PARAQUAT IN PERSPECTIVE

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Introduction

Opponents and supporters of paraquat are in agreement about one thing, that it is one of the world's leading herbicides. The unique properties of paraquat mean that there is no true, viable alternative in markets such as soil conservation and tropical smallholder agriculture, which supports the rapidly growing populations of many developing countries. World-wide, paraquat's use brings substantial benefits to food production and sustainable agriculture; farmers remain enthusiastic about the value that it adds. In contrast to this, some groups have been very vocal in their demands for its restriction or banning and this has led to the production of a number of reports that contain allegations regarding its safety in use. Syngenta treats any expression of concern over safety very seriously and continues to work with authorizing bodies, academics and local organizations to understand and improve the safe handling of pesticides, including paraquat. The objective of this paper is to consider the need for and the benefits of paraquat alongside the issues raised by its critics and thereby to put paraquat in perspective.

The Benefits of Paraquat

The combination of properties that make paraquat unique are broad-spectrum non-systemic activity, fast action and rapid deactivation in contact with soil. This profile gives farmers unique opportunities in many crops for cost effective weed control and sustainable agriculture which are unmatched by any other chemical or system. The availability of paraquat on the market triggered the growth of minimum and conservation tillage (Bromilow, 2003) one of the most important environmental innovations in agriculture in recent years and it remains important to these systems today. Paraquat's unique properties result in the continued growth in demand for "Gramoxone" which is now the herbicide of choice for 25 million farmers world-wide. It helps them to produce food free from residues in more than 70 crops in over 120 countries, giving farmers a range of efficacy and sustainable agriculture benefits that are unmatched even after 40 years in the market.

Mode of Action

In order to understand fully the unique agronomic properties of paraquat, it is important to understand how it works. Paraquat is not systemic and only desiccates the green foliage that it touches; it kills annual weeds but woody crops and the roots of perennial plants remain unaffected. When in contact with the soil, paraquat is deactivated rapidly. These properties explain why paraquat is known as a **precision herbicide**. It acts only where it is applied and is then deactivated within an hour, substantially limiting the exposure of non-targets and the environment in general. The rapid desiccation of green plant material requires the presence of both light and oxygen. Conning *et. al.* (1969) showed that molecules of paraquat divert electrons from the iron-sulfur centres in chloroplast Phytosystem I and are reduced. The reduced paraquat reacts with oxygen to form superoxide (O_2^-) that in turn generates hydrogen peroxide radicals that attack the plant cell membranes. This causes the characteristic browning of the leaves, which can occur within as little as 30 minutes of treatment under strong light conditions, and complete desiccation within a few days.

Agronomic and Social Benefits

Paraquat's activity is relatively unaffected by sudden, heavy rainfall or other adverse weather conditions, due to its rapid action. This is extremely valuable, especially in tropical agriculture where high rainfall and rapid weed growth make hand weeding a lengthy, tedious and backbreaking occupation. Typically, hand weeding accounts for over half of the labor input for smallholders (Parker, 1972) and is often undertaken by women and children. Hand weeding has been determined a "real and substantial risk of back injury" by the California Department of Occupational Safety and Health (Associated Press, 2004), which has banned it in all but organic agriculture, as Californian organic farmers successfully argued that they have no alternative. The use of paraquat in many developing countries has freed women and children from these tasks and the time and energy released has been used to advance education and the economic independence of rural communities (Srinivasan, 2003). Paraquat's rapid action gives farmers confidence that weeds have been controlled and avoids the temptation to spray again.

The precision contact action of paraquat makes it safe for weed control near shallow-rooted tropical crops and in trees, nuts and vines. Negligible effects on green crops not

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Precision use around a shallow rooted tropical crop, taro in Samoa. No other herbicide could be as effective as paraquat for this use as it is not taken up into the taro. Photograph property of Syngenta Crop Protection, AG.

directly sprayed and banana 'mats', from which the fruiting stems grow and lack of drift due to low volatility, are of great value to both tropical smallholders and in commercial plantations such as palm oil, banana, rubber and pineapple. Paraquat's speed of action and absence of residues in crops make it the best practical choice of herbicides in the production of many tree and vine fruits in southern Europe and for the control of suckers that grow from some varieties of vine roots.

