

PSAC

NOTES ON THE FIRST MEETING OF
PARAQUAT STRATEGIC ACTION COMMITTEE

COMPANY
SECRET

Held at Fernhurst on Friday, November, 22, 1985

Present:-

Dr A K Stapleton (Chairman)	: Herbicides
Dr D H Brooks	: Manager, Development Department
Dr G M Farrell	: Development Department
Mr C S Major	: Public Affairs
Dr T B Hart	: PSRG
Mr G A Willis	: PSRG
Mr T A Sampson	: Americas Region
Mr D F Manning	: FEP Region
Mr W C Stonebridge	: EMA Region
Mr A G Potter	: WER Region
Mr P J Bramley (Secretary)	: Herbicides

- 1 AKS outlined the objectives of the Committee as follows:-
 - 1.1 To review and propose for Executive approval overall strategy in the field of paraquat 'defence'.
 - 1.2 To ensure effective co-ordination of detailed strategies adapted for individual territories.
 - 1.3 To identify in-house resource needs to ensure effective implementation of these strategies, to monitor resource spending and to ensure correct priorities are allocated to work programmes.
 - 1.4 To ensure that internal/external communications in this crucial and rapidly-changing area are highly efficient and streamlined.
 - 1.5 To meet on an 'ad-hoc' basis as necessary to provide rapid and effective decision-making.

2 JAPAN

DFM presented an update on the situation in Japan where the 'Gramoxone' registration is under intense pressure because of the continuing high levels of suicide poisonings with 'Gramoxone' and the recent spate of homicides involving the 'spiking' of soft drinks. ICI's objective is to avoid a reclassification of 'Gramoxone's registration to the highest toxicity category which would effectively prohibit sales. A reclassification of 'Gramoxone' itself would apply to all paraquat formulations.

The MAFF (Agriculture Ministry) remain supportive of paraquat and in particular of our 'Preglox'(45 gm ion paraquat + 45 gm ion diquat) strategy because of paraquat's immense benefits to Japanese agriculture. However, MHW (Health Ministry) are under heavy pressure particularly because of the homicide incidents and need to be convinced that MAFF/ICI are taking sufficient measures to combat the situation.

ICI Japan is being asked to take effective measures in the market place to limit 'Gramoxone' sales only to farmers and to ensure proper storage of the product by retailers and farmers. In addition, ICI is being asked when 'safer' formulations of paraquat will be available. ICI's strategy is based on a 1Q 1986 limited launch of 'Preglox' followed by a complete switch from 'Gramoxone' by 4Q 1986. The 'Preglox' strategy offers the following potential benefits to the suicide/homicide problem:

- Name change
- Livery/label change
- Change in bottle size
- No mention of paraquat on label
- 4-5 x increase in acute oral LD₅₀ level
- Higher level of emetic (see below)
- Addition of a bittering agent ('Bittrex' type)

Because of the homicide problem, a bittering agent is now considered relevant for Japan (in other circumstances the speed of action is too slow). Taste trials, costings and storage tests are urgently being carried out to select the best agent and optimal inclusion rate.

ACTION : PJB/ICI JAPAN/WED, YALDING/TAL

The Japanese Ministries have also strong leanings towards a straight dilute liquid paraquat formulation (50 gm ion per litre). This would cost an additional £2.5-3.0/kg ion) compared with the current costs of 'Gramoxone'. ICI Japan is continuing attempts to promote the 'Preglox' strategy with both MAFF and MHW. To date both MAFF and MHW have resisted arguments from various lobbies for a solid paraquat formulation but such formulations are actively being championed in the media.

3 EFFECT ON OTHER MARKETS

Regions considered that an adverse outcome of the current crisis in Japan need not have an immediate impact in other markets. The developing world (particularly in EMA and Americas Regions) is more influenced by regulatory trends in West Europe/USA whilst in West Europe itself there are already plans for launching 'Preglone'-type formulations and pressures exist for diluting 'Gramoxone' itself (see France, below). Even in the Far East it was felt that an adverse outcome in Japan should not pose insurmountable regulatory problems.

