Monsanto

FROM (NAME & LOCATION) Dept. of Medicine & Environmental Health St. Louis - General Offices

DATE 4/18/78

CC:

SUBJECT

REFERENCE

TO M. C. Throdahl
D1D

Enclosed is the information you requested on PCB's. In addition, I have taken the liberty of including a document prepared by Barney Wander encompassing many other questions about PCB's. In addition, I have also included a summary on toxicity and environmental effects of PCB's prepared by George Levinskas. You may already have copies of both of these but while preparing this report, I felt it might be best to answer as many peripheral questions as possible at the same time.

Ernest Tillman, M. D.

ET/mjb

MONS 213452

Monsanto

FROM (NAME & LOCATION) Dept. of Medicine & Environmental Health St. Louis - General Offices

DATE 4/18/78 CC

SUBJECT Health Effects of PCB's

REFERENCE

TO Monte C. Throdahl
D1D

PCB's are oily liquids which are poorly absorbed from the gut. Therefore, a single dose ingested would be largely excreted and minimal acute toxic effects would be expected. About all we would expect to see would be nausea, possible vomiting and diarrhea. The effects would be similar to ingesting a large dose of mineral oil. No other acute toxic effects resulting from PCB ingestion are known.

Repeated ingestion of small quantities of PCB's is an entirely different matter. This was the case in the Yusho incident. Here, small quantities of the material would be absorbed and stored in the body and chronic toxic effects have been identified in this situation. In Yusho there was repeated ingestion and the symptoms and signs resulting from this began to occur in 1968. The objective findings resulting from this include the following:

acne-like skin eruptions on the face, the buttocks and in areas where two skin surfaces are in contact.

skin pigmentation

swelling of the eyelids

inhibition of growth and abnormal teeth in children

smaller than average infants at birth

total body pigmentation at birth

bronchitis

bursitis

a decrease in triglyceride levels in females

anemia

increased lymphocytes in the white blood cell count

decreased blood levels of albumen

slowed electrical conduction in sensory nerves

In addition, the persons exposed complained of the following symptoms:

fatigue
headache
abdominal pain
numbness and pain in the extremities
cough and sputum
menstrual disturbances

As analytical methods improved, after the onset of this problem in Yusho, it was found that the cooking oil in addition to containing PCB's also contained polychlorinated dibenzofurans. With a second contaminant identified, a question as to which material actually caused the symptoms and signs exist. We do not know the answer to this question and I doubt that it would be possible to ever make a distinct determination.

Ernest Tillman M. D.

ET/mjb

Toxicity and Environmental Effects of Commercial PCBs

Introduction

Polychlorinated biphenyls (PCBs) are not a single chemical entity. They are produced by chlorinating biphenyl to acheive a final product with specified properties. These products, sold under the trade name AROCLOR by Monsanto, are mixtures of chlorine-containing biphenyls with different numbers and positions of the chlorine substituents.

Over the years, a series of investigations have been conducted to assess potential health and environmental hazards of PCBs. The 3 predominant commercial mixtures (AROCLORS 1242, 1254 and 1260) have been studied most intensively. Toxicity tests performed on these 3 commercial mixtures were typical in scope of those designed for the evaluation and establishment of the safety of direct and indirect food additives.

It may be noted that AROCLOR 1260 no longer is produced in this country since it does not meet the physical specifications for its restricted uses.

Conclusions Based on Monsanto Studies

1) As a class, the AROCLORS are relatively harmless materials for routine industrial handling under ambient conditions.

2) Threshold Limit Values of 1 mg/m^3 and 0.5 mg/m^3 have been established for materials containing average chlorine values of 42% and 54%, respectively, of the available sites.

3) The no-effect level for these materials in chronic

rat and dog feeding studies is about 10 ppm in the diet. No hepatocellular carcinomas were present.

4) The no-effect level on rat reproduction is between 1 and 10 ppm in the diet since higher levels result in low mating indices.

5) No teratogenic or mutagenic effects were observed in studies with rats and mice.

6) In chicken reproduction and teratology studies, AROCLOR 1242, which produced the most severe effects, had a no-effect level of 2-4 ppm in the diet.

7) Acute toxicity to fish varies from less than 1 ppm to greater than 100 ppm depending on the specific AROCLOR and species of fish tested.

8) PCBs containing 3 or less chlorine substituents per molecule are reasonably biodegradable.

Summary of Monsanto's Long-term Toxicity Studies on Commercial PCBs.

These tests consisted of 2-year (lifetime) feeding to rats, 2-year feeding to dogs, 3-generation rat reproduction studies with 2 litters cast per generation, rat teratology studies and dominant lethal mutagenic studies in mice. Toxicity and reproduction studies in chickens were performed to evaluate possible untoward effects in birds such as decreases in eggshell thickness. In addition, biodegradation and tissue accumulation studies have been conducted.

The highest dietary level (100 ppm) in the lifetime rat feeding studies produced a weight depression at 24 months in females fed AROCLOR 1254 and liver weight increases in all

groups except males fed AROCLOR 1242. As with other halogenated hydrocarbons, the important histopathologic changes were present in the livers of animals sacrificed at the end of the study. These consisted of hepatocellular alterations such as focal hypertrophy, cytoplasmic lipid changes and in some animals from the 100 ppm groups, hepatomas or cholangiohepatomas. No evidence of hepatocellular carcinogenicity of the AROCLORS was found.

In the dog 2-year studies, some slight decreases in body weight gain were noted. At the highest feeding level (100 ppm), AROCLOR 1260 produced an increase in serum alkaline phosphatase activity and liver weights without concomitant histopathologic changes. However, there was evidence of gastrointestinal inflammatory lesions and ulcerations which appear to be similar to those found by Allen in rhesus monkeys fed AROCLOR 1248. (AROCLOR 1248 was an experimental product which never was commercialized.)

In the rat reproduction studies, none of the AROCLORS produced adverse effects in the 2 litters of the first generation. In the second and third generations, there was a reduction in the mating index at the 2 highest feeding levels (10 ppm and 100 ppm). The ability of females to conceive, carry the delivery process to parturition, and to successfully nourish the young was not affected by the 3 AROCLORS. No changes were produced in the reproductive tracts of either male or female rats by any of the 3 AROCLORS.

There was no evidence of teratogenic or mutagenic changes with any of the PCBs at maximally tolerated dose levels in

rats and mice.

In the chicken toxicity/reproduction study, AROCLOR 1260 was without effect at all test levels. AROCLORS 1242 and 1254 at 100 ppm in the diet decreased egg hatchability. In fact, poor hatchability of eggs was found from hens fed 8 ppm of AROCLOR 1242. In addition, AROCLOR 1242 at 10 and 100 ppm and AROCLOR 1254 at 100 ppm were associated with reduced eggshell thickness. Chick viability was affected by both substances at a dietary level of 10 ppm.

Biodegradation studies were conducted using semi-continuous activated sludge systems and tissues of rats fed PCBs were analyzed to measure accumulation and retention of these materials. These factors are influenced by the number and position of the chlorine substituents. Higher chlorine-containing members are more resistant to biodegradation and they accumulate more readily and are less readily metabolized and/or excreted from lipoid tissue in animals. PCBs containing 3 or less chlorine substituents per molecule are reasonably biodegradable.

Comments

The conclusion that "No evidence of hepatocellular carcinogenicity of the AROCLