off-specification" product.

- **Non-Government Organisations' Viewpoint**

Representatives of the Federation of Malaysian Consumers' Association, the National Coalition Against the Misuse of Pesticides, the Pesticides Action Network and "Tenaganita" (Womens' Force) all disputed the views of government officials, paraquat's producer and grower groups on the incidence of poisoning by paraquat and its safety for use in Malaysian agriculture.

An alarmingly increased rate of-human and animal poisonings by paraquat was alleged. It was claimed that plantation workers, rice farmers and smallholders were being adversely affected in that order. In their collective view, inadequate attention was being paid to training in safe use and to occupational monitoring of exposure to pesticides, including paraquat. It was recognised that the more established plantations did provide better equipment and training than that which was available from newer plantations or to individual farmers. Nonetheless, there often was inadequate training in first-aid and safety measures. Essential hygiene measures, such as provision of clean water for drinking, washing and first-aid were often unavailable in the workplace. Other perceived problems included:

- lack of appropriate protective equipment;
- inadequate label warnings and directions of use, including labelling in the Tamil language;
- ready distribution of paraquat concentrate by "estate suppliers" and pesticide retailers;
- illegal sale of decanted paraquat in drink bottles; and
- improper disposal of paraquat containers into domestic garbage.

It was felt that inadequate attention was being paid to the use of physical (ie non-chemical) means of weed control.

According to "Tenaganita", the majority of herbicide sprayers in Malaysia now are women, there being more than 30,000 female pesticide sprayers employed throughout the country by the plantation sector alone. A joint study by Tenaganita and PAN Asia and the Pacific on the "impact" of pesticides on women plantation workers, including socio-economic factors, was cited (Arumugam, 1992). The 50 women interviewed were chosen at random from six estates from the State of Selangor. Complaints of nausea, dizziness, fatigue, dermal infections and fingernail damage were associated with the use of paraquat. Other less specific complaints of menstrual irregularity and uterine prolapse are difficult to reconcile with herbicide usage. There does not seem to have been a comprehensive occupational health investigation of these complaints.

- **CAB International**

CABI Malaysia representative supported the need for greater emphasis on non-chemical means of pest control because of the negative aspects of pesticide use as occurred with paraquat. Recent success with integrated pest management in rice growing in Indonesia provides an excellent example of what can be achieved. CABI believes that pesticides should be relegated to a supplementary role and only serve as a "stop-gap" measure whilst comprehensive Integrated Pest Management programmes are developed.

- **Faculty of Medicine, U.K.M.**

Members of the Department of Community Medicine, Faculty of Medicine, University Kebangsaan, Malaysia, have investigated the incidence of headache, fever, conjunctivitis, acute asthma or "stomach ache" in a cohort of 3041 subjects in a paddy farming area exposed to pesticides and rice dust. The relative risks for exposure to pesticide and rice dust were 1.8 and 1.6 respectively. The incidence of acute symptoms were higher in children aged less than 4 years. Thus, exposure to pesticides and/or paddy dust may contribute to acute symptoms of disease (Noor Hassim and Rampal, 1992a).

A subsequent cross sectional study compared the pesticide spraying practice on a "mini estate" and by individual paddy farmers. Occupation practice was significantly better on the mini estate with significant differences in wearing gloves, aprons and goggles and avoidance of eating and drinking during spraying. This was attributed to the better organisation by the mini estate management, provision of protective equipment and enforcement of good spraying practice and the regulations. Individual farmers relying on their own initiative were relatively less well protected (Noor Hassim and Rampal ,1992b).

The Faculty members interviewed considered that paraquat spraying by paddy farmers, mostly by knapsack sprayer, presented little real occupational health problem. They further considered that the agrochemical industry was making a serious educational and training effort to overcome the occupational and poisoning hazards of pesticides and that this was having a positive effect.

These developments were occurring against a background of increasing awareness of occupational health and safety issues in Malaysia. The proposed Occupational Health and Safety Act would strengthen the scope and coverage of occupational health and safety measures. In response to this recognised need, increasing education and training of the medical and paramedical workforce in the occupational aspects of pesticide use and safety was already taking place (Rampal, 1993).

Suicide by paraquat or other pesticides was not raised as a particular concern by these groups.

Pesticide Poisoning in Malaysia

Although death by poisoning is a matter which requires coronial investigation in Malaysia, epidemiological definition of the extent of pesticide poisoning has been hindered by limited collection and recording of data. The best available sources of information are government hospital "in-patient" data and laboratory analytical reports. The Ministry of Health receives and collates reports of cases of poisoning and their investigation from each State office which, in turn, have been compiled from district hospital records.

According to Lum *et al* (1993), most pesticide poisonings in Malaysia from 1979 to 1986 were due to paraquat with 49.1% being intentional and 37.8% accidental. Areas that include large numbers of plantations and farms where pesticides are likely to be used in quantity, tend to record high levels of mortality due to pesticide poisoning. Also mortality from pesticide poisoning correlates strongly with suicidal intent.

. Medical Unit, General Hospital, Kuala Lumpur

At the Medical Unit, General Hospital, Kuala Lumpur, in 1987, there were 603 cases of poisoning of which 298 cases were associated with pharmaceuticals, 185 with household products, 95 with pesticides, including 35 with herbicides. About half of the cases (49%) were intentional ingestion (suicide/parasuicide) and 39% were accidental. Poisoning was most common amongst those of Indian descent (41%), followed by Chinese (33%) and Malays (22%).

