MEMORANDUM OF INTERNAL CONFERENCE
April 7, 1970

PRESENT:

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| Dr. O. G. Fitzhugh | - | Assoc. Director for Toxicological Review (BF-203) |
| Dr. L. Friedman | - | Director, Division of Toxicology (BF-140) |
| Dr. C. Williams | - | Residue Toxicology Branch (BF-218) |
| Dr. F. McFarland | - | Division of Regulations and Petitions Control (BF-321) |
| Dr. H. Jones<br>Mr. J. Cummings | - | Petitions Evaluation Branch (BF-216) |
| Dr. J. McLaughlin | - | Division of Toxicology (BF-147) |
| Dr. J. L. Svirbely<br>Dr. G. E. Whitmore<br>Dr. H. Blumenthal | - | Division of Toxicology (BF-148) |

SUBJECT: Cabaryl teratology

This conference was called to try to establish an in-house response to the most recent data relative to the teratogenic potential of cabaryl. Dr. Blumenthal presented a review of the past history up to the time that the FDA had reported this compound as a teratogen in dogs. At this time the Union Carbide Company had responded by establishing that, for urinary metabolites there was a definite difference between the dog and the guinea pig, on the one hand, and the rat and the human on the other hand. Further, that this difference in metabolism was reflected in the teratogenic differences for the species involved. On the basis of this reasoning, and the fact that the levels that caused teratological response in dog was high enough to allow for the tolerances in force, there was no action taken to revoke such tolerances for carbaryl. Since that time the "Bionetics Study" had established the teratological response for a strain of mouse. The possible teratological response in sheep had been reported. Union Carbide had repeated the FDA dog work. The Albany Medical College Group had done some monkey studies.

Dr. McLaughlin, who had recently visited with the Albany Group, then discussed his impression of the monkey study. He stated that at this time it was impossible to come to an overall conclusion with reference to the teratological response of monkeys to cabaryl. However, he felt that there was sufficient doubt engendered by the work to date to suggest the need for carrying the monkey teratology further.

There was then some general discussion with reference to questions of residue. What the real residues on crops were, and whether, if one were aware of the real residues would there be need for new toxicological data?

The fact that cabaryl had not been found in the total diet studies was not too meaningful since the methodology used was sensitive to about 1 part per million, and did not respond at all to possible plant metabolites. After much further discussion it was concluded that the Union Carbide people should be informed of our concern. Further that they should be asked to respond to the total teratology data and possibly repeat the monkey studies. Finally, they should also be asked for more up-to-date residue analyses to establish the metabolic picture in plants.

It was suggested that Dr. Blumenthal draft for Mr. McFarland the type of questions that should be asked of Union Carbide.

H. Blumenthal, Ph.D.

cc: BF-140
BF-203
BF-218
BF-216
BF-321
BF-147
BF-148

HBlumenthal:cms 4-16-70