Monsanto

4

FROM (NAME & LOCATION) George Roush, Jr., M. D.

DATE July 30, 1975

SUBJECT PCB's

REFERENCE Memo HSB to FJF 7/17/75

TO H. S. Bergen
B2SL

cc G. L. Bratsch - B3NA
D. L. Eby - A3NA
J. T. Garrett - A2SA
T. L. Gossage - B2SL
G. J. Levinskas - A2SC
W. B. Papageorge - B2SK
R. G. Potter - B3SA
K. W. Easley - 1920
W. W. Withers - B2SA

Attached is a draft for the toxicity section of the Monsanto statement under Action No. 5 of the reference memo.

I believe this draft contains the essentials which must be included. It will undoubtedly need to be revised before it becomes a part of the final statement which should be completed in late August.

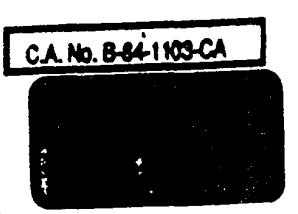
Comments are solicited.

GR

George Roush, Jr., M. D.

GR/ln
att.





SCM 019723



WATER_PCB-SD0000015412

PCBs

Recently, we were informed that liver carcinomas were observed in female Sherman strain rats fed AROCLOR 1260 for 20 1/2 months. This prompted us to re-examine livers from male and female rats of the Charles River strain which had been fed AROCLOR 1242, AROCLOR 1254 or AROCLOR 1260 for 2 years in earlier studies conducted by Monsanto. In addition, we have discussed our findings and those reported to us with scientists working in the field of carcinogenicity.

There are 4 elements which are closely interwoven in this matter: (1) differences in test procedures, (2) differences in results obtained by various investigators, (3) definition of what is a cancer, and (4) evaluation of potential risks, if any, to man. These will be summarized briefly.

(1) Several animal studies have been conducted with various brands of PCBs. In some studies, the test material has been

SCM 019724



WATER_PCB-SD0000015413

identified by trade name (AROCLOR, KANECLOR). In others, there was just a general reference to PCB. Consequently, the quality of test material with respect to the amounts and nature of contaminating impurities or by-products cannot be determined in all cases. In addition, several strains of test animals were used, the duration of the experimental periods varied, and there was a wide range in the depth of detail with which the observations were reported. Consequently, it is difficult to make comparisons between these studies.

(2) In general, studies have shown mice to be more susceptible than rats and females to be more sensitive than males to the liver effects of PCBs. Beyond these generalizations, the results have not been consistent. Some investigators have reported liver carcinomas. Others have observed only benign tumors. Several have noted changes in liver tissue without detecting tumor formation. For the reasons just cited, it is difficult to determine the bases for these different results.



WATER_PCB-SD0000015414

The most direct comparison can be made between the 2 studies on AROCLOR 1260 since the same high dosage level of the same lot of AROCLOR 1260 was employed in both experiments. In the studies reported to us, liver carcinomas occurred in approximately 8% of female rats of the Sherman strain (the only sex used). In Monsanto's study, none of the liver lesions had progressed beyond the stage of benign tumors (hepatomas) despite a slightly longer duration of feeding of AROCLOR 1260 to rats of Sprague Dawley, Charles River strain. The Monsanto study employed rats of both sexes and it did confirm the previously noted greater sensitivity of female rats to liver effects of PCBs.

(3) In the traditional pathologic sense, liver alterations seen with all 3 AROCLORS in Monsanto's studies were benign in character. Lesions of the type seen may be induced by other chlorinated aromatic and aliphatic hydrocarbons such as aldrin, dieldrin, and carbon tetrachloride. In fact, the experts whom we consulted expressed opinions that the potential carcinogenicity of PCBs was comparable to that of DDT, aldrin, dieldrin and carbon tetrachloride.



WATER_PCB-SD0000015415

The Environmental Protection Agency (EPA) and the National Cancer Institute (NCI) have redefined the traditional concept of benign and malignant tumors. Those agencies now view any tumor induced by a chemical as malignant despite the absence of the classical histologic features of malignancy. The legal division of EPA has used this redefinition of carcinogenicity to cancel the registrations of dieldrin and aldrin and it is about to launch litigation against chlordane and heptachlor. In this connection, it should be noted that, by virtue of their intended use as pesticides, these materials were intended to be used in a dispersive manner.

(4) Commenting upon EPA's reclassification of tumors, the Food and Drug Administration's (FDA) Associate Commissioner of Science remarked that . . . "It should be emphatically emphasized that there is by no means universal acceptance of . . . the above . . . classification of tumors." In addition, it should be noted that FDA has had the microscope slides of tissues, including livers from

SCM 019727

013708

WATER_PCB-SD0000015416

rats on the Monsanto studies with the 3 AROCLORS for about three years, and that the FDA has been informed of the more recent study on AROCLOR 1260. To this date, no adverse comments have been received.

After a review of all information available to us, we conclude that AROCLOR 1260 has been shown to be a carcinogen in one strain of rat. It is not carcinogenic in the traditional meaning of that word to all commonly used strains of laboratory test animals. Our overall interpretation of the available data is that AROCLOR 1260 has a carcinogenic potency comparable to that of DDT and carbon tetrachloride.

AROCLORS 1242 and 1254 have not been shown to be carcinogens.



SCM 019728

WATER_PCB-SD0000015417