Intentional poisoning was most prevalent amongst the Chinese followed by the Indian sector. Accidental poisoning was most common amongst the Indian followed by the Malay sector. It was suspected that intentional self-poisoning amongst the Malays was under-reported and accidental poisoning over-reported because of the stigma associated with suicide in the Muslim population (Tariq, 1989).

According to Sinnaia (1989), analysis of the national poisoning morbidity and mortality data for the 1980s indicated a slow rise in mortality, largely due to an increasing number of pesticide poisonings.

In 1986, the Ministry of Health introduced a standardised reporting format on all cases of pesticide poisoning.This was later extended to all poisonings.

- Hospital Admission Data

1987
In 1987, 1,077 reports were received from Government hospitals. Of these, 292 fatalities were recorded (27%). The diagnosis of poisoning was based either on history, clinical examination or laboratory tests (24.7%) or from history and clinical examination only (75.3%). The following features emerged from this analysis:

Sex
There were 589 poisoning cases (54.6%) male and 489 (45.5%) female. Deaths occurred in 160 cases (54.7% male and 45.2% female).

Age
The highest number of cases was recorded in the 15-24 age group, comprising 362 cases including 92 fatalities. Mean age for males was 29 years and for females 24.3 years. The 25-34 age group had a relatively high representation, comprising 22.2% (239 cases) and 21.6% (63 deaths) of total cases.

Disturbingly, amongst those who consumed poisons for suicidal purposes, 33.6% were in the 15-24 year age group, 22.2% in the 25-34 age group and 7.5% in the 35-45 year age group. In each group there were more females than males.

Cause of poisoning
Of all cases, 46.5% were suicides and 40.7% were accidents, out of which only 4.4% were work related. Some 4.3% of poisonings were of undetermined origin. Of those who died, suicides constituted 72.6% of the deaths, accidents comprised 16%, of which only 0.2% were occupational.

Occupation
The occupational status of all cases were not ascertained. However, available information on 102 deaths showed housewives formed the largest group, 22.5%. There was also a significant proportion of general labourers, farmers, estate workers and rubber tappers (45%). Students formed about 9%..

Poison Type
In 258 fatal cases, 99.2% were attributable to pesticides. Drugs and other poisonings were a comparatively lesser problem. Mortality due to poisoning predominated in districts and areas having large numbers or wide areas of plantations where pesticides were likely to be used (Sinnai, 1989).

1988
Information compiled from inpatient records of Government hospitals by ICI Agrochemicals (Malaysia) indicate that the incidence of suicide with paraquat in Malaysia peaked in 1988 and has declined thereafter. In 1988 there were 418 deaths due to pesticide poisoning: 386 deaths due to paraquat, and 18 due to organophosphates. Of the remaining 9 deaths, 3 were due to glyphosate, 1 due to a chorophenoxy herbicide, 3 were due to organochlorines and 6 were unknown.

1991
In 1991, there were 893 admissions for pesticide poisonings (278 deaths; 31.1%) in Malaysia of which 494 (55.3%) were associated with paraquat. Of the latter, 338 poisonings were classified as suicide or attempted suicide (204 deaths; 73.4% of paraquat poisonings). Accidental exposure to paraquat resulted in far fewer admissions (129; 26.1%). There were no deaths attributed to occupational exposure to paraquat whilst the number of accidental occupational paraquat exposures resulting in hospital admission was low (13; 2.6%). For comparison, there were 102 hospital admissions due to organophosphate poisoning which resulted in 17 deaths. There were 47 admissions and 2 deaths due to glyphosate.

Response to Pesticide Poisonings in Malaysia

. Ministry of Health

As described above, the Ministry has taken steps to improve its data collection on pesticide poisonings in order to develop appropriate response. It has also improved the education and training of its personnel engaged in pesticide application in public health programmes.

. The Pesticides Board

According to Lum *et al* (1993), in response to reports of misuse of and poisoning by pesticides, the Pesticides Board, in 1984, launched a nation-wide campaign to promote the safe use of pesticides. The campaign had 3 main objectives:

- to create awareness amongst the general public of the dangers associated with the use of pesticides;
- to educate consumers and end users about safety procedures for handling pesticides; and
- to inform the public about the 1974 Pesticides Act.

The campaign included lectures, talks, exhibitions, pamphlets and posters, radio publicity and television programmes on the safe use of pesticides.

With respect to paraquat, the Board, in 1985,approved proposals from ICI Agrochemicals Malaysia, the principal manufacturer of paraquat, to add a blue dye and a stench (pyridine derivatives) to paraquat formulations as a warning against accidental ingestion. An emetic may also be added to paraquat formulations but is not required by regulation.

In recent times, the Board has been rationalising the number of registered pesticide products. The number of registered concentrations of paraquat that can be present in registered products is being reduced from 18 to 3 (i.e. 200 g/L, 150 g/L and 100 g/L).

The pack sizes of paraquat products have similarly been rationalised. Currently available in Malaysia and their approximate market share are:

- 1 L (6-7%) used by smallholders;
- 4 L (55-60%) used by more general smallholders;
- 20 L (8-10%) used by contractors and larger smallholders; and
- 200 L (15-20%) used by plantations.

It was, however, stated that some 250 ml packs of paraquat are still available for smallholder use.

It was considered that this rationalisation of the available pack sizes of paraquat has decreased the incidence of poisonings arising from the decanting of paraquat into inappropriate containers such as soft drink bottles.

Additional restrictions on the availability and use of paraquat under the "Highly Toxic Pesticide Regulations" have been under consideration for some time.

. Malaysian Agricultural Chemicals Association

The Malaysian Agrochemicals Association, in collaboration with its membership, has introduced a 3-year education programme to improve the general awareness and knowledge of Malaysian agricultural workers in safe use of pesticides. A modular training manual has been developed. Efforts are being made to promote common messages across the industry so that farmers and users do not become confused by inconsistent messages. The first step, a "train-the-trainers" programme is now nearing completion. Secondary training of farmers and other pesticide users will then begin. Funding is being sought from Government and international aid organisations to extend the programme to all pesticide users.

. Other Organisations

Semigovernmental agencies such as the Malaysian Agricultural Research Institute, the Rubber Research Institute of Malaysia, FELDA and FELCRA have also organised short training courses on the safe use of pesticides.

. ICI Agrochemicals Malaysia

Since 1969, ICI has conducted in Malaysia an extensive series of studies to determine the degree of occupational exposure and occupational health problems associated with the use of paraquat.

A considerable body of knowledge has been accumulated to show that, when used in accordance with approved practice and the taking of appropriate precautions, especially during mixing, paraquat may be used safely. Most of these studies have been published and are reviewed elsewhere in this document.

The degree of exposure encountered from proper application of diluted paraquat has been found to be insignificant, providing good working practices are followed. The use of elaborate protective clothing and equipment is unnecessary.

In response to the continuing problem of poisoning by paraquat, formulation changes were introduced to paraquat liquid concentrate, namely the addition of a blue dye, a stench and an emetic aimed at alerting the user or unwary at the potential hazard of paraquat ingestion.

In addition the packaging and label of its paraquat had been improved not only to comply with regulation but also to alert the user to the hazards. The currently registered Malaysian label for a 4 L "Grammoxone" container carries a red band to indicate high hazard, a "skull and crossed bones" symbol to indicate a poison as well as the warnings,

"HIGHLY POISONOUS"
"KEEP AWAY FROM FOODSTUFF AND CHILDREN".
and
"PARAQUAT CAN KILL IF SWALLOWED"

The latter warning statement precedes the following safety directions, printed in red and contained with a panel:

"USE AT LEAST 40 PARTS OF WATER TO ONE PART OF 'GRAMMOXONE' PP910 DO NOT USE ANY APPLICATOR NOZZLE WHICH INVOLVES USE OF CONCENTRATIONS ABOVE THE RECOMMENDED RATE. DO NOT APPLY THROUGH 'ULTRA LOW VOLUME (ULV)', 'CONTROLLED DROPLET APPLICATOR (CDA)' OR 'MISTBLOWER' IN ANY CIRCUMSTANCES DO NOT REPACK FROM ORIGINAL CONTAINER"

Additional warnings and cautions, the symptoms of poisoning, first-aid directions and instructions for medical treatment in case of ingestion, including an emergency telephone number are so displayed. The warnings and statements are written in English, Malay and Chinese. Pictograms illustrating the need for locked secure storage, use of face shield, protective gloves when handling the concentrate and washing after use are also displayed.

In 1985, ICI Agrochemicals Malaysia introduced a product stewardship programme for responsible and ethical management of its products. It is currently funded to about $1 million annually with education and training as its principal features.

A primary objective has been the education of management, supervisors and workers on rubber and palm oil estates about the hazards of paraquat and its safe use. A company medical officer has visited some 1200 Malaysian estates for this purpose since 1985. Direct safety education of farmers has been introduced as part of normal sales promotion. Education of technical and advisory staff has been introduced at agricultural colleges, training schools and in the Department of Agriculture. An increased acceptance of the use of protective clothing designed for tropical use during mixing (e.g. Tyvac aprons) was claimed as a direct result of this type of education.

A training programme on management of paraquat poisoning introduced for doctors, paramedics in hospitals and for medical assistants employed on the estates has been introduced. Based on experience gained, the programme has been modified and improved. Thus, in 1993, the following additional measures were introduced to increase awareness of paraquat's hazard potential:

- pictograms on labels;
- leaflets attached to packs;
- a poster campaign at distribution points;
- a campaign in print, radio and electronic media;
- an "incentivised" learning scheme aimed at users and school children; and
- a media campaign.

ICI (Malaysia) considers that these measures will have an increasingly positive influence on improving the understanding for safe handling and use of all agricultural chemicals and not just its products.

Observations

The Malaysian experience with the use of paraquat combines the diverse elements of acute poisoning and extensive occupational exposure experience and monitoring under tropical conditions.

Paraquat poisoning in Malaysia presents two distinct problems, acute poisoning due to either suicidal or accidental ingestion and the sequelae of occupational exposure. Suicidal ingestion is by far the major problem.

In contrast to its use on plantations where paraquat is applied by dedicated sprayers for up to 10 months of the year, smallholders farm only about 3 ha per family and would usually apply paraquat only 2-3 times per year. Consequently, occupational exposure to paraquat should be significantly less in the smallholder sector.

There is increasing awareness of occupational health and safety issues in Malaysia. Training of medical and paramedical personnel is increasing. Anticipated new occupational health and safety legislation should better define responsibilities and promote improved occupational health and safety. The agrochemical industry has responded to this challenge through its programme of education and training.

The results of supervised occupational exposure trials and field surveys generally indicate that occupational exposure to paraquat during the mixing and application operations should not be a problem if operator training and supervision is adequate and if appropriate protective clothing and facilities for personal hygiene are available. ICI Agrochemicals (Malaysia) has undertaken serious attempts to warn of paraquat's hazard and to educate trainers and users in its safe use.