The population of the world will increase by more than 2 billion (40%) over the next 20 years and comparatively more growth will come from Asia where the population will double by 2025 (United Nations 1997). The staple food in Asia is rice, so substantial increases in productivity are needed in the very short term. In Indonesia, with one of the fastest growing populations, typically only two crops of irrigated rice are obtained per year. If seedbeds can be prepared rapidly, then a third crop of direct seeded rice can be obtained (Sembiring & Kartaatmadja, 2003). Because of its rapid action, paraquat is a cornerstone of this practice. Unlike other broad-spectrum herbicides, paraquat leaves the grass roots intact that stabilize the paddy field 'bunds' under the usual conditions of heavy rainfall on cleared fields. In Guandong Province, China, over 1 million hectares are used for high quality vegetable production, with up to eight crops grown per year. Paraquat's unique rapid action and precision attributes make it an essential tool both in rapid seedbed preparation and management of weeds in the growing crop without uptake into the vegetables.

Sustainable Agriculture Benefits

In many parts of the world, tillage in conventional and organic agriculture has left the soil vulnerable to erosion by wind and rain, resulting in losses of around 10 tonnes per ha per year for croplands in America (Crosson & Ostrov, 1988). Topsoil and nutrients are washed from fields, where they are needed, into the drainage and river systems where they create an environmental problem. Sedimentation is the greatest cause of impairment of waterways in the USA. To combat these problems, methods of reduced tillage were proposed as early as the 1920s, but could not be implemented because of the problem of weed management. The introduction of paraquat in the 1960s finally enabled these theories to be implemented on a large scale as Minimal Tillage (Bromilow, *loc. sit.*) and led to the modern practice of Conservation Tillage, which increases soil fertility, while decreasing energy inputs and soil and nutrient loss in erosion (Fawcett & Caruana, 2001). Soils hold vast reserves of carbon, three times that held in trees and twice that in the atmosphere. Conventional tillage promotes the microbial mineralization of this carbon, decreasing the quality of the soils and increasing the carbon dioxide released into the atmosphere, thus contributing to global warming. Minimum tillage substantially decreases such losses. Paraquat was the key ingredient for the adoption of such systems and because of its unique properties, remains important today. Conservation tillage is now adopted on 60% of US corn acres and 85% of the soybean acreage, as well as in vegetables and many other crops. In Europe, the ability of paraquat to control green foliage but to leave soil-stabilizing roots intact has been incorporated into erosion-prevention programmes that have been shown to decrease the loss of soil by 66% (138 t/ha) in French vines (Llewelyn, 2004) and by 98% (48 t/ha) in Spanish olives (Gomez, 2004).

Terraces, conservation tillage and conservation buffers save soil and improve water quality on this farm in Woodbury County in northwest Iowa, USA. Photograph by Lynn Betts, USDA Natural Resources Conservation Service.

Paraquat is used in European vines to control 'suckers' and to manage grass cover crops, where it preserves grass roots. This helps maintain the soil stability and decreases erosion, improving water quality and safeguarding farm productivity for the future.

After application, free paraquat is rapidly degraded in the environment or becomes irreversibly deactivated by soil. This means that green plant material exposed to paraquat is desiccated and no residues are taken up from the soil into the treated or following crops. This residue profile is valuable to the food industry.

Weed Shift and Resistance Management

Due to the increased use of glyphosate in recent years, there has been some change in the spectrum of weeds from grasses to broadleaved weeds, against which glyphosate is comparatively less effective. In addition, there has been a rapid increase in the number of species resistant to glyphosate (Neve *et al*, 2003). In Malaysian Oil Palm, a switch to glyphosate in the 1990s led to a shift in the weed spectrum towards more pernicious broadleaved weeds (Quah *et al*, 1997). In order to manage such weed shifts and potential resistance problems, in markets where both paraquat and glyphosate are appropriate, farmers tend to alternate them to preserve their options for cost effective weed control.

