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CHEVRON CHEMICAL CO. ORONITE DIV. R & D DEPT. 15 '75

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PARAQUAT
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Dear Ken:

Please forgive my delay in acknowledging your, Mike's, and Mrs. Whitaker's recent correspondence. Thank you for the timely review and comments on the paraquat bulletin. We have revised it according to your suggestions.

I have a number of items to discuss with you and two rather specific requests. I am enclosing reports on 2 poisoning incidents which you are already aware of, one dermal and one parenteral. In addition, I have been informed of a possible fatality from ingestion of paraquat in Florida. A man supposedly stored both paraquat and drinking water in similar "Clorox" bottles and drank from the wrong one. I would appreciate your not publicizing this case, as we are still investigating it and have not, as yet, been able to confirm it.

I was sorry to learn that the monkey studies on superoxide dismutase (SOD) could not be done. As long as the people at Hammersmith do not publish the fact that SOD does not appear effective, I believe that we are going to be asked to supply it. A possible way of studying the effect of SOD on paraquat victims has been suggested by Dr. MacGregor of our staff. Data supplied by D.D.I., Inc. (the U.S. supplier of SOD) indicates that subcutaneous administration of SOD produces a sustained blood level, as opposed to a very quick disappearance following a single I.V. injection. We believe that a study, in the rat using subcutaneous injection of SOD following oral paraquat administration, would provide more meaningful data than the type of study done by Autor, where only I.V. doses were given. Will you undertake to do or sponsor such a study so that we may better advise on the use of this drug? Incidentally, I would be interested in receiving any information you may have from Huntingdon on doses used, signs, survival time and autopsy findings in the monkey.

With regard to problems of nosebleed and sore throat in our own plant workers, I would like more detail, if possible, on problems PPD has had in manufacture or liquid packaging. Has PPD a record of any such complaints from packaging paraquat? Have your industrial hygienists ever taken air samples near liquid or solid packaging lines and/or urine samples from the workers? Could this data be made available to us? I would also be interested in what precautions PPD takes for protecting their plant workers.

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such as use of respirators, gloves, etc. We are currently undertaking a study to determine possible exposure levels, and the information requested would be of use to us.

In my April 28 letter, I asked if you were doing or sponsoring, or acquainted with any research using the hemoperfusion device, other than clinical trials. We are anxious to see if this type of unit can be of significant value in treating paraquat victims.

Mike's May 30 letter, in answer to mine of May 21, made no mention of whether or not you have ever had reports, confirmed or not, of injury such as Mr. Fales claims to have suffered. Anything you have on the question of permanent injury from paraquat, or any follow-up evaluations several years after spraying would be of benefit to us. Fales and several others have alleged permanent CNS effects from paraquat. Several papers describe transient CNS-type effects following administration of paraquat in the rat. Also, the pathologist who read slides of spinal cord from Thomas Paul, found evidence of an acute degenerative process similar to that seen in anterolateral sclerosis (ALS). This patient was also heavily curarized for at least 10 days. There was no history of signs or symptoms relating to ALS, and the pathologist felt that the lesion was recent. She is not "convinced" that it was due to paraquat, but she is suspicious. Have you seen anything like this? Your opinion and supporting data would be very valuable to me. This appears to be a growing problem in the litigation area and is of concern to state and federal regulatory agencies.

We have completed our first round of antidoting studies. The dose of paraquat used was 126.5 mg cation/Kg. This caused 13/15 deaths in 14 days with purified paraquat and 10/15 for Ortho Paraquat Cl. The treatment regimen used was identical to that described in Smith, et al., except that Robinson's Bentonite or Robinson's Fuller's Earth were substituted for the bentonite.

Previous studies done by Ortho indicated that Robinson's Fuller's Earth was a relatively weak binder of paraquat (6,000-7,000 ppm "tightly bound") while the Robinson Bentonite was a strong binder (54,000-56,000 ppm "tightly bound"). Additional groups received cathartic only, without any clay, on the same schedule. Treatment was delayed 4 hours, but in one group, treatment with Bentonite and cathartic was delayed 24 hours. Results were as follows:

Treatment	Mortality (14 days)
Purified Paraquat (PP) No Treatment	13/15
Ortho Paraquat Cl (OP) No Treatment	10/15
PP/Bentonite/Cathartic	1/10
OP/Bentonite/Cathartic	0/10
OP/Fuller's Earth/Cathartic	2/10 (one died very early and may have aspirated)
OP/Cathartic	9/10
OP/Bentonite/Cathartic/24 hour delay	6/10

As you can see, the strong and weak binding clays were effective at 4 hours, but not at 24 hours, and the cathartic alone was not effective. I will send you a full report as soon as it is available.

We would like to see more of these studies done using various activated charcoals, "universal antidotes," and perhaps even several types of soil. Will CTL undertake to do these follow-up studies? We feel these are necessary because of the prevalence of such materials in the Emergency Room or hospital and the lack of clays in these establishments. If you will do this work, we can supply you with the materials likely to be encountered in the U.S. We had occasion recently to recommend the new treatment in a case where a field worker splashed paraquat concentrate into his mouth. Although the hospital was located in Southern California near a major highway and with commercial airline service, the soonest we could get bentonite to them was 24 hours. They did initiate treatment with activated charcoal and magnesium sulphate. A sample of urine taken 8 hours after exposure, but prior to treatment, and 5 samples taken during the next 24 hours were all negative for paraquat and treatment was discontinued at that time. As far as I know, the patient is alright, and probably did not actually swallow any paraquat. However, this case does point out that we, in the U.S., will probably be treating more cases with charcoal than with bentonite, and I would certainly like to see a definitive study done using the commonly available charcoals.

I appreciate your attention to these questions, and look forward to seeing you in October.

Very truly yours,
Original Signed
R. D. CAVALLI

R. D. Cavalli
Staff Product Toxicologist

RDC:ln
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