Although there is, as yet, insufficient information to gauge the effectiveness of these measures, they should continue and be encouraged vigorously.

Available statistics indicate that paraquat became the principal agent for self-poisoning in Malaysia in the 1980s. The incidence of paraquat suicide seems to have peaked in 1988 and declined thereafter. The influence of the formulation changes aimed at deterring accidental ingestion is not established but may have contributed to this decline.

It was commonly recognised that paraquat has gained notoriety as a suicidal agent. Consequently, suicide with paraquat was often seen as a "social issue" rather than a consequence of its availability.

As mortality from pesticide poisoning closely related to suicidal intent, the control of sale of hazardous pesticides to only *bona fide* agriculturalists and horticulturalists has been advocated. Similarly, the substitution of highly toxic substances with less hazardous ones has been proposed to reduce poisonings and deaths. In response, it was often stated that another poison would be substituted for suicide should the availability of paraquat be restricted. There is some historical evidence to support this view.

As a consequence or the changing profile of Malaysian agriculture, paraquat is now more widely available in the Malaysian community than when it was previously largely confined to plantation usage. This now seems to be reflected in an increased tendency for suicidal use of paraquat in the sub-urban population.

Hitherto, suicide with paraquat has been thought to be more common amongst the Hindu and Buddist sectors of the population and less frequent amongst the Chinese and Malays for social or religious reasons. This pattern is apparently changing with increasing incidence of suicide amongst Malays and Chinese. This may be attributable to factors such as the relatively decreased number of plantation workers or to factors such as changing social patterns, altered familial control, including the changing influence of role models and/or other elements which are neither identified nor fully understood. Hopefully, the improved poisoning epidemiological data collection being implemented by the Ministry of Health will enable this question to be answered.

Appendix 4: Persons Consulted

The consultant would like to thank all of those who assisted in this project, including:

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Dr Chew Soo-Ton, Environmental Affairs Manager, Monsanto (Malaysia)

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Mr George Diatloff, Senior Agronomist, Queensland Lands Department, Brisbane, Australia

Mr Peter J.Edwards,Environmental Biologist, Environmental Sciences Department, Zeneca Agrochemicals, Berkshire U.K.

Ms Irene Fernandez, Director, Tenaganita and Chair, Pesticide Action Network, Asia Pacific, Kuala Lumpur, Malaysia

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Mr John R. Finney, Development Director, Zeneca Agrochemicals, Surrey U.K.

Dr George B. Fuller, Director, Product Registration & Regulatory Affairs, Monsanto Agricultural Company, St. Louis, Missouri U.S.A.

Dr. Charles E. Hastings, Toxicology Manager, roundup and Residential Products, Monsanto Agricultural Company, St. Louis, Missouri U.S.A.

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Ms Lily Hor, Malaysian Agricultural Chemical Association

Mr Wong Hoy Yuen, Senior Pharmacist, Division of Pharmaceutical Services, Ministry of Health, Malaysia

Dr Charles E. Hastings, Toxicology Manager, Monsanto, St. Louis, Missouri U.S.A.

Mr Stephen Kinder, Managing Director, Shell Chemicals, Malaysia

Dr P. Krishnan, Honorary General Secretary, Malaysian Medical Association, Kuala Lumpur, Malaysia

Dr Lim Guan-Soon, Scientific Adviser, CAB International, Kuala Lumpur, Malaysia

Mr Lim Ah Hooi, Marketing Manager, Monsanto (Malaysia),

Dr Karl-Heinz Leist, Hoechst AG, Germany

Mr Zahari B Hj Mahfudz, Business Manager, ICI Agrochemicals (Malaysia) Sdn Bhd.

Mr Tuan Hj Mohd Noor Maidin, Chief Executive Officer, Malaysian Rubber Producers' Council

Dr Noor Hassim Ismail, Faculty of Medicine, University Kebangsaan Malaysia, Kuala Lumpur

Dr Gobindram B. Nainani, Deputy Director, Health Division, Ministry of Health, Malaysia

Dr A.D. Parkinson, WHO Representative for American Samoa, Cook Islands, Nuie, Samoa and Tokelau, Apia

Professor Susan Pond, Department of Clinical Pharmacology, University of Queensland, Brisbane

Mr Pow Kam Wah, Plant Protectionist, Sime Darley Plantations, Selangor, Malaysia

Ms Maheswari Ramasamy, Director, Federation of Malaysian Consumer Associations.

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Ms Sarojini Rengam, Executive Director, Pesticides Action Network, Asia and the Pacific

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Dr Yusoh Salleh, R & D Manager, Dupont Agricultural Products, Du Pont Far East Inc. Kuala Lumpur, Malaysia

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Dr Robert C. Scott, Product Manager, Product Management Section, Zeneca Central Toxicology Laboratory , Cheshire U.K.

Mr Anil Somani, Senior Environmental Specialist, The World Bank, Washington U.S.A.

Mr Tan Soo Hian, Secretary, Pesticide Board, Malaysia

Dr M. Shukor Ussof Adon, Assistant Director, Occupational Health Unit, Ministry of Health, Malaysia

Mr Mike Watson, Pesticides Safety Directorate, Rothamsted, U.K.

Mr Mike Whitaker, Product Usage Manager, Stewardship and Safety, Zeneca Agrochemicals, Surrey U.K.