Alternatives

Paraquat is the only broad spectrum, rapid action precision herbicide. Other broad-spectrum materials are slow acting, strongly or moderately systemic and are sensitive to post-application weather. They are not alternatives to paraquat in the markets requiring rapid, precision use, crop safety and soil conservation through the retention of root masses. As these materials have a different spectrum of activity to paraquat and entirely different modes of action, in markets where they are complimentary, it is useful to alternate the chemicals used, to avoid weed shifts and resistance. The maintenance of a variety of herbicidal modes of action is a key element of the practice of integrated weed management.

Human Safety

Undiluted paraquat formulations can be moderate to severe skin irritants, but intact skin is an effective barrier against the absorbance of paraquat (Lock & Wilks, 2001). Splashes of the undiluted formulation concentrate can be injurious to the eye and must be washed away immediately; eye protection must be worn while handling the concentrate. Potentially, paraquat is toxic by inhalation, but it is not volatile and the particles produced by agricultural equipment are many times bigger than those that can be respired. Regulatory bodies have considered this point and, for example, the US EPA concluded that,

> *"particles used in agricultural practices are well beyond the respirable range and therefore inhalation toxicity is not a toxicological endpoint of concern"* (US EPA, 1997).

The World Health Organisation classifies paraquat as Class II, moderately hazardous (WHO, 2002). The acute oral toxicity of paraquat is higher than that of many herbicides, but paraquat is of similar or lower toxicity than many other pesticides or commonly used household chemicals. As with all herbicides and the vast majority of other chemicals, there is no specific antidote that acts systemically. There are however, widely available treatments that can limit the absorption of paraquat into the body as well as strategies for the management of intoxication.

Experts in the regulatory authorities of the USA (US EPA, 1997), Europe (EC, 2003) and the World Health Organization (JMPR, 2004) have independently conducted exhaustive reviews of paraquat's chronic toxicology. Their conclusions based on the study of the entire body of scientific work are somewhat different to the claims frequently made by paraquat's opponents. They all concluded that paraquat is rapidly excreted; is not a genotoxin *in vivo*; does not cause cancer; is not a teratogen; does not cause reproductive toxicity, is not a neurotoxin and is not an endocrine disruptor. The apparent structural similarity between paraquat and MPTP, an agent known to cause 'Parkinson's like symptoms', led some researchers to inject large doses of paraquat and other pesticides into a strain of laboratory mice used in the study of the disease. Paraquat and MPTP have outwardly similar structures but have very different chemical properties. This means that MPTP is taken up very easily into the brain whereas paraquat is not. Opponents of paraquat have used this work to suggest that paraquat is implicated in the etiology of the disease however most scientists do not share this view. The World Health Organization's recent review of the evidence stated that,

> *"..the available mechanistic and other animal studies did not support the hypothesis that paraquat residues in food are a risk factor for Parkinson's Disease in humans"* (JMPR, 2004).

Smallholder application, Guatemala, 2003. The applicator is wearing long trousers, a long shirt, a sun hat, boots, and a plastic sheet over his back, to protect from leaks. He washed his hands after each fill. He carried water for 3 miles to the field and a plastic bag with clean clothes to walk home in. His work clothes are always washed separately. He has sprayed for 30 years with no incidents. Photograph property of Syngenta Crop Protection, AG.

Consumer Exposure

There is very little exposure to paraquat for the consumer of treated crops as the vast majority of paraquat uses do not result in detectable residues (<0.05mg/kg) in foodstuffs. The US EPA concluded,

> *"that there is a reasonable certainty that no harm will result to infants and children or to the general population from aggregate exposure to paraquat dichloride residues. Further, based on the available data, the Agency does not believe that the effects produced by paraquat would be cumulative with those of other structurally related compounds."* (US EPA, 1997).

