APR 14 1969

Industrial **BIO-TEST** *Laboratories, Inc.*
1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062
AREA CODE 312
TELEPHONE 272-9030

April 10, 1969

Mr. Elmer Wheeler
Monsanto Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63166

Dear Elmer:

I am enclosing a revised protocol for a chicken study with the Aroclors.

After much discussion among ourselves, we have concluded that a relatively conventional study should be conducted with the addition of certain specific parameters which might be of importance in reproduction and mineral metabolism. The study has been made flexible at the end to allow for the possibility of mechanistic studies, should these be indicated, based on gross findings. It seems to us irrational to attempt definition of mechanism until we have demonstrated an effect.

It is our opinion that the studies to elucidate mechanisms, to determine rate of accumulation, and to define no-effect levels for enzyme induction might best be done as separate studies specifically designed for the purpose. Although these studies would require the utilization of more refined techniques, the duration of treatment and the numbers of animals required would not be excessive. To attempt to combine all things in one study would introduce massive complications and, in our opinion, would be excessively expensive and wasteful if it should be that the significant effects are not observed with the species selected for study.

We have also elected to recommend dietary levels of 1.0, 10 and 100 ppm. We feel that 100 ppm is high enough since, if effects are not observed at this level, it is probable that the test material does not cause the effect of concern or that the chosen species is unresponsive.

Since 2 ppm has already been found to be a no-effect level of DDT for microsomal enzyme induction in rats, we see little virtue in going below 1.0 ppm at this stage. If effects are observed at this level, our shorter term mechanistic studies can be confined to lower levels.

The mallard duck study would be conducted according to the same protocol except for the change in species.

The cost for these studies, exclusive of Part E and the other detailed studies, would be:

Chicken or duck study using 3 dosage levels plus controls	
One material	$ 9,000
Two materials (common controls)	15,750
Three materials (common controls)	22,500
Four materials (common controls)	29,250

I am in the process of acquiring more insight into the biochemistry which might be involved, and will develop cost estimates for other studies which might be indicated.

We see no cause to modify the fundamental design of the mammalian studies which, in our opinion, should be conducted as classical toxicological studies to define no-effect levels. We will, however, propose the addition of certain biochemical parameters which might be significant to the overall purpose of the program. I will forward to you our thoughts on this (including consideration of the suggestions of Drs. Mehler and Metcalf) together with revised cost estimates in the very near future.

Since duck egg production is somewhat seasonal, the fowl studies should be started soon.

Because of the time involved, the chronic feeding studies, and the rat reproduction study should be initiated at an early date.

Sincerely yours,

Otis E. Fancher, Ph.D.
Director

OEF/JM
Encl.

MONS 090110