Mr Andrew Yeo, Director, Mastra Corporation Sdn Bhd, Kuala Lumpur, Malaysia

Dr Zakiah Ismail, Institute of Medical Research, Malaysia

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Ms Josie Zaini, National Consumer Protection Council, Selangor, Malaysia

Appendix 5: A Farm Level Framework for Pesticide Training

A FARM LEVEL FRAMEWORK FOR PESTICIDE TRAINING*

Introduction

Pressure to increase agricultural productivity, particularly in developing countries, will intensify into the next century. World population continues to expand. The World Bank expects the total to rise from 5.3 billion in 1990 to 8.4 billion in 2025. Most of this expansion is centred in Asia and Africa. It is not before 2075 that overall population growth is expected to level off completely at 10.2 billion. At the same time, the FAO has shown that the availability of new land is severely limited in many parts of South East Asia, Africa and Latin America.

These conflicting trends point to severe pressure on agricultural productive capacity in large parts of the developing world. Maximization of crop yields/ha will be imperative, and can only be-achieved by use of available technology, including chemical crop protection.

* *Based on a paper prepared by M.J. Whitaker, ICI Agro-chemicals to the Third International Conference on Plant Protection in the Tropics organized by the Malaysian Plant Protection Society (MAPPS), Genting Highlands, Malaysia, 20-23 March 1990. The original paper is referenced and carries a large number of illustrations which have been omitted in the present version. Complete copies can be obtained either from ICI or ARSAP.*

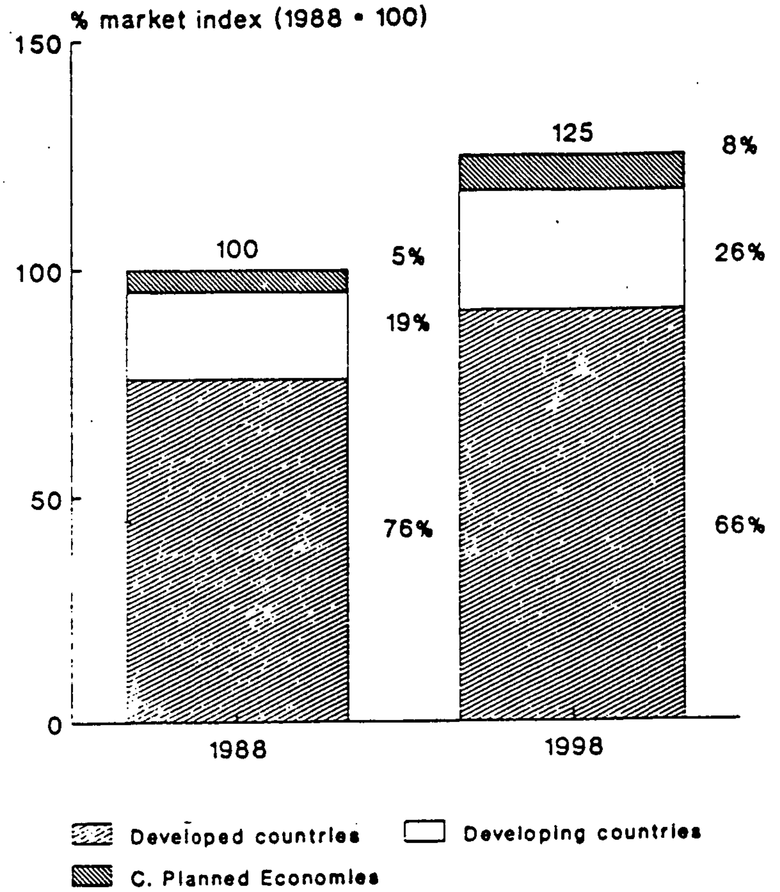
Biotechnology is making rapid progress and can be expected to play a major role in crop protection in the long-term. However, for the remainder of this century and the beginning of the next, effective crop protection will continue to depend, to a considerable extent, on intelligent use of agro-chemical technology. Adoption of national Integrated Pest Management (IPM) strategies, integrating the full range of varietal, cultural, biological and chemical pest control methods testifies to the continued role to be played by agro-chemicals in sustained long-term improvement of agricultural productivity and quality.

World agro-chemical usage (figure 1) is forecast to continue growing at around 2.5 per cent per annum over the next 10 years, particularly in developing countries. Further analysis suggests that most developing country growth will stem from the wider use of agro-chemicals by smallholder farmers.

These developments, together with the need to improve existing standards in the use of agro-chemicals by smallholder farmers, and plantation workers, emphasizes the importance of implementing effective education and training programmes across much of the developing world. Demand for increased education and training support in agro-chemical usage, will come from the World Bank, international aid organizations, as well as national governments. In addition, the wider adoption of IPM and insecticide resistance strategies will make greater demands on product-support skills and capabilities.

Education and training

Figure 1. World agro-chemical market growth



Source: Hayes, A. (1990). Global Trends in Agro-chemicals and Seeds. US Co-operative Society's Annual Conference, Georgia, USA, March 1990.

There can be little doubt that the quantity of international and national resources devoted to agro-chemical education and training, as a component of improved pest management, will increase in the 1990's, in both public and private sectors. The FAO's International Code of Conduct on the Distribution and Use of Pesticides highlights the shared responsibility of both sectors in the achievement of improved standards. This is supported by GIFAP in its guide to industry on the code's implementation.

For success, it is crucial that public and private sector resources invested in agro-chemical education and training are managed to maximum effect.

Farmer education and training in ICI agro-chemicals

It is important to realize that agro-chemical companies have been carrying out a wide range of education and training activities for the past 20 years or more, as a part of normal market development. However with the establishment of the FAO Code of Conduct, growth in use of pesticides in developing countries, an increasing realization of the need to raise standards and the implementation of company product stewardship policies, the importance of establishing farmer education and training as a professional company activity alongside development, marketing and sale of products becomes all the more apparent.

ICI's Farmer Education and Training Section (FEATS), based in the United Kingdom, provides the focal point for improving standards in company extension support across its world markets. Its primary functions include:

1. Assessment of standards in use
2. Education
   - Design and pre-testing of materials
   - Planning and implementation of programmes
3. Training
   - Design and pre-testing of materials
   - Planning and implementing internal (ICI staff) and external (Extensionist, Retailer, Paramedic, Teacher) training programmes
4. Monitoring the impact of programmes

This paper outlines FEATS thinking on the design of effective programmes and the methodology it is encouraging overseas marketing companies to adopt.

Components of effective programmes

Targetting activities

Programmes which are developed locally and tailored to local circumstances stand the best chance of reaching and influencing target audiences.

The key to successfully targetting education and training programmes is improved understanding of target populations. In particular, actual standards in the handling and use of agro- chemicals and hence the priorities for improvement; literacy levels; technical language skills; cultural acceptability of pictures and symbols to communicate safe and effective product use; the relative importance of different communication channels reaching into these populations, as well as the impact of past initiatives on them.

Where possible representative base-line surveys of target audiences are being integrated into the company programmes. To date FEATS has conducted knowledge, attitude and practice surveys in Malaysia (rubber and oil palm), Central America (maize), Brazil (bananas), Indonesia (rice), Paraguay (cotton), Thailand (maize, cassava, rubber and fruit), Pakistan (cotton), Colombia (coffee, maize, rice and potatoes) and has plans to extend such surveys to other situations in Asia, Africa and Latin America.

Information gained from such surveys has been shared with national authorities. It explains actual standards in the use of ICI Agro-chemical products as opposed to perceived standards, and explains the rationale for the education and training programmes implemented. The broad steps FEATS intends to follow in each area to ensure properly targetted programmes is illustrated below. The need is stressed to pretest education and training materials, and the desirability to monitor the impact of programmes, so that they can be refined and developed. In this way, education and training could become a dynamic, on-going management process.

1 Base-line survey to define:
- Actual user needs
- Effective communication methods

2 Design and implement targetted mass education and training programmes, using pretested materials

3 Monitor the impact of programmes and revise them

Integrating activities

There is no unique solution to the improvement of standards. Improvement requires a sustained effort, and the need to integrate complementary mass education techniques, with direct and indirect training in properly managed programmes. Without this, the impact of resources would be dissipated in fragmented and unco-ordinated activities.

The main components of integrated programmes from a company point of view are as follows:

Education (Definition: the systematic transfer of information on improved practice)

(a) Label

(b) On-pack leaflets

(c) Wall posters

(d) Mass media - radio
- TV

(e) Educational videos

(f) Educational aids - materials/devices

Training (Definition: the demonstration of improved practice)

(a) Direct to farmers - mobile field units - Flip charts
- Video/film
- Slides

(b) Indirect via:

Distributors - "Train the Trainers" programme
Extensionists - "Train the Trainers" programme

The potential contribution of each component is briefly examined.

Mass education

Labels

Product packs have to become fully self-educational, if agro-chemicals are to be used safely and effectively in developing countries. Labels are an essential part of this process. They are a vital and primary point of contact with end users, and every effort must be made to improve their quality. The principles of good labelling have been well-defined and recently set out in GIFAP's "Guidelines for Writers of Pesticide Labels and Literature" published in 1989.

In many parts of the world, colour-coding schemes have been introduced for some time, to illustrate the relative hazards of different products. This has been stimulated by WHO and supported by national governments. Nevertheless, many smallholders remain unclear about their meaning. This results from insufficient public education during their introduction. It must not happen with 'pictogrammes', which are potentially very useful aids to safety.

However, one cannot simply rely on labels, even with improvements to bring about significant changes of standards-in-use. They lack the space and flexibility required for really imaginative campaigns. Large numbers of users cannot read and those who can, do not necessarily read labels before use. In a great many cases, users also lack the technical language skills to understand them fully. It is vitally important therefore to supplement label information with other methods of communication if packs are to become fully self-educational, and satisfactory standards in the use of products are to be achieved. Supplementary on-pack leaflets have a key role to play in the area.

On-pack leaflets

From among all the educational materials that have been produced over the years to support ICI Agro-chemical products, on-pack leaflets, transferred in attachments such as neck-tags have the greatest potential, by far, of transferring information to the end-users in an appropriate form. They are particularly suited to smallholder markets in developing countries, being highly visible and tending to attract the attention of end users, which labels do not. They provide the space required for good communication - using illustrations and simple texts almost 100 per cent comprehension levels can be achieved. This gives the flexibility to run complete series of short-term education campaigns covering all aspects of improved practices. Research also shows that, smallholders who receive such leaflets tend to retain them and show them to other members of their families.

Clearly, the full potential of on-pack leaflets as a method of communication to smallholders has just begun to be developed. They need to be used responsibly. However because these are not necessarily constrained by lengthy bureaucratic procedures required to change label contents or formats, short-term imaginative on-pack communication could become possible, and permit time for the use of novel techniques such as incentivised learning schemes. Two incentivised learning campaigns were tried in Malaysia.

