

Exhibit 48

PARAQUAT AND DIQUAT

LIAISON MEETING WITH CHEVRON CHEMICAL COMPANY, USA

17-19 FEB 1976

TOXICOLOGY

The discussions on the toxicological aspects of paraquat usage and registration in the USA were between Dr R D Cavalli, of Standard Oil Company of California, and myself.

1. Action to counter the possible rebuttal presumption by EPA against paraquat. Dr Cavalli had not received my draft of the case for the existence of a treatment for paraquat poisoning, although he had the other enclosures of my letter of 15 January 1976. I gave him another copy of the draft which was discussed briefly. After analysing this document with other members of the Chevron Group, he will send comments. His first reaction was that it was suitable but required emendation with the addition of more US cases and some redrafting of the text.

Some additional experimental work is also needed on minor aspects of the rebuttal proceedings and also for classification of Ortho paraquat. This will entail a small amount of acute work and Dr Cavalli will try to get this done in his new facilities. A letter has been sent to him (KF to RDC, 4 Mar 76) giving ICI's views of the required work.

2. Legal actions involving paraquat. There are three known possible actions against Chevron with damage suits which could total around £15m. None of them appears to be founded on good evidence and allege effects not known to be caused by paraquat. Two of these (McKinsey and Mendes) claim paraquat has caused blood dyscrasias. Only two literature papers (one of them nonsense) give any support to this whatever. CTL has recently done some experimental work to see if these are possible effects and a literature search. These were discussed. The other actions (2) involve multiple vague symptoms after chronic exposure. Arising from these, Cavalli said that the chronic animal studies done with paraquat were inadequate for good defence. This is probably true. I agreed to

discuss with PPD the possibility of further studies. It is accepted that such experiments would be difficult to make completely satisfactory, since the nature of the allegations is so vague. In addition to the animal tests, Chevron are keen to have a human epidemiology study on workers chronically exposed to paraquat. Two semiacute studies have already been done in Malaya and Eire, but what is required is one extending over at least one to two years. The USA is unsuitable since sprayers use a multitude of compounds. I had already talked about this to Dr Howard and agreed to raise the subject again. Although Chevron have not yet lost a large law suit involving paraquat, this is obviously an area where they feel very vulnerable and the potential losses are large. Dr Cavalli has agreed to send as full details as possible of all the cases for CTL evaluation.

3. Testing of antidote adsorbent formulations. The protocol for this study has been agreed and will be done in the USA. If the Dowex resin treatment works, further experiments will be done to assess the effect of lessening the amount of resin and testing other resins which may be available in the US.

4. Chevron is partially supporting an experiment in dogs being done at ULA, testing the effect of extracorporeal oxygenation in paraquat poisoning. The experiment will be limited, but involves the measurement of paraquat in blood and biopsy samples of lung, together with tissues *post mortem*. I questioned the availability of suitable methods at either Chevron or ULA and offered the facilities of CTL. I also agreed to send a copy of our GLC method of analysis.

We also talked about the possibility of support of research in the USA, particularly the ideas expressed by Dr H K Fisher of the VA Hospital, University of Arizona. (After the meeting in San Francisco, I visited Dr Fisher. He will shortly be moving to head a larger group on pulmonary disease at ULA. Although he retains an interest in paraquat, he had not intended any large amount of work. He will consider whether, with support, he could justify a programme. Any proposal would probably require a postdoctoral Fellow and cost around \$20-30 000.) Chevron would be keen to see such support, but would not fund it themselves.

5. I was shown the experimental animal facilities in the Environmental Health Center. These are very new and, as yet, scarcely furnished. Although fairly small, they are modern and, when complete, should be very satisfactory for toxicology work up to, and possibly including, 90-day trials.

6. Dr Cavalli was told that I shall cease having responsibility for bipyridyl toxicology at the end of March and that Dr Litchfield will take over this role as far as liaison with Chevron is concerned. Dr Rose will be in charge of all research into the action of paraquat and diquat and the search for treatment of poisoning.

7. At the general meeting the possibility of the introduction of a closed mixing system was raised. Whilst few details of this are known, its applicability to paraquat or diquat solutions needs careful study. Descriptions of having to cut the neck of the container do not inspire confidence, and we must take all precautions to avoid adding accidents in the field to our other problems.

K Fletcher

KF:EKW
18 Mar 76

CIRCULATION

Dr J T Brauhnoltz, Plant Protection Division
Dr A Calderbank, Plant Protection Division
Mr G Jenkins, Plant Protection Division
Mr D Walker, ICI US Agricultural Division
Mr T Frears, Plant Protection Division
Dr D Barrett, Plant Protection Division
Mr D Blows, Plant Protection Division
Mr J A Turner, Mond Division
Mr D A Knowles, Plant Protection Division
Mr A W Waitt, Plant Protection Division
Dr M H Litchfield, Central Toxicology Laboratory
Dr M S Rose, Central Toxicology Laboratory
Dr R A Herrett, ICI US, Goldsboro
Mr R C Hampel, ICI Americas, Wilmington
ICI Australia Ltd, Report Centre
ICI Australia Ltd, Library, Merrindale
ICI New Zealand (fao Mr W F Leonard)
PPD, Jealott's Hill Report Centre
PPD, Fernhurst, Reports Centre
Dr J N Ospenson, Chevron Chemical Co
Dr R D Cavalli, Standard Oil Co of California