Occupational Exposure

As with most pesticides, the most likely population to be exposed are the applicators. Appropriate personal protective equipment for working with paraquat is no more than would be recommended for any other product. During handling of the concentrated formulation the use of gloves and eye-protection is recommended; a long-sleeved shirt, long trousers and boots should be worn during application. Separate washing of clothes used during spray operations and attention to personal hygiene by those handling all pesticides is also important. Minor predictable deviations from these recommendations will not lead to serious health effects.

The principal route of exposure for users is the skin, as it is with most other agrochemicals. During normal occupational exposure, paraquat is poorly absorbed through human skin and the very small amounts that may be absorbed, are rapidly excreted and are well below the level needed to induce toxic effects in the lung, the most sensitive target organ for paraquat. The question of enhanced uptake through damaged skin has been raised. When applicators follow normal good working practices, this is not a significant route of exposure. However, the potential for adverse effects continues to be assessed through in-use surveillance. Reviewing the information concerning operator exposure, Europe's independent committee of experts, the Scientific Committee on Plants (SCP) observed that,

> *"Based on the field exposure studies, corroborated by information on health surveys on operators, the SCP is of the opinion that when paraquat is used as a plant protection product as recommended under prescribed good working practices, its use does not pose any significant health risk for the operators"* (SCP, 2002).

There is a substantial body of evidence in the medical literature regarding the question of long-term effects from occupational exposure to paraquat (e.g. Howard *et al*, 1981; Lock & Wilks, 2001; Sabapathy & Tomenson, 1992; Senanayake *et al*, 1993). All these studies agree that under the normal use conditions prevailing in developing countries there is no evidence from detailed medical examinations that paraquat causes any long- term health effects. Contrary to the previously published operator exposure studies, Castro-Gutierrez (1997) and Dalvie (1999) expressed concern that, though they could find no relationship between paraquat exposure and impaired lung function, some respiratory effects may be evident. This concern was investigated independently by a team from the University of California, Davis and was critically reviewed by an independent expert advisory panel. The study was conducted in a large group of paraquat sprayers in Costa Rica, representative of the user population potentially most exposed. This study represents the most extensive and detailed medical survey of paraquat-exposed workers ever undertaken. It strongly supports the position that paraquat does not cause any clinically or functionally important adverse health effects in occupational use and with respect to the concerns expressed above concluded that,

> *"overall these findings are consistent with no clinically significant increases in interstitial thickening or restrictive lung disease among this population."*
> (Schenker *et al*, 2004).

Occasionally, problems of skin irritation or nail damage have been reported. Such irritation and damage is reversible upon cessation of exposure and the incidence due to paraquat is very low. For example, the reported frequency in Vietnam (0.2 – 0.3%) is the same for paraquat as for other pesticides (Ministry of Health and Preventative Medicine, 2002). Such effects are indicative of the need to improve working practices and standards of hygiene. Syngenta takes this very seriously as these farmers likely also use other pesticides, which unlike paraquat, may be more readily absorbed through the skin. Since 1975, Syngenta and its legacy company, in partnership with stakeholders committed to improvement of working practices, have been running detailed product stewardship programmes world-wide to address these and other product safety issues, particularly for small holders and other applicators in developing countries.

Accidental Exposure

When paraquat was first introduced in the 1960s a common malpractice was to decant pesticides into smaller containers such as drinks bottles, without any appropriate labelling. The original paraquat formulations were odourless reddish-brown liquids, which led to them being mistaken for drinks such as cola, tea or red wine. Regrettably, a series of fatal poisoning incidents due to mistaken ingestion began to occur. From 1975 onwards a blue colour and a stench (foul smell) were added as alerting agents to avoid 'mistaken consumption'. From the mid 1980s a powerful emetic was also included to induce rapid vomiting in case of ingestion (Sabapathy, 1995). Improvements in treatment were also developed. These measures were accompanied by changes to pack sizes and product labelling. The formulation changes initiated by Syngenta are now reflected in the FAO standards. Though all Syngenta brand paraquat products comply with these specifications, many generic paraquat products supplied in developing countries do not.