The first campaign aimed at increasing awareness of improved on-farm storage methods. Survey research had highlighted the extent to which storage methods were improvised and inadequate on rubber and oil-palm smallholdings. Entrants were offered appropriate prizes for correctly differentiating good from bad practice. Approximately 50,000 smallholders responded to the scheme.

The second campaign incentivised the reading of product labels. Again, survey research showed that large numbers of literate rubber and oil-palm smallholders do not read product labels before use. Entrants were asked to check actual product labels and identify key safety words. Prizes were offered for correctly finding the right words. Approximately 20,000 smallholders entered the scheme.

Different response rates for the two campaigns probably reflect their relative complexity. The readership campaign required more disciplined effort on the part of the entrants than the safe storage campaign. This shows that industry would have much to learn about the design of such campaigns for greatest effect. The good response levels to both campaigns, together with attendant press and media coverage, illustrates the potential use of such campaigns in raising awareness of improved practice and of creating interest in it.

A significant impact on standards in the 1990 cannot be expected by simply recycling the same low-key educational methodology of the past. This is social marketing work and requires a good level of management efficiency. Methods which permit new imaginative approaches must be adopted. On-pack leaflets, if properly developed, represent one such method, and should be adopted on a wide scale.

Posters

Posters have a useful supporting role in properly integrated educational programmes, provided they are well designed and adequately distributed. Good design is essential to ensure that posters are visually attractive and easily understood. The illustration should show good and bad practice, in a deliberately structured way, at each stage in the handling and use of agro-chemicals from purchase to disposal.

In a campaign in Central America written reminders and explanations were included, as well as illustrations and symbols, to aid comprehension and hopefully motivate change. This amount of text was incorporated because research had been undertaken on individual and family illiteracy rates in these target populations (smallholder maize farmers using 'Gramoxone'). These are at relatively low levels - approximately 30 per cent among male heads of households, but down to less than 5 per cent among families because smallholders' children, who have usually received some primary education, have higher literacy rates than their fathers, and are used to fill the gap for illiteracy with older members of the family.

Table 1. Access to selected mass media in different markets

Percentage population owing	Central America					
	El Salvador Maize	Honduras Maize	Java Rice	Paraguay Cotton	Malaysia Rubber/Oil palm	Brazil Bananas
Radio	62	81	80	82	85	89
TV	-	-	24	11	90	74
(Sample size)	(124)	(121)	(450)	(458)	(401)	(300)

However the final impact of this, and other posters, on the rural communities these are aimed at, depends to a great extent on the distribution they receive. This has to be wide and appropriate.

There is considerable variation in the exposure potential of different poster sites. In Malaysia, research shows that safety posters displayed in agro-chemical retail shops, received only 2 hours/annum exposure, while those displayed in the rubber dealer shops, where many independent Chinese and Malay smallholders sold their rubber, received 30 hours/annum exposure to the average rubber and oil-palm smallholder.

There is a need to improve understanding of the exposure potential of different poster sites in the rural communities dealt with, to ensure that the time and effort spent in developing posters are displayed in these communities. This is not easy for individual agro-chemical companies which usually may not have adquate number of employees living and working in rural areas. For this reason, increasing co-operation with public sector organizations is being sought (e.g. Ministries of Health, rural banks, national extension services) in joint design and distribution campaigns, to ensure that posters reach right into rural areas, and are not just left with agro-chemical retailers.

Mass media campaigns

Smallholder access to t..e principal forms of mass media (newspapers, radio, TV) in rural areas, varies widely between countries. Results from some of the survey research in the ICI markets illustrates this variability for TV and radio (table 1). Such data is essential in judging the appropriateness of different media.

However, it is equally important to assess both the advantages and disadvantages of mass media before investing heavily in them. For commercial companies buying time on TV or radio can be more expensive than running poster or on-pack leaflet campaigns and may not necessarily be more effective.

Although mass media can ensure wide and quick coverage of target audiences who have access to them, they are seen by rural populations as sources of news and entertainment and are judged to be of limited value in the systematic transfer of technical information. However, they are very good at creating awareness and in helping to change attitudes. It is in this respect that mass media should be used to work towards improved standards in the use of agro-chemicals. Synchronization of messages between

IRRI

Monitoring to determine economic spray thresholds on-pack leaflets, poster campaigns and mass media is essential if impact is to be maximized.

To date FEATS has done little of its own mass media work. Instead they have financially supported mass media campaigns launched by national pesticide associations and have tried to synchronize the company's messages with those of associations' campaigns to create greater impact. For example, in Malaysia, the National Pesticide Association (MACA) mass media campaign in 1989 to encourage readership of labels coincided with the 'read the label' competition launched by FEATS.

Educational videos

These can be an important audio-visual aid to agro-chemical education in rural areas, particularly in situations where direct access to smallholders and estate workers is a practical proposition for training. In situations, where large numbers of smallholders have access to video players and TV sets, distance learning through educational videos becomes feasible for the smallholder.

Clearly such situations are rare in smallholder agriculture. However they do exist, for example, vegetable growers in the Cameron Highlands of Malaysia. Most members of this small population of 3 to 4,000 mainly Chinese vegetable producers have both video and TVs. In 1987, there were 3 or 4 video lending libraries serving these communities. The distribution of educational videos through them may persuade these growers of the importance of adhering to pre-harvest intervals, if the risk of agro-chemical residues in vegetables is to be avoided.

