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September 22, 1970

Trip Report - Meeting on Aroclors (Monsanto) in Washington, D. C. - 9/15/70

Bill Pappageorge, Elmer Wheeler and Jack Early from Monsanto, Dr. Fitzhugh, Dr. Clara Williams and Mr. John Tigley from FDA as well as myself attended the meeting. The one-year progress reports from the chronic rat and dog studies were presented and the results were discussed. The report of the first generation of the three-generation reproduction study in rats was presented and preliminary results from the second generation were discussed. A copy of the second generation report was not available for dissemination. Copies of the chicken reproduction study also were given to FDA and the results were discussed.

One point which was very important in our discussions was that if the animals in the reproduction study are still alive, we probably should breed for a third litter and do caesarian on the females.

During the meeting, we found that FDA is doing some work with Aroclors 1254 and 1260. Dr. Williams' group in Washington is doing liver microsomal enzyme work. They are checking aniline hydroxylase, aliesterase, nitrogen reductase and glucuronidase. Feeding levels are 25, 75, 150, 300 and 500 ppm in the diet. The enzyme activities are measured after 30, 60 and 90 days. There are slight effects from feeding 25 ppm for 30 days.

There was some reduction in body weight gains in females fed 500 ppm for 90 days and perhaps a slight effect in those fed 300 ppm for 90 days. Histology on livers and other tissues from rats after 90 days has been done. The report of the pathologist indicated that there might possibly be some changes in the liver, but indicated that they could not make a conclusive statement about the possible changes. They are planning to do electron microscopy on these tissues.

They also have done some work on liver protein. After 90 days on test at 500 ppm, the liver to body weight ratios were 77 compared to 37 for controls. However, the protein content of the liver remained relatively constant. Therefore, it was assumed that the changes were fatty in nature.

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The next work planned with enzyme induction is to check potentiation with other chlorinated hydrocarbons, such as the pesticides.

Dr. Farber at Beltsville also intends to do some work with Aroclors 1254 and 1260. He wants to do liver microsomal induction studies on dogs and pigs. He does not plan to do any subacute or chronic testing in either of these species.

We also found out that Tom Gaines and Renate Kimbrough in Atlanta are doing some work with Aroclors. They have done acute oral studies in rats and also reported wanting to do some chemical analyses in the tissues after a single dose. High doses were fed to rats (10,000 ppm) and there were very marked effects, as we would expect. Only 1,000 and 10,000 ppm were fed. They were trying to find the 90 dose LD_{50}, and probably will not be able to do so with compounds such as these. They do intend to continue the studies, however. They also plan to do some 90-day feeding in rats to determine effect and no-effect levels. It was also mentioned that they would do reproduction studies, but there was no definition of what they meant by a reproduction study.

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