In a review of poisoning incidents, Garnier *et al* (2003) concluded that poisoning as a result of accidental ingestion of paraquat was now rare in Europe because of improved training and the addition of alerting agents and emetic to commercial products. A 20 year survey from the National Poisons Information Centre (London) noted in 2001 that most of the cases of poisonings from mistaken ingestion occurred at the start of the study in the early 1980s with the last one recorded in 1992, confirming the virtual disappearance of accidental fatalities since their peak in the early 1970s (Northall and Wilks, 2001). There are no comparative statistics available for developing countries, but it is believed that the introduction of safety and alerting agents (colour and stench) and emetic have made significant contributions to the reduction in mistaken ingestion (Sabapathy, 1995). In Costa Rica, an investigation by Wesseling *et al* (1997) showed that all fatalities associated with confusion of bottles occurred before 1987, the year when the formulation changes were introduced.

Deliberate Exposure

Regrettably, notoriety linked to the mistaken ingestion problem, attracted the attention of those intent on harming themselves. Suicide is a tragic fact in many societies and cultures. While crop protection products are one of the methods used, they are not the most frequent method and paraquat is not the most frequently used product (WHO 2001; FDA 2003; Ministry of Agriculture, India, 2000). There are no reliable global estimates as it is practically difficult to collect statistics in many countries and the true facts are often hidden or obscured for religious, financial or social reasons. What is known however, is that following a peak in the late 1970s and early 1980s suicide fatalities involving paraquat have decreased (Sabapathy 1995) and in countries where overall strategies for the prevention of self-harm are adopted, the overall number of suicide incidents can be decreased (WHO 2002). In South-East Asia where pesticide-related suicides are significant, hospital-based surveillance has shown that paraquat accounts for only a very small proportion of cases (WHO 2001, FDA 2003). Of the 7 countries with the highest rates of suicide in Europe, paraquat is not available, due to restrictions or the lack of a relevant market, in 5 of them. In the 8 with the lowest rates of suicide, paraquat is sold in all of them. This has been the situation for a number of years and shows that the frequency of self-harm is determined by factors other than the availability of paraquat.

Environmental Safety

Typically, the target weeds intercept up to 95% of the paraquat applied, where it is degraded by photolysis and microbial action to non-toxic degradates (Lee *et al*, 1995). Paraquat is non-volatile and the diluted formulation is sprayed in large droplet sizes to maximise efficacy, this also minimises spray drift. Thus paraquat reaches the field soil either directly, or through incorporation of decomposing sprayed vegetation. On contact with soil, paraquat is subject to extremely rapid and strong binding (Summers, 1980). Binding to clay and organic particles massively reduces the bioavailability of paraquat in soil pore water, resulting in no risk to earthworms and soil microorganisms (Roberts *et al* 2003). Bioavailable paraquat is rapidly degraded by soil microorganisms in a matter of days to natural products, such as CO_2 and water (Ricketts, 1999). As this is an equilibrium process, the net result is that the build up of paraquat in soil is prevented, as demonstrated by long-term field trials conducted around the world over the last 30 years (Roberts *et al* 2002). A schematic describing the environmental fate of paraquat is shown in Figure (1).