ACTION : REGIONS to monitor trends closely

However, it was agreed that in this situation, ICI would probably have to mount an 'intensive' communication exercise internationally.

In preparation for this, a briefing note should be drafted for ICI staff covering the Japanese situation giving clear guidance on the correct information to be released internally and at Government level. At an appropriate moment when the situation in Japan has settled down, this note should be finalised and circulated at the relevant senior level.

ACTION : CJM

4 THICKENED FORMULATIONS

Against the background of the arrêté constraining the paraquat content in future formulations to 40 gm ion per litre, Sopra recently displayed samples of the newly-developed thickened 'Gramoxone' 200 gm/litre formulation based on calcium carbonate to the Commission de Toxiques in an attempt to maintain registration of a high strength paraquat formulation. The initial response of the authorities has been favourable and they have indicated that such formulations could suit their own particular conditions.

However, the authorities want to limit the paraquat content in the thickened formulation to around 100-120 gm ion per litre. Sopra are therefore urgently investigating the feasibility of formulations diluted to 100 gm ion per litre 'Gramoxone' and a 120 gm ion per litre paraquat + 80 gm ion per litre diquat mixture ('Preglone'). Field tests will be undertaken in 1986 at the end of 1987/1988. Further work on storage stability/spraying properties and farmer acceptability need to be undertaken before these new formulations are proven for development. A meeting is to be held at Yalding on 11 December 1985 to review the situation and to put into place a work programme to product launch.

ACTION : WER/SOPRA/GMF/PJB

5 SOLID PARAQUAT FORMULATIONS

Over recent years, PPD has been involved in evaluating a number of alternative solid formulations of paraquat:

- Weedol-type extruded grains based on magnesium sulphate
- Paraquat/diuron mixtures (Hodogaya)
- Sodium chloride 'coated' granules
- Carbowax granules (Chevron)
- Alginate additives (Kelco)

The attached note summarises the state of progress of these developments. At the current time only the magnesium sulphate-based technology is sufficiently developed to provide a commercial formulation but only then at low ion content.

All the options suffer the common problem of a high fixed capital cost penalty for formulation and packaging capacity (approximately £10 m for 2,000 te ion) together with varying levels of plant cost penalties. The recent Executive Paper confirmed that the solid option does not, at the present time, provide ICI with a worldwide solution to the poisoning problem because of those heavy cost penalties together with potential dust hazards in both manufacture and use. However, the pressures on ICI to launch solid paraquat formulations continue particularly in Japan and Italy.

It was therefore agreed that as a matter of priority PPD should put in hand a work programme to evaluate the alternative options of solid paraquat formulations with the clear objective of producing a high strength formulation capable of commercialisation on a fast timescale. The target is 20% bipyridyl ion content and the work should cover both straight paraquat and paraquat/diquat mixtures. For preference the product chosen should be non-dusty - otherwise suitable special packaging will be needed. The programme should cover both the product-in-use and operator-hazard, safety aspects and include an estimation of the full capital and plant cost implications. Interest on a longer timescale was also expressed in paraquat/diuron 'Gramocil'-type solid formulations.

ACTION : PJB/GMF working with PSD/WED, YALDING to produce a detailed work programme and timetable and report back by early January 1986

6 INCREASED EMETIC CONCENTRATION (Report of Sub-Group)

Recent work by CTL (note attached) has indicated that, in dogs, substantially higher concentrations of emetic than the current 0.5 gm per litre in 'Gramoxone' induce vomiting in a much shorter time period, thus reducing paraquat plasma levels. CTL believe that this work offers the prospect that a 5-10-fold increase in the emetic concentration in 'Gramoxone' could improve (significantly) the survival rate from paraquat poisonings in man. Whilst doubts remain over the use of these dog studies as a model for poisoning in man (viz the efficacy of gastric emptying in man under all conditions), it was agreed that the work is sufficiently encouraging to warrant testing in 'field' conditions on a limited scale.

