

Monsanto

FROM (NAME & LOCATION)

W. R. Richard - Research Center

DATE

April 4, 1969

CC:

SUBJECT

REFERENCE

TO

M. Farrar

E. Wheeler

~~H. Bergen/D. Olson~~ / Return H. Bergen

E. Kelly

J. Springate/W. Shalk/W. Waychoff

R. Keller

E. Tucker

Enclosed are notes by Dr. Alan Mehler
on chlorinated biphenyl.

W. R. Richard

ms

Att.

DSW 201051

March 25, 1969
Alan H. Mehler

COMMENTS ON AROCLOR

There are several independent aspects of the problem, which should be considered separately.

I. Are the substances detected in nature driven from Aroclor?

- A. Are they really PCB? Evidence cited indicated that they are. A question remains about relative proportions of biphenyls with various amounts of chlorine; the compounds identified do not include the lower members, which are major components. Therefore, it must be determined whether the compounds with less chlorine escape detection, are degraded in nature or fail to accumulate in animals.
- B. Are there "natural" sources of PCB? The proposals to look for PCB in potential sites of production are long shots but they are not difficult or expensive and should be given high priority. Examples include automobile exhaust and other chlorinated hydrocarbons, (e.g., insecticides) which conceivably could contain trace contaminants of PCB.
- C. What is the source of the PCB reported in animal bodies? This question is somewhat dependent upon the answer to IA and IB. A partial answer will also come from projected analyses of water and stream bottoms downstream from the manufacturing plant. The difference in geographical distribution between the users of Aroclors and the affected animals is evidence that the PCB detected in carcasses does not originate in Aroclor. I doubt, however, that a completely convincing case can be built on this logic. A possibility to be considered seriously is the production of PCB biologically from other halogenated hydrocarbons, such as DDT or lindane.

II. Is Aroclor toxic?

- A. Questions of general pathology are not acute at this time and do not seem to require major effort or attention.
- B. Reproduction in birds has been implicated in the literature. This is the area of greatest concern and should be attacked most vigorously. The general approach of using chickens and ducks has several advantages that make it practical. If effects of Aroclors on any component of the reproductive process are found, these organisms should be studied further to learn more about the basis for the effect. This opinion is not based on a general scientific curiosity about unfamiliar phenomena but on the possibility of finding means to counter the effect or to find a valid method for screening individual Aroclors or other materials to find safe substances for various uses. If, however, the results with chickens and ducks are negative or inconclusive, consideration should be given to conducting analyses on birds more closely resembling the species whose survival has been questioned. It may be difficult to use hawks but it must be considered that hormonal control of reproduction can have great quantitative differences and that the interpretations of Risebrough et al., may be correct even if chickens and ducks do not give positive results. For example, PCB could induce a microsomal oxidase that could form polar estrogens but in vivo the chicken could still respond normally to the amount of estrogen that escapes oxidation, whereas in a falcon the

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increased oxidation of hormone could reduce the effective amount below a critical level. This example uses an oversimplification - the actual interplay of many hormones in vivo gives even more opportunity for differences among species to be critical.

- C. What is the significance of induction of microsomal enzymes? A reasonable argument links an increase in one or more enzymes that can hydroxylate steroids with damage to avian reproduction. This correlation should be tested.
1. A dose-response curve for enzyme induction can be determined easily and quickly. If the relatively large doses reported to induce increased enzyme levels in pigeons are necessary to produce a biological response, the significance of the phenomenon can be discounted. However, if doses at levels comparable to those found in the prey of falcons (1-10 ppb) produce responses, the suspected relationship will be strengthened and a more complete analysis may be required to determine exactly what causes the induction and whether there is a positive correlation between enzyme level of effects on reproduction.
 2. Studies on doses should be concerned with concentration build-up in animals. That is, a small amount of PCB in the diet may not give a response in the time that a larger amount is effective. However, if PCB is retained (dissolved in lipid depots, for example), eventually the concentration in the animals may become sufficient to cause metabolic disturbances. In any studies along these lines enough animals should be used so that entire carcasses can be analyzed at intervals during and after extended periods of feeding to determine the rate of accumulation and elimination of PCB.
- D. Do Aroclors have significant effects on mammals and other animals? There is no evidence at this time that the amounts to which humans or other mammals might be exposed cause any pathological changes. However, the present social and political climate seems to make it expedient to obtain conventional data to establish safe limits of exposure. Similarly, the potential danger to fish seems to be a question only because PCB has been detected in water and this does not seem to be very urgent. However, if fish studies are done, it would be desirable to use impregnated food or coated particles to give a realistic test of toxicity at levels greatly exceeding the solubility in water. Adsorption on silt seems to be a sufficiently realistic possibility to warrant testing at high levels.
- III. Is Aroclor metabolized? This is not a major question at this time. It may become of some significance eventually if it is necessary to explain a distribution of components in nature different from the composition of Aroclors. It may also be relevant to elimination of some or all of the components from animal bodies. It may be found that ability to induce enzymes is related to ability to be metabolized but this would be a subject for investigation only if earlier investigations indicated relevance. Adequate methods for determining whether PCB's are metabolized may not exist at this time. The amounts to be detected may be small even for radio-isotope methods.
- IV. Is Aroclor degraded in nature? This is a long-term question that does not seem to require a major effort at this time. It is of importance only because a general question of toxicity has been raised and ultimately it may be necessary to demonstrate that toxic components do not accumulate forever.

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