Rapid and strong binding to soil also renders paraquat immobile due to its lack of availability for off-site transport in the water phase. Hence, groundwater and surface water

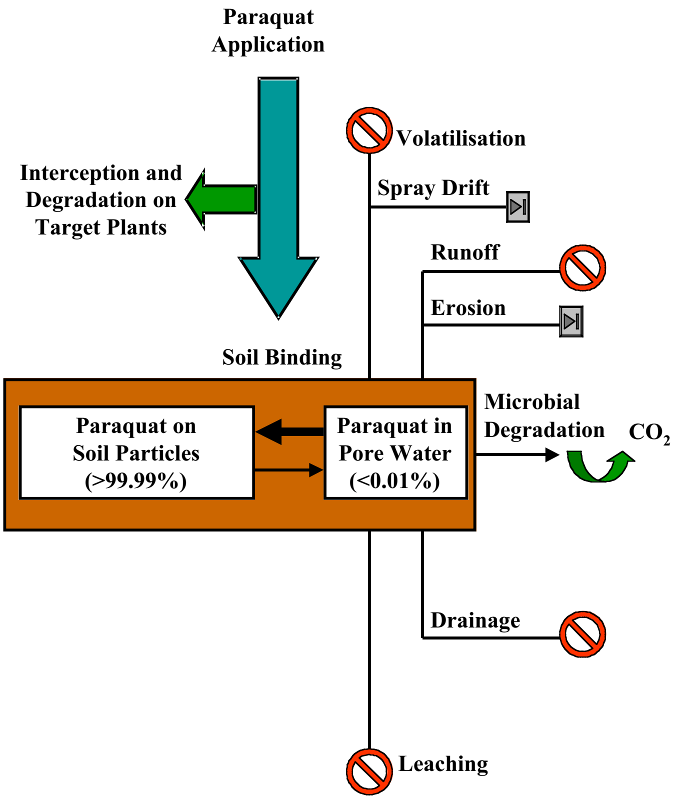

Figure 1. **Schematic of the fate of paraquat in the terrestrial environment**

are not exposed to biologically available paraquat by leaching, drainage and runoff water from soil. Any paraquat residues on eroded soil during runoff events remain subject to strong binding, preventing release into streams and rivers. In fact, the way paraquat is used in sustainable agriculture minimises soil erosion (Bromilow, *loc. cit.*). If any spray drift enters surface water from normal use, the concentration is very rapidly decreased, mostly by binding to suspended particulates and sediment followed by degradation (Summers, *loc. cit.*). This precludes chronic exposure of aquatic organisms and paraquat does not pose an acute risk to any aquatic organisms (US EPA, 1997). As with all herbicides, consideration must be given to mitigating any acute exposure of aquatic plants.

Paraquat is suitable for use in Integrated Pest Management (IPM) programmes as it is classified as "low risk" to honey bees in the field and 'Harmless' (Category 1) to ground dwelling beneficial arthropods, according to the EPPO and IOBC classification schemes, respectively.

Practical experience and detailed monitoring in the UK over 40 years use has shown that though there have been a very small number of isolated incidents, birds and wild mammals are not at risk from exposure to paraquat when labelled directions are followed. Paraquat does not bioaccumulate in birds and mammals and will not build up in the food chain as a result of predation and scavenging. The evaluation within the Standing Committee on the Food Chain and Animal Health gave careful scrutiny to the small but potential risk to ground-nesting birds and hares and "*concluded that the risk would be acceptable, provided appropriate risk mitigation measures are applied*." (EC, 2003)

Product Stewardship

Detailed product stewardship activities have been run in relation to paraquat since 1975. In addition to the formulation and pack changes discussed above in "Accidental Exposure", Syngenta and its legacy company have partnered with stakeholder groups committed to practical improvements. In the early 1980s, formal and globally managed stewardship activities were established. Education and training programs were set up directed in particular towards smallholder farmers in developing countries. Commentators have noted the beneficial effect of these stewardship activities in countries such as Malaysia and Costa Rica (Sabapathy, 1995; Wesseling *et al*, 1997). A paper from the National Poisons Centre in the UK noted in 2001 "most of the these cases (mistaken ingestion) occurred in the early 1980s with the last one recorded in 1992, confirming the virtual disappearance of accidental fatalities since their peak in the early 1970s" (Northall and Wilks, 2001).

