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Your ref	Our ref	Tel ext	Date
	PS/AP		30 June, 1976

SAFER FORMULATIONS OF PARAQUAT

1. Emetic Formulation

Since my letter of 27 April to Area and Regional Managers about the emetic formulation, technical development work in PPD and at Pharmaceuticals Division has shown that most of the early promise of the project is being fulfilled. Animal work has demonstrated that the formulation causes vomiting shortly after its ingestion. Stability trials carried out so far give every reason for belief that a stable formulation is available. Field work has shown that the emetic formulation results in no loss of herbicidal activity. Environmental and residue studies have started, but no problems are likely to arise in this area. Extensive spray operator trials are to be carried out in the UK in July and August, but all the scientific evidence suggests that there will be no effects on operators.

The planned rate of addition of the emetic agent should ensure that 80% or more of the people who ingest 10 ml of 'Gramoxone' will vomit. The present indication is that this rate of addition will add approximately 6.5p to the cost of a litre of 'Gramoxone', although it is hoped that process development work at Pharmaceuticals Division will reduce this cost.

We can therefore remain extremely optimistic that this development represents a real breakthrough in our attempts to overcome the problems arising from accidental or deliberate drinking or 'Gramoxone'. However, it seems prudent to continue to keep the information in-house as far as possible and to delay announcement of the project to any of our distributors (including ICI Companies overseas) until the animal work is fully complete and the operator trials have been carried out. This should be by late August.

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It seems worthwhile for us to begin discussions on the next phase of the development. Current plans are to market 'Gramoxone' plus emetic in part of the UK and in Eire early in 1977, followed by full-scale UK marketing from autumn 1977. We believe that we should plan for a worldwide introduction as soon as possible. It is hoped that supplies of the emetic formulation will not be limited beyond 1977 but we should in any case establish which countries have priority for its introduction. In some cases, of course, delay in registration may be the limiting factor, and we shall need to know what is required for registration country by country. Needless to say, registration of an emetic formulation as the only permitted paraquat product would be highly desirable and we need to determine in which countries this might be achieved.

2. Other aspects of a safer formulation

Since we are now proposing a proactive, global policy on the introduction of a safer formulation we should also consider what else needs to be done. The Reduction of Hazard project team believes that there should also be a deterrent to drinking, even with an emetic formulation. There is a strong view in the Business Area supporting this, but it is a topic which needs further debate. The reasons for including a "warning signal" in Gramoxone are firstly that the emetic formulation may not be successful in preventing all deaths (because of differences in susceptibility in the population) and secondly that even with the emetic there could still be adverse public reaction if people drink Gramoxone accidentally. It is therefore important that if we are to include a deterrent to drinking it should be the best one. From the point of view of production and minimising stocks and working capital, a single, globally-used formulation would be the most desirable.

It is therefore proposed that we should make a determined attempt to establish as objectively as possible whether colouring or stenching the product is the best method of warning against accidental drinking. We are trying to obtain guidance from Market Research people as to the best method for assessing this, but the difficulties of choosing a suitable population sample for the assessment are very large since what we need to know is whether members of the general public (worldwide!) are warned more by a colour than by a stench.

Already planned is a survey in the UK to establish whether introduction of pyridine base-stenched 'Gramoxone' has had any adverse effects on use of the product - a factor which may become more important when competition from glyphosate becomes more severe.

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The questions about a deterrent which needs to be answered are:

1. How do we assess which is best - colour or stench?

2. How practicable is a single global formulation?

3. What are the registration problems?

4. Is the marketing of a distinctive coloured/or stenched formulation likely to be of value in meeting competitive threats?

5. What are relative costs?

6. How serious is the problem of accidental contamination of foodstuffs by paraquat likely to be in the future? The coloured formulation is probably better than the stench in countering this.

I should like to arrange a meeting with Area Managers to discuss the issues arising from the above during the next few weeks. Daphne Bartholomew will contact you shortly to arrange a suitable date.

P SLADE