In practice, the amount of extra emetic that can be added to 'Gramoxone' may be limited to 1.5-2.0 gm per litre because of solubility problems (WED, Yalding are currently checking this). However, it was noted that it is the ratio of emetic : paraquat ion content which is crucial so that in the case of a dilute paraquat product this constraint will not be binding (ie, a higher absolute dose of emetic to man can be achieved in the larger, lethal dose of the dilute formulation at lower concentrations of emetic in the formulation).

A sub-group has considered possible additional operator hazards, environmental hazards and constraints on emetic availability and concluded that these should not pose constraints to the limited field test. An initial screen of possible countries has revealed Japan and France as immediate candidates.

The ability to effect a name change to the formulation is seen as an important method of ensuring that meaningful quantitative feedback is received on the efficacy of this change together with the injection of extra resource to analyse poisoning statistics.

ACTION : SUB-GROUP to organise on fastest timescale Japan 1986? France 1987? and to consider further other markets (UK, Fiji, Malaysia?)

7 RESEARCH PROGRAMME AND RESOURCES

Research is co-ordinated by a Work Group led by K P Parry and E Chrystal, set up some 18 months ago. Some research effort at Jealott's Hill, and some funded external work is in hand together with CTL, in the search for antidotes/alternative methods of treatment. The major objective of the Work Group however is the search for forms/formulations of paraquat with significantly reduced toxicity in suicide attempts.

7.1 Paraquat Chromotropate and Other Ion Pairs

The chromotropate is about 5 x less toxic than paraquat dichloride, but requires relatively large quantities of an anionic surfactant to restore herbicidal activity. Even so, there is some reduction in activity, and because of this together with high cost, the chromotropate has been shelved. Research effort has shifted to other ion pairs and complexes using the same principle, ie a lower toxicity form of paraquat which is reactivated by tank mixing with an appropriate anionic adjuvant. There are some very encouraging ideas in early stages of assessment which, if successful, would be less costly than chromotropate.

7.2 Double Encapsulation

This approach is based on Exxon polymer technology. Interest was stimulated by the fact that Exxon were able to formulate cyanide to be non-lethal to rats. After many long delays we now appear to be close to an agreement with Exxon by which samples of the polymers will be made available. Chances of success are unknown, but the idea is well worth following as in principle it offers the hope of a reduced toxicity formulation which just might be of value globally. Formulation Section are prepared to allocate an Experimental Officer to this research full time.

7.3 Resources

These projects require resource in Formulation, Syn Chem and Weed Science Sections, field trials effort and supporting research at CTL. Requirements will be quantified, but we can expect allocation of probably 3-5 man years at Jealott's Hill for each of the next two years, which is the timescale thought to be necessary for completion of these projects.

8 PROCEDURE FOR RELEASE OF INFORMATION

Events during the recent crisis in Japan have highlighted the need for rapid but effective screening of confidential information prior to release outside ICI. It was agreed that Regions should provide the basic screen but that PSRG and HPM would need to be consulted. The PSAC itself provides a forum for rapid decision-making in this area. As a safeguard all confidential information should be copied to HPM.

9 REGULATORY AND COMMRCIAL INFORMATION BASES

The current crisis in Japan has thrown up the need to ensure that all information on the regulatory and commercial status of paraquat released to external bodies should be as accurate and up-to-date as possible. In the commercial area, because of the different management accounting systems it is particularly important to ensure consistency of information. It was agreed that PSRG and HPM would review current systems and if temporary resource was needed to overhaul these then approval for this would be sought.

cc Those present
Dr D Cornthwaite
Dr P Doyle/Mr J R Finney
Mr J C Francis

Mr R A Woods
Mr T C Frears
Mr Lewes Smith

PJB/WJM
13/11/85
A 541