Today, Syngenta has active stewardship programs in more than 45 counties and in excess of 1.3 million users receive safe use training every year, in the context of IPM programs to demonstrate the relevance of these practices to a profitable approach to farming. Of these 1.3 million people, around 125,000 users receive in-depth safe use training. These programs are constantly reviewed and revised to reflect new ideas, standards and approaches.

Syngenta is committed to the FAO International Code of Conduct on the Distribution and Use of Pesticides. The FAO

Training demonstration, citrus in Spain, measuring and loading Gramoxone. Photograph property of Syngenta Crop Protection, AG.

Safe use training in Paraná, Brazil, January 2004. Locally manufactured, water resistant, light cotton PPE with an apron for mixing. Over 500,000 sets of these have been distributed in Brazil and they are popular with users. Photograph property of Syngenta Crop Protection, AG.

defines product stewardship as "the responsible and ethical management of pesticide product from its discovery through to its ultimate use and beyond". Syngenta believes that good product stewardship is a business imperative. Our vision is that Syngenta be recognised by stakeholders to be foremost in responsible and ethical product management.

Why FAO Specification Paraquat Products Should Remain Available

Given the immense value of paraquat to farmers, to sustainable agriculture and the exceptional level of product stewardship that has and continues to be, conducted by Syngenta, it is strange that the product should be subject to an intense, political campaign to ban it. The roots of this campaign can be seen in the early 1980s when there was an increase in the number of accidental paraquat poisonings and following on from this, deliberate poisonings. This resulted in the withdrawal of registrations in some countries where the market was small and concern for deliberate misuse was high. At this time, the Pesticide Action Network, (PAN) included paraquat on their list called the "dirty dozen" which now comprises 18 chemicals. Of these 18 chemicals, all but three have now been listed under the Rotterdam Convention for Prior Informed Consent, or "PIC listed", which places practical barriers to their international trade and is a useful point of leverage to challenge western corporations.

Paraquat is not "PIC listed" as its profile does not meet the agreed criteria; however, it is one of only three chemicals listed by PAN not to be PIC listed and is now the focus of an intensified campaign by a coalition of groups who find opposing paraquat a convenient vehicle to achieve a number of different political objectives. As part of this campaign, allegations have been made in press releases, publications and Internet sites concerning the chronic toxicity of paraquat, which are answered above, and sometimes confuse the social tragedy of suicide with normal occupational exposure e.g. Wesseling *et al*, (2001); Fernandez *et al* (2002); Madeley (2002); Watts (2003) and (PAN Germany). Attacks on paraquat frequently cite a reference concerning Western Samoa (Bowles, 1995), which purports to correlate a sharp decrease in the frequency of suicide with "control of paraquat". In fact, no new "control of paraquat" was implemented at this time but a counselling program targeted at suicide prevention by all methods.

Syngenta and its legacy company have conducted an enormous amount of environmental and human safety research over the last 30 years in order to understand in detail the safety in use of paraquat. Where issues have been identified, appropriate changes in the formulation, use recommendations and training have been made and monitored to assess their success. When the true risks of the use of the product are put into the perspective of the enormous benefits to users, global food production and to soil conservation in sustainable agriculture, it is only possible to conclude that Gramoxone gives an enormous net benefit and that banning of the product would further disadvantage farmers in developing countries by removing a valuable tool. The FAO now mandates the formulation changes pioneered by Syngenta that have led to a decrease in the number of adverse incidents, but has to rely on national authorities to enforce them. Organizations sincerely committed to the wellbeing of the developing world should be campaigning for effective regulation and the enforcement of these standards rather than for actions that will drive the trade in this valuable and unique product into an unregulated black market. Not to do so would be a victory for short-term politics over careful long-term science, with the losers being farmers in developing countries. Paraquat products meeting or exceeding FAO specifications should be allowed to continue bringing benefits to sustainable agriculture and food production in a world increasingly challenged by a rapidly expanding population.

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