

29 MAR 1976

COMPANY SECRET

To: Dr A Calderbank  
Dr P Slade  
Dr A H Todd  
Dr R Hemingway  
Dr D Riley  
Dr R Ford  
Mr R D Wiseman  
Mr G R Lee  
Mr G C Hackemer  
Dr C B Barlow  
Dr M H Litchfield  
Dr M Rose

R.50796 EMETIC AGENT

A meeting was held on Monday 22 March 1976 to establish a programme for the evaluation of R.50796 (I.C.I.63197) as an emetic agent to be added to formulations of paraquat.

The present objective is to consider presenting a case to PSPS in October of this year for limited clearance in 1977. It is recognised that, if the project gains momentum, then the process of registration may be accelerated by external factors.

The following points for action were agreed upon:

Action

- 1) Until the patent position is clarified the evaluation of R.50796 will remain a company secret and documentation will be treated accordingly. CBB
2. Dr R Ford will retain our sample of R.50796 and act as source of supply within PPD. RF
- 3) From existing human data a concentration of 0.5g/litre is likely to produce emesis upon ingestion of 10ml Gramoxone. This concentration will be regarded as the one for most intensive investigation.
- 4) Dr R Ford will immediately seek to formulate R50796 in Gramoxone and will examine its stability and analysis. RF
- 5) Mr G R Lee will arrange for the following trials to establish that R.50796 does not interfere with paraquat activity.

Potatoes	8 sites	April
Grass	6 sites	May

The above trials will employ a 0.5g/l formulation and the crops will be retained. Further 1m box grass studies at Jealott's Hill and Fernhurst to be conducted in May will compare various inclusion rates of R50796 (0.5, 1.0 and 2.0g/l). The results from these trials will be reviewed at the end of June.

GRL

6) The expected inclusion rate of R50796 is so small that it will probably represent a limited environmental threat nevertheless certain environmental aspects should be covered prior to discussion with PSPS. These are:

- |     |   |                          |
|-----|---|--------------------------|
| 6.1 | An analytical residue method should be available by end October.  | <u>Action</u><br>RJH     |
| 6.2 | A limited soil and water breakdown study should be undertaken.  | RJH                      |
| 6.3 | Dr Foulkes will discuss with Dr Riley a soil leaching study.  | DMF                      |
| 6.4 | Further radiolabelled material will be required from Pharmaceuticals and, in addition a synthesis of "hotter" material instigated.  | DMF                      |
| 6.5 | The toxicity to rainbow trout should be established.  | RDW                      |
| 7.  | The potential for R50796 to produce taint in potatoes and water will be examined.   | DMF/to<br>contact J Page |
| 8.  | Pharmaceuticals will provide an estimate of price for the compound. It is impossible to provide any sensible forecast of PPD requirements at this stage. In the interim Pharmaceuticals will be asked to provide a further 1.0Kg of material. | AHT                      |
| 9.  | G C Hackemer will provide a network to cover the 1976 evaluation programme to be circulated to those parties actively involved.   | GCH                      |
| 10. | CTL will arrange for studies in animals to show that R50796 is likely to maintain its emetic properties in the presence of paraquat. These studies are required as a matter of urgency.   | MHL/MR                   |
| 11. | It is believed that, by mid August, the major technical questions related to the project will have been answered. The project will be reviewed at that time to provide clear proposals for a future global registration strategy.             |                          |

23 March 1976

DMF/imt