

NOTES ON ICI/CHEVRON MEETINGS

4-6 OCTOBER 1978 - JEALOTT'S HILL AND FERNHURST

PART I - PARAQUAT AND DIQUAT GENERAL MATTERS (4 OCTOBER)

Those attending for Chevron: Dr J N Ospenson  
Dr H G Franke  
Mr L Hopkins

ICIA: Dr D W Barrett

DIQUAT

Aquatic Tolerance Petition

EPA have now issued a draft document (Appendix 1) which is undergoing internal EPA review prior to eventual publication in the Federal Register. It proposes that the interim tolerance of diquat in potable water (0.01 ppm) becomes a permanent tolerance. The Agency is also proposing a fundamental change in policy regarding aquatic use of herbicides - "... from one of naming the user agency to one which delineates the conditions of safe use". If this is accepted and published it would be a significant step forward, but Chevron could not guess as to the outcome or timing of the internal EPA review of the document.

Alginates

ICI Nothing further to report. A meeting on the subject is shortly to be held in the UK and Chevron will be provided with details about mid November.

Chevron have allocated resource to the project for 1979 and will outline their program at the next (spring) liaison meeting.

Potato Tolerance Petition

It was agreed that the full tolerance petition should not be submitted to EPA - at least until after the available chronic feeding studies had been audited and the need for any repeat studies evaluated.

Small Grain Desiccation

Chevron ICI This outlet has now been abandoned. Chevron will forward copies of residue data when completed. ICI handed over a draft summary of the photoproduct research (prepared for FAO/WHO). A full report of this work will be forwarded when completed.

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Ethylene Dibromide

Levels of EDB in the product are now down to 40-60ppm using solvent extraction. Samples will be held at Organics Division to confirm EDB content before despatch. Organics Division would like as much notice as possible of US requirements.

ICI

Some drums of product recently arrived in the US containing hexane. Organics Division will be asked to check drums before despatch using a "sniffer".

EDB is still going through the RPAR process. Chevron have had no response from EPA about their confidential statement of formula.

Status of Long Term Toxicological Studies

- (i) Two year rat studies Three studies have been carried out and in combination give some support to the fact that diquat does not produce any serious long term effects in rats, other than cataract formation. Two of the studies used dichloride salt and had poor survival due to respiratory disease. One of these was an IBT study (1965) and the other CTL (1964). The third study (Pharm. Div. 1976) was designed to find a nel for cataract only. This was in general agreement with the earlier studies.

Chevron

The early CTL study is being audited. Chevron agreed to forward microfiche copies of what data was available from the IBT study.

(CTL comment: It seems unlikely that the two earlier studies would pass a present day EPA review. However, there are mitigating factors which indicate that diquat is unlikely to pose a hazard from long term administration. The 3 studies were undertaken in 3 different laboratories and two strains of rat were used. On the evidence of cataract formation there is a close similarity between the results showing consistency between these studies. The combined evidence from the two earlier studies gives no indication of any adverse finding other than cataract formation despite administration at levels up to 1000ppm. It should be noted though that DQ appeared somewhat more toxic in the CTL study where the level of 1000 ppm had to be abandoned because of mortalities).

The need to carry out a repeat 2 year rat study will be discussed further at the next (spring 1979) liaison meeting, when it is hoped that more detailed assessments of the "old" studies will be available.

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- (ii) 80 Week Mouse study This is a more recent study (Life Sciences Research - 1976), and appears to be in good shape. There was a clear no-effect level of 30 ppm diquat.

Chevron/ICI

The report would be evaluated in more detail by Chevron and CTL would be asked to check on the pathology results.

The status of the two other chronic studies remains unchanged, viz.

- (iii) Rat Reproduction Study: A CTL study (1972) used the dibromide salt and appears reasonable on paper. It has not, however, had an in-depth evaluation.
- (iv) Long term dog study (CTL, 1966): Feeding with dichloride salt was carried out from 2 to 4 years. A no-effect level for cataract appears to have been well established but a considerable amount of effort would be needed to upgrade the report.

The supporting studies on teratogenicity (evaluated in 3 species) and mutagenicity (from 3 tests) are all clean.

Although we have to respond to EPA on validation of the IBT 2 year rat study, one approach regarding repeat tests is to wait to be asked. The presentation of new tolerance petitions would undoubtedly precipitate this action. It was agreed to review the situation at the next meeting.

#### PARAQUAT - NONE RPAR MATTERS

##### Safer Formulations

Chevron are anticipating change over to the stench (n-valeric acid) formulation in the period October-December 1978.

The emetic submission is still hung up in F & DA. The ways in which an approval for an emetic formulation could help counter introduction of competitive PQ was stressed. There is also new data from Huntingdon showing an effect of the emetic in delaying gastric emptying in animals (report in draft stage). It was agreed that Don Dye would contact the responsible people in EPA to get an update of the situation, which would then be reviewed (early November) to decide what further action should be taken. ICI offered support in any proposed visit to EPA to press this case.

Chevron

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ICI is introducing coloured formulations only in those countries where it is being forced to do so.

### Competitive PQ

Recent analysis of Taiwanese PQ using reduction followed by GLC has shown the presence of up to 38% quaternised 2,4'-bipyrylium salt and smaller quantities (2.5%) of quaternary 2,2'-bipyridyl.

Chevron Mr Assad will be asked to explore ways of obtaining a sample of Taiwanese PQ presently impounded at Los Angeles by EPA.

Since IBT have now finished toxicological testing, it seems highly probable that the Otsuga tests contracted there on PQ have had to be aborted.

### Round-up

Monsanto now claim that the toxicology problem (IBT data) has now been resolved with EPA. They believe that 15-20 tolerance requests held up for 1 year in EPA will be cleared in the next 2-3 months. Dr Barrett has a list of the outlets.

There are indications that Monsanto are reducing the recommended rate on annual weeds. In comparison with PQ on no-till corn and soyabean a two fold improvement with PQ (in tank mixes with residuals) has been demonstrated by Chevron (0.5 lb PQ = 1 lb glyphosate)

### Registration Status

The current status (at July 1978) regarding petitions for paraquat (and diquat) is shown in Appendix 2.

The oleoresin submission has now been approved by EPA and an agreed label printed (Appendix 3).

The State of California (Dept of Food and Agriculture) has issued permit conditions for the use of PQ for cotton harvest aid (aerial application, specifying nozzle sizes and using a thickener such as nalcatrol) see Appendix 4.

ICI Assuming PQ survives the RPAR process (see Notes Part II) then it will come up for re-registration with certain data gaps. Repeat chronic studies are underway to fill these data gaps. It was considered necessary that we would also need a repeat dog study, of 6 months or 12 months duration to provide a no-effect level in a non-rodent species. It was agreed this should be started - there is a suitable space at CTL about mid 1979. A draft protocol for this study will be forwarded to Chevron.

### Hydrogen evolution

The background to this was discussed at the last meeting. In tests carried out by Chevron PQ liberates hydrogen from aluminium faster than does glyphosate from mild steel,

galvanised steel and zinc. Monsanto have a warning on their label ( Appendix 5).

Chevron have concluded that EPA will need to be advised of the PQ situation and a label statement submitted. ICI A will be given the opportunity of commenting on the draft.

Balcolm Chemicals Private Label

There was no time to discuss this problem.