**Monsanto**

FROM (NAME, LOCATION, PHONE) J. Zack Dept. of Medicine & Environmental Health -A2SD-4-5410

DATE January 11, 1979

SUBJECT PCB Epidemiology Study

TO Clarence F. Buckley-1740

cc F. C. Meyer-A2SA

Enclosed is a draft report on the PCB epidemiology study for your review. I would appreciate your looking over the section on page 4 dealing with PCB exposure levels. I want to make sure that I have not misstated the information obtained by Dr. Meyer and David Musch last summer on PCB exposure levels.

Thank you.

Judy Zack

Judy Zack

mo
Enc.

MONS 001555

IN 10M (REV. 2/79)

A Brief Mortality Study of

Workers Exposed to Polychlorinated Biphenyls

Background

The term "polychlorinated biphenyls" (PCB's) describes a group of mixed chlorinated biphenyls which vary in consistency from oils to sticky resins in direct relation to the degree of chlorination of the phenyl rings. Mixtures of PCB's have been in use since 1929 for various periods in transformers, capacitors, lubricants, "carbonless" duplicating paper, fireproof sealants, plastics, adhesives, and other products. Their electrical, chemical, and biological stability contributed significantly to their value for many industrial uses. These properties also made PCB residuals more persistent in the environment, as technical developments in gas chromatography and mass spectrometry for detection of trace quantities began to demonstrate in the mid-1960's [1,2,3].

While acute biological effects from relatively high PCB exposure levels are known and can be avoided by appropriate control measures, attention has been focused on the chronic effects resulting from long-term low levels of exposure to PCB's. In extensive two-year animal chronic oral toxicity tests of AROCLOR 1242, 1254, and 1260 (42, 54, and 60% chlorinated PCB products) conducted for the Monsanto Company, no carcinogenic effects were observed in the rats and beagles tested. Hyperplasia, hypertrophy, and several benign tumors were observed in the livers of the rats, but there was no evidence of malignancy in any of the test animals.

Other investigators have reported liver tissue effects ranging from hyperplasia to well-differentiated hepatocellular carcinomas in rats or mice fed with various PCB-containing diets. For example, Kimbrough, et al fed rats with AROCLOR 1254 and 1260, and observed hypertrophy, lipid accumulation, and adenofibrosus, but no malignancies, in the livers of the test animals.[4] In a later experiment, the same investigator fed Sherman rats 100 ppm of AROCLOR 1260 for 21 months and reported the induction of hepatocellular carcinomas and neoplastic nodules in the test animals' livers whereas, control animals showed little or no effects.[5]

A 1978 National Cancer Institute report of carcinogenicity tests on AROCLOR 1254 concluded that the substance was not carcinogenic in Fischer 344 rats under the conditions of the bioassay. Although the incidences of hepatocellular tumors and gastrointestinal carcinomas were not statistically significant, an excess incidence of hepatocellular proliferative lesions (hyperplastic nodules) appeared to be related to administration of the chemical.[6]

The first report of possible PCB effects on humans occurred in 1968, when over 1200 Japanese were involved in an epidemic of Yusho, an acne-like skin disease which was later traced to the consumption of a rice-oil contaminated with PCB's from a leaking heat-exchange unit. However, it was later shown that the rice oil also contained a high

level of polychlorinated dibenzofurans (PCDF's), possibly due to the high temperaturc of the heat exchange unit. The highly toxic PCDF's were shown to be relatively more concentrated in the liver than PCB's, and these findings clearly indicated the necessity to pay greater attention to PCDF's for clarification of the nature of Yusho.[7]

There have been very few epidemiological studies of human populations exposed to low levels of PCB's over a long period of time. The Mobil Oil Company released a study in 1976 conducted by Bahn[8] in which a significant number of melanomas and pancreatic cancers were found in PCB-exposed plant workers and research personnel. However, the study has been severely criticized due to deficiencies in the identification of the study cohort, failure to identify other potentially carcinogenic chemical exposures, and other problems which left the results of the Mobil study highly in doubt.[9]

Shortly after the Mobil study, a preliminary study of PCB-exposed workers was begun at the Monsanto Company, focused on workers at the W.G. Krummrich plant in Sauget, Illinois, where PCB's were manufactured from 1936 until production ceased in 1977. This preliminary study failed to support the Mobil study results. No melanomas or pancreatic cancers were found but an apparent excess occurrence of lung-cancer deaths was found in the incomplete study cohort. However, due to the preliminary nature of the study, no minimum time of exposure criteria was applied for the workers and no follow-up was done on over 30% of the study cohort who had left the company. Further definition of the exposed population was needed.

The study reported here is an attempt to complete the epidemiological evaluation of the worker population of Monsanto's W.G. Krummrich plant, and evaluate the chronic effects of PCB-exposure on humans. Thus, the mortality experience of workers exposed to PCB's in their manufacture has been followed and evaluated under accepted epidemiology criteria for follow-up of all active, retired and terminated employees with exposures to PCB's for at least 6 months.