

CONFIDENTIAL - CATEGORY B

NOTES ON MEETINGS HELD AT CTL 6-9 OCTOBER 75

I INTERNATIONAL PARAQUAT MEETING - 7 OCTOBER

The meeting was held to enable clinicians and research workers to exchange views on the treatment of paraquat poisoning with the objectives of agreeing the best treatment and determining future research programmes. The programme and list of participants is attached in Appendix I.

A detailed account of the meeting will be issued and these notes are to highlight one or two aspects and minute relevant discussions with some of the delegates.

The very positive approach by Drs Okonek, Lau, Fisher, Douse and McGeeon to the treatment of poisoning cases was sadly contrasted by the hesitant approach by U K doctors. Nevertheless, the meeting was timely and the discussion indicated several points worthy of further research.

- Highest priority should be given to determining a rapid method of analyses of paraquat in the blood as the present method takes about 18 hours. The availability of such a method would enable doctors to apply the most effective treatment. There was strong opposition to the use of forced diuresis being universally applied as in some cases it could be detrimental and/or unnecessary.
- Douse and Fisher's work suggests that high or normal O_2 in lungs could accelerate paraquat action in the lungs. Douse uses N_2 to reduce O_2 tension but because of other treatments applied the benefit of N_2 is not clearly established. It may even be deleterious. Dr Fisher by extra-corporeal oxygenation, by-passing the lungs, has suggested another approach which should be investigated.
- The value of haemodialysis and haemoperfusion should be studied in relation to dosage of paraquat.
- A wider range of animal species should be studied for treatment of paraquat poisoning to facilitate extrapolation to humans.
- The effects of forced diuresis on blood plasma levels of paraquat should be investigated.
- Past, present and future information on the treatment of paraquat poisoning should be collated and circulated.
- Antidote studies should continue to attempt to find a chemical which will either displace paraquat from the lung or prevent its entry into the lung.
- There is a need for a regular exchange of information between those actively involved in paraquat work. Consideration should be given to further meetings and to the means of disseminating information.

PH EXHIBIT 23
WITNESS: *Antkowiak*
DATE: 3-5-20
Araas Winberley, CSR 7778

L-618

CONFIDENTIAL - PARAQUAT LITIGATION

SYNG-PQ-02491648

Author's note: There is an obvious requirement for the coordination of paraquat research and for keeping in close contact with research workers and clinicians handling paraquat. This is particularly important as more requests for financial support are likely.

PERSONALITIES:

- Dr Douse (Holland) and Dr Okonek (West Germany):** Both very forceful and enthusiastic workers; they provided a very refreshing approach to the problems of paraquat poisoning. Their methods are becoming increasingly successful.
- Prof K Lau (Malaya):** Very positive. He was categorical on the use of Fullers Earth in the treatment. He indicated a high number of deaths in Sarawak, figures were obtained from the Director of Medical Services, where paraquat is replacing other corrosive materials previously used to commit suicide. In the Pacific it seems important that suicides visibly suffer as a manifestation of their expiation.

	Total	Suicide	Accidental
1972	4	1	3
73	6	4	2
74	27	17	10
75	23	14	9
Total	60	36	24
Not fatal	27		
Fatal	33		

Prof Lau believes that the rate of deaths is similar in Malaysia. He was concerned over lack of apparent action by the local company. He informed him that tests were under way with a stenciled and unattached/coloured formulation in Malaysia, but there were technical problems to resolve. He hoped that a safer formulation would be possible and that the label provided unequivocal warnings of the hazards of misuse.

Dr Lau appeared very reasonable and it would be of value to keep him fully informed of developments in the treatment. He could prove a very useful cooperator in the event of government pressure.

NOTE: These topics have been discussed with the Marketing Department.

- Dr Fisher (U S A):** A very diplomatic and likeable person who during the discussion, by his calm and rational approach frequently relaxed the atmosphere between research workers and clinicians. He appeared to be a competent and knowledgeable research worker.

- 2 -

CONFIDENTIAL - PARAQUAT LITIGATION

SYNG-PQ-02491649

- Dr R Davies (Australia):** Very likable with good personality who introduced a highly practical note into the conference. As a result of the conference will immediately revise 'Treatment Booklet'. His report into the paraquat deaths in Samoa is attached (Appendix II).

Dr Davies could greatly assist PFD by representing ICI/CTL at the interface with the NH & MRC. Also he could provide information on changes of attitude and protocols with the addition of presenting our views to the authorities when required. He was enthusiastic at this suggestion, as was Dr Swan and the proposal has been accepted by our Regional Marketing Department. Dr Swan will approach Dr Whitton, Director of ICI Australia with the proposal. It is believed that the active assistance of Dr Davies to Mr F Milk will provide a strong registration team. (Action taken).

- Dr J McElligot (Canada):** Dr McElligot was some years ago the senior pathologist at CTL and is now Senior Pathologist at a hospital in Kingston, Canada. His services have been used to a limited extent in a consultancy capacity by CTL for PFD products. There is a need to formalise the position as Dr McElligot is now being approached at odd hours of the day to give advice. Additionally, because of his many useful contacts within and outside official circles, more use should be made of his services on behalf of PFD and to this he agreed and it was endorsed by Dr Swan.

NOTE 1: Since agreed by the Regional Marketing Department.

NOTE 2: It will be necessary to ensure that both Dr McElligot and Dr Davies are kept fully informed by CTL on the toxicological dossiers for our products.

- MEETINGS WITH:** Dr Ospenson
Dr Cavalli
Dr Swan (part time)
Dr Fletcher
A Waitt
Chevron Chemical Company
Standard Oil Company
CTL
CTL
FPD

HELD ON 8 AND 9 OCTOBER 75

- COMMUNICATIONS:** A breakdown in communications had occurred between Chevron and CTL resulting in considerable misunderstandings over work programmes and supply of information. After lengthy discussion it was agreed that:
 - K Fletcher and D Cavalli would be the major point of contact between CTL and Chevron respectively.
 - All correspondence should be copied to Dr Calderbank and Mr Waitt who, in turn, would feed in any background information for the two parties.
 - In matters of major concern Dr Ospenson and Dr Swan should correspond directly.
 - For paraquat a quarterly report should be written by K Fletcher/M Rose for Chevron. An annual report would be required for diquat.
 - In order to provide CTL with a better background to the American scene Dr Fletcher should attend the Chevron/FPD marketing and technical discussions. Dr Ospenson proposed that the toxicologists could meet one day prior to the general discussions for exchanges on their own topics which would be summarised for presentation at the meeting of marketing and technical representatives from the two companies.
- CASE HISTORIES:** It is important for the EPA to have supporting evidence of a palliative treatment for paraquat poisoning and therefore to assemble complete case histories on paraquat poisoning cases where only small intakes of paraquat were recorded. Dr Fletcher agreed to select the most relevant cases to follow up with discussion with Chevron and Dr Swan considered that Dr Howard may be able to assist. It would be highly necessary to ensure that the confidentiality of these medical records be maintained and the ethics of transmitting this type of data is to be resolved by CTL.
- ADSORBENTS FOR THE TREATMENT OF PARAQUAT POISONING:** There was a need to examine as to their suitability for treatment of paraquat poisoning, other adsorbents such as charcoal, resins and other clays. This work was to be done at Huntingdon Laboratory but Dr Cavalli requested that it be carried out at his laboratory where they were familiar with the technique and had spare animals. It was agreed that this should be done subject to suitable coatings. It was also agreed that this biological study should be linked to the studies of the chemical adsorbence of the material under test.

- 4 -

CONFIDENTIAL - PARAQUAT LITIGATION

SYNG-PQ-02491650

CONFIDENTIAL - PARAQUAT LITIGATION

SYNG-PQ-02491651

- 4 IIRS REPORT ON PARAQUAT SPRAYS. It was agreed that this report could be copied to the Californian State officials.
- 5 CHRONIC TOXICITY. Chevron are concerned on the chronic effects of paraquat sprays resulting from 4 cases reported by the State of California. The syndrome is reported as injury to the CNS, non-specific liver/kidney injury. It is said the syndrome can be confused with heat effects from working in the sun. However, prompted by Ide Honaroff, a journalist, one of the 4 is suing Chevron. Refutation of this claim is extremely difficult and Chevron would like more positive data to use in litigation cases. It is suggested that a critical epidemiology study is carried out and a long term toxicity study using sprays on animals. These proposals are to be discussed at future meetings.
- 6 ACTIVITY OF PARAQUAT ON CNS. In a recent autopsy on a paraquat poisoning the pathologist discovered lesions on the motor neurons. The lesions were sufficient to cause debilitation. It is not clear from the case history whether the therapy might have induced this effect which is similar to arterio-sclerosis. Fisher has also reported ataxia from paraquat administered by any route and Dr Fletcher has received a few enquiries on peripheral neuritis. It was agreed that this effect was difficult to check but evidence might be obtained from an epidemiological study. This topic is to be given further consideration.

III VISIT OF DR WANDEKAR (WHO) TO CTL ON 9 OCTOBER

It was believed that Dr Vandekar could provide CTL and PPD with advice on the presentation of data to WHO and on the ability of WHO to discuss toxicological problems with the manufacturer. Unfortunately his interest lies solely on insecticides for public health use and he suggested we contact Dr Lu or Dr Vettorezani. This action has been taken.

Circulation:

Dr J F Braumholts	Dr K Fletcher/Dr N Ross/Dr M Mitchfield (2)
Dr A B Swan	Mr R Moore/Mr A Higgins
Mr A J Maier	Mr J Denise/Mr R Sprinnett
Mr R R Vetch	Dr R Davies, ICI Australia
Dr A Calderbank	Dr P McElligot, Canada
Mr A G Bates, ICI U S	Dr K Howard
Mr R Hampel/Mr D Walker, ICI U S	
Mr W C Jenkins	
Dr G Watson/Mr I More/Dr D Borrett	
Dr A Schumacher	

AWN/LAN/17 Nov 75