Educational aids

Some aspects of improved agro-chemical use and pest management are potentially complex, and need to be simplified into educational aids, which end-users or their advisors can easily use. Good designs is a prerequisite for success in this area. Examples that FEATS has worked on recently include a knapsack-calibrator for extension workers, and a pegboard threshold monitor for cotton insect pests in Paraguay.

Knapsack Calibrator: Using correct spray volumes and product concentrations is an important component of the safe and effective use of agro-chemicals. Yet few smallholders know how, or even, why it is important to calibrate their sprayers. The design of a simple field calibrator for extension workers provides a useful first step in correcting this situation.

The six-step knapsack calibrator has been well received in various parts of the world including Malaysia, India and Zimbabwe. All the advisor needs is the pocket calibrator, and measuring stick, graduated measuring beaker and pencil. It is a simple method, cuts out the need for direct calculations and is ideal for the advisor working with farmer groups or spray gangs.

Pegboard Monitor: Not only is educating smallholders in pest recognition and appropriate monitoring procedures necessary, but smallholders should also be taught the economic spray thresholds for individual pests. This is an essential component of effective IPM programmes. The pegboard has been developed for important cotton pests (aphids, alabama, heliothis, pectinophora) in Paraguay. It reduces the assessment of pest populations and spray thresholds to a simple field procedures. It has been well received by both smallholders and authorities.

Training

It is essential that mass education is integrated with training programmes. As far as the individual agro-chemical company is concerned, the key question is what level, and hence type of training it should, and can afford to undertake. Seeking a sensible answer to this depends to a great extent on the size of the target population to be trained.

Where the target population is small, locationally restricted or well organized, for example into co-operatives, then direct training support becomes a viable proposition and the operation of mobile field units feasible. In most countries, ICI Agro-chemicals operates some form of direct training. However, in few countries does direct company training have a significant impact on the great mass of the smallholder population.

Results from surveys (table 2) illustrate the limited impact of direct company training programmes, highlight the importance of product packs becoming more self-educational and emphasize the importance of national extension services and agro-chemical retailers as sources of direct advice for smallholder farmers in developing countries.

It is for these reasons that FEATS is concentrating future developments on indirect training activities, mainly through national agricultural extension services and agro-chemical retail outlets, but also through rural health and education networks. By concentrating efforts on the creation of multiplier effects, through existing infrastructures, it is anticipated that the impact of training programmes will be maximized.

To achieve this, it is important to use the best training methodologies. In particular, practical participative training methods as opposed to purely theoretical learning is recommended. Publication by GIFAP, at the end of 1988, of training manuals developed in the United Kingdom by Wolverhampton Polytechnic for extension workers and agro-chemical retailers in developing countries, represents an important opportunity for the

Table 2. Sources of agro-chemical advice most used by smallholders in selected parts of the developing world

Sources of information (% sample)	El Salvador Maize	Guatemala Maize	Honduras Maize	Java Rice	Paraguay Cotton	Malaysia Rubber/Oil palm	Brazil Bananas
External							
Ag Co advice	6	18	19	-	1	4	8
Product labels	6	25	10	1	36	34	29
Extension service	9	3	7	36	11	67	3
Pesticide outlet	30	25	21	53	14	21	23
Internal							
Neighbours	19	31	21	48	21	56	33
Own experience	11	17	23	-	23	15	16
(Sample size)	(124)	(120)	(121)	(450)	(458)	(401)	(300)

achievement of consistent standards in practical agro-chemical training.

GIFAP has been operating its own "Train the Trainer" programme on behalf of the agro-chemical industry since 1987, when a series of pilot training programmes were run to develop final materials for inclusion in the training manuals. To date GIFAP training programmes have been run in many parts of Asia, Africa and Latin America.

To support this programme, and ensure that improvements in training standards reach the markets as soon as possible it is FEATS strategy to:

(a) Establish and train an international network of master trainers through ICI Agro-chemicals overseas technical development and marketing network;

(b) Implement in-market training programmes of extensionists and retailers *et al* to support GIFAP's overall initiative, and fulfill ICI Agro-chemicals' product stewardship objective that appropriate training is provided where possible to ensure that products are used safely and effectively; and

(c) Ensure that appropriate packages of training materials are developed and supplied to extension workers, agro-chemical retailers and other useful rural change agents, to facilitate the training process for smallholders and plantation workers.

Collaboration between public and private sectors

There is little doubt that the integration of mass education techniques with practical training methods, in properly managed programmes, tailored to fit local circumstances and targetted at local needs is the best strategy for improvement, even for the individual company. However, success requires active collaboration between private and public sectors. Both sides need to recognize their shared interests and work towards common goals.

Collaboration in the private sector

The same is true in the private sector. In market situations where common interests in improved standards of safe and effective agro-chemical use are shared between companies, and do not compromise normal commercial competition, collaboration between companies should be encouraged. This will increase the chances of crop sector campaigns having significant impact, and minimize the risks of negative overlaps occurring. Collaboration can be organized through national agro-chemical associations, or on a bilateral basis.

Resources

The quantity and quality of international and national resources devoted to agro-chemical education and training will need to be increased in the 1990 if standards in their use are to be improved. In large, valuable agro-chemical markets it will not be difficult for the private sector to justify investment of the resources required to develop and implement effective programmes. However, in small markets this will not necessarily be the case.

Agro-chemical markets in many parts of Asia, Africa and Latin America are small, relative to the costs associated with the improved agro-chemical education and training support methods being advocated. Yet, these are probably the areas where the greatest need for improved agro-chemical use exists. In these circumstances, international aid agencies will need to become increasingly involved if effective, collaborative projects are to be introduced.