

Exhibit 49

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Dr R D Cavalli
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U S A

KF:EKW

4 Mar 76

Dear Dick

PARAQUAT : SAN FRANCISCO MEETING

I thought it as well to write to you to give my own impressions of our meeting and the area for future work.

1. We agreed that we would try to do the analyses on the experiment on extracorporeal oxygenation in dogs if this was agreed by the experimental group. I enclose a copy of our experimental method.
2. You will send me, when available, the case histories of the possible litigants with as full a description as possible of the blood effects. We shall continue with our work on the effects of paraquat and diquat on the blood and bone marrow of rats. We will also continue to try to get further information from clinical cases of poisoning where blood or marrow effects have been reported. In this context, I think it would be useful to have some bone marrow pathology from fatal cases. I will try to get some here and you might bear this in mind if you are unfortunate to have another case.
3. Since there would seem to have been some mix-up over my letter of 15 January and all enclosures, I am sending further copies.
4. You will continue with adsorbent/survival studies in rats with more emphasis on the effect of using Dowex resins in lesser amounts if they prove effective.
5. I have discussed with Calderbank and Waitt the possibility of doing further chronic studies of paraquat in rats to try to obtain evidence to combat possible litigation on a multitude of alleged effects of paraquat. Their view is that PPD would be reluctant to do this, since no experiment could be all embracing and any lack of immediately relevant evidence could be fully exploited. Furthermore, the extrapolation from animal to man is always attackable and no arguments can contradict the case of the 'sensitive' individual. At present, therefore, PPD do not intend to carry out extra studies without more persuasive argument.

The possibility of an epidemiology study is, however, being pursued and I hope this can be done, although there is nothing further to report.

6. I have discussed your proposal that work on Chevron Ortho paraquat required for US registration/rebuttal proceedings be done at your labs. This is agreed to be appropriate and we have discussed what might be required. It is, of course, assumed that the work will be done to the EPA protocols. I enclose copies of a summary of the areas where information might be required and the PPD view of where we might be deficient. This suggests that the following work might be necessary.

Rebuttal presumption requirements

iA1 Dermal LD50 of undiluted formulation. Although we have no direct work on Ortho paraquat, there is a considerable amount of other formulations and, hopefully, this would suffice. If requested the test can be done rapidly and therefore this should be left out. I would be interested to hear your thoughts on this.

iA2 Dilute spray dermal LD50. This requires to be done but hopefully only on the most concentrated spray in use. Aerial strengths need to be considered separately.

iA3 The inhalation toxicity of undiluted formulation. On this we must seek your guidance, since I do not know the appropriate test. Gage's work gives the toxicity of a respirable aerosol of pure paraquat and an estimate of respirable fraction from sprayers. We also have back-up information on the two field trials in Malaysia and Eire. Exposing rats to practical agricultural sprays will give uninterpretable results. Can you please advise what you consider appropriate?

iB1 & 2 Toxicity of residues to wild-life. Here we consider the available information adequate.

iB3 Toxicity to aquatic life. The information is inadequate but will be obtained by PPD.

iiA. We will collect all available data on oncogenic/mutagenic tests which should be adequate. The data will, of course, not be obtained from Ortho paraquat, but this should not matter.

iiB Other chronic effects. No more experiments to be done, but the developments to be reviewed periodically.

iiI Present data should be sufficient.

iii I have a few comments for amending my draft paper and you will also look at it from the USA point of view. Consideration will be given to including well described unpublished cases, both from UK and USA. The document will be maintained up to date at frequent intervals.

Restricted use requirements

Most of these will also be covered by the above, but on 162.ii(c) 1 iiD and E we believe we lack the relevant work and this should be done. I am not clear whether this refers to concentrated or dilute formulation and would seek your judgement on the appropriate tests.

You will also presumably need to do some work on the formulation lacking corrosion inhibitors and a sample of this will be sent when available.

I had a very interesting morning with Ken Fisher. He is moving to the University of Los Angeles, probably in July, to take over a much larger department. He does intend to carry on with some work on paraquat but had intended to do no further clinical research on poisoning. I told him that if he was interested and could formulate a worthwhile programme, then we might be prepared to support a worker in his lab. He will give this some thought.

May I say how much I enjoyed my stay in San Francisco, and thank you for your royal hospitality. One of my regrets at leaving my present job is that it may be some time before I have an opportunity to return. I will do my best to brief Mel Litchfield on the various lines that are running so that he may be able to cooperate with you rather better than I.

My best wishes,

Yours sincerely

K Fletcher

Enclosures

cc Dr J N Ospenson, Chevron
Dr A Calderbank, PPD
Mr A W Waitt, PPD