Mr. Easley

MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
CENTER FOR DISEASE CONTROL
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

DATE: JAN 13 1976

TO : For the Record

FROM : Senior Research Reviewer, DCDSD

SUBJECT: Meeting with Representatives of Monsanto Industrial Chemicals Co., the National Institute for Occupational Safety and Health, and other Federal Agencies.

The following information is provided in accordance with NIOSH Administrative Issuance Number 8, dated October 30, 1975.

On November 13, 1975, at the request of Monsanto Industrial Chemicals Co. (Mr. K. Warren Easley, Director, Government Affairs), a meeting was held to discuss the results of certain polychlorinated biphenyl experimental animal exposure studies and their interpretation.

The meeting was held in the NIOSH Conference Room, Park Building, from 9:30 a.m., to approximately noon. Richard A. Rhoden, Ph.D., Senior Research Reviewer, DCDSD, served as the NIOSH Coordinator for the meeting. A list of attendees is attached.

The meeting opened with Dr. Finklea presiding, and Dr. Roush, Monsanto's Medical Director, laid the historical background of the request for the meeting, Monsanto's previous Medical Director (Kelly), having been approached, in November 1974, by CDC personnel in regard to certain rat feeding studies of a polychlorinated biphenyl product once marketed by Monsanto. The study had been conducted by CDC's Dr. Renate D. Kimbrough and others, and certain of the hepatic lesions found by these investigators were described as hepatocellular carcinomas, i.e., in 26 of 184 female Sherman rats killed 2 months after approximately 21 months of feeding exposure at 100 ppm Aroclor 1260.

Monsanto brought the CDC findings to the attention of its toxicology consultant, Industrial Bio-Test Laboratories, Inc. (represented at the meeting by Dr. J. C. Calandra, President), which then undertook a reassessment of its own PCB toxicologic findings. Dr. Calandra stated that Industrial Bio-Test Laboratories, Inc. (IBL) reviewed its original histopathological preparations as well as some new ones (made by IBL's Drs. Gordon and Richter) from preserved materials, and found no reason to alter its original conclusions that none of the observed hepatic lesions were malignant. Dr. Calandra further observed that the U.S. Food and Drug Administration had indicated no disagreement with those conclusions, that Drs. Kimbrough and Gordon (both pathologists) had reviewed

the IBL materials together, and that IBL had submitted its materials for review by the Eppley Institute's Dr. Paur, who also concurred with IBL's conclusions. [Two observations are interjected here: (1) The IBL rat studies were conducted with a considerably smaller initial set of Charles River rats (both sexes), and were designed for serial (3,6,12,24 months) sacrifice, so that relatively few animals (27 for Aroclor 1260) were available for sacrifice after full-term feeding, with concomitantly less likelihood that a lesion whose incidence was only 26/184 (14%), possibly only in females, would be observed. (2) According to the written report submitted by Dr. Calandra, Dr. Paur seemed, to this reader, to equivocate as to the pathologic description of the disputed lesions, and it seemed clear that the lesions described in the CDC study as hepatocellular carcinomas were different from other observed lesions that more closely resemble some of those observed in the Monsanto-sponsored studies.]

Dr. Calandra noted that two traditionally distinguishing features of carcinomas were not characterized in the lesions so described in the CDC report, i.e., invasion and metastasis. He noted further that there are recognized authorities who maintain that "hyperplastic nodules," etc., represent adaptive responses to PCBs that might even, in some cases, be reversible. Indeed, Kimbrough, et al., in their report (Induction of Liver Tumors in Rats by Polychlorinated Biphenyl Aroclor 1260., submitted to J. National Cancer Institute), stated that" ...No definite intravascular invasion was noted and no metastases were found." Dr. Kimbrough added that known carcinogens, e.g., Butter Yellow, 2-AAF, elicit identical responses to those seen in the Aroclor 1260 study.

Dr. Finklea interjected that, in his opinion, the human health significance of the findings, regardless of what the lesions ultimately are called, should be the primary concern of NIOSH. He, having to attend to other matters, then charged Dr. Fairchild with the conduct of the remainder of the meeting.

Mr. Brown announced that NIOSH (DFSCI) program plans call for a retrospective mortality study (and 2-year follow-up) to be conducted among workers in some PCB-using industry, and that it hopefully would begin in calendar 1975. [A NIOSH team visited the Westinghouse capacitor plant in Bloomington, Indiana on December 4, 1975, to conduct a preliminary investigation of plant personnel records.]

Dr. Shapiro elicited agreement from Dr. Calandra that, in view of the accumulated data on Aroclor 1260-induced pathologies, that product deserves "suspect carcinogen" status.

The meeting adjourned shortly thereafter, the Monsanto team previously having arranged to make similar presentations to CEQ, NCI, FDA, and EPA, on November 13th and 14th. [Drs. Rhoden and Shapiro attended the NCI meeting on November 14th. The NCI representatives were Drs. Peters, Kraybill, and

Flamm. It was agreed that the Kimbrough-Calandra differences warranted consideration by the DHEW Committee to Coordinate Toxicology and Related Programs, and that steps would be taken to bring the matter to that body's early attention.]

Richard A. Rhoden

Attachment

cc: D. Brown
J. Calandra
K. Easley
E. Fairchild
J. Finklea
E. Harris
R. Kimbrough
J. May
S. Morris
L. Murthy
A. Russo