AROCLOR 1260: Meeting at NCI, January 31, 1975

Present

Renate Kimbrough - ~~EPA~~ HEW	Donovan Gordon - Industrial BIO-TEST
Robert Squire - NCI	Ward Richter - Industrial BIO-TEST
Morton Levitt - NCI	George Levinskas - Monsanto

A summary report of the meeting held at NCI is attached.

A copy of Dr. Kimbrough's remarks also is attached. This is essentially the same material presented by her at Monsanto on November 22, 1974. This information led to the meeting.

Dr. Kimbrough conducted a 2-year feeding study using 200 female rats to follow up on an earlier study in which she had detected a bladder tumor in rats fed AROCLOR 1260. At a meeting held in Quail Roost Conference Center, North Carolina in December, 1971, she presumably was dissuaded from her belief that the single bladder tumor she had observed in a female rat was due to AROCLOR 1260. However, she must have been unconvinced since she started the present study on January 14, 1972. She used a Sherman strain of rat which had been derived from an Osborn-Mendel strain by cesarean section and thus could be labeled as specific pathogen free (SPF). The Sherman strain has been maintained as a random bred closed colony. Since the bladder tumor had occurred in a female, she put 100 females on a diet containing 100 ppm of AROCLOR 1260 and she kept 100 females as controls. Animals had been born between December 18 and 22, 1971. Thus, they were about 3½ weeks of age when the study started. After 20½ months, on October 2, 1973, feeding of AROCLOR 1260 was stopped. Approximately one month later (November 4), animals were sacrificed.

It may be noted that Dr. Kimbrough did not detect bladder tumors, the original aim of this study. A control female did develop a bladder papilloma.

Control animals in this study had very "clean" livers. The incidence of spontaneous changes was quite low. Insofar as could be determined, Dr. Kimbrough has no data from other 2-year studies which could be used to assess the spontaneous tumor incidence of this strain of rat. Despite the absence of historical control data, her results would be hard to refute.

Animals were fed PURINA Laboratory Chow. It was analyzed periodically for several contaminants. Mycotoxins, naturally occurring products of mold growth which can cause liver tumors, were reported to be less than one part per billion.

There was no specific resolution of this issue. As an observer, I wanted to get the reaction of BIO-TEST's pathologists before

deciding what to do. There was no opportunity to caucus while at NCI. After we left, and they conceded the occurrence of hepatic carcinomas, there was little else to do. Although the subject wasn't raised, I got the distinct impression that Dr. Kimbrough plans early publication of her findings.

About the only palliative course of action would be to publish our 2-year study on AROCLOR 1260 before Dr. Kimbrough gets into print. This would at least blunt the impact of her publication. Another course of action would be to repeat the study and to include additional animals which would be fed AROCLOR 1260 for 18 months only. This would permit a determination of whether or not the liver lesions would regress after feeding of the product was interrupted. Obviously, it would be 2-3 years before the results of such an experiment would be available.

George J. Levinskas

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2/4/75

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The purpose of this meeting was to review sections of liver tissue from Dr. Kimbrough's 2-year study in which female rats were fed 100 ppm of AROCLOR 1260.

Drs. Kimbrough and Squire had studied and classified the findings. Dr. Levitt, either a visiting fellow or a post-doctoral trainee did not participate to any great extent. He was mentioned as having a good knowledge of liver.

Dr. Richter had viewed the slides from our 2-year study in which rats of both sexes had been fed 100 ppm, 10 ppm or 1 ppm of AROCLOR 1260. Subsequently, he and Dr. Gordon reviewed sections of liver from all animals in this study.

Three conclusions can be drawn.

1. In our earlier study, the severity of liver lesions was greater in females than in males.

2. To a large extent, substantially the same type of lesions were observed in both studies except that the lesions seemed to be more advanced in Kimbrough's study. Although there was some variation in terminology, the findings were reasonably close.

3. There were definite liver adenocarcinomas in Kimbrough's study. Dr. Richter expressed the view later that 2 animals in our study approached the type of lesion Kimbrough had observed, but there was agreement by Drs. Gordon and Richter that Dr. Kimbrough's rats had developed a lesion which they had not observed in our earlier study with AROCLOR 1260.

If. Drs. Gordon or Richter feel that I have not summarized this meeting correctly, or if they desire to amend or expand my remarks, I invite them to let me know.

GJL

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AROCLOR 1254: NCI Toxicity Testing at Stanford Research Institute

At the meeting at NCI on January 31, 1975 regarding AROCLOR 1260, Dr. Squire mentioned that AROCLOR 1254 was under test at SRI. This material is being tested in their "bioassay" program which he defined as consisting of groups of 50 male and 50 females on test at each of 3 levels. Dr. Squire either was reluctant to divulge too many details, or more probably, he was not overly familiar with this program.

AROCLOR 1254 is one of 20 chemicals being tested in an experiment which Dr. Squire described as "unique" and having an "enormously complex matrix". Apparently, each chemical is being tested by itself and with each of 3 other compounds. When the 3 dose levels and the various combinations are considered, this can get very complicated in short order.

Beyond that bon mot, Dr. Squire sayeth no more. We shall attempt to learn more of this study through other contacts at NCI.

George J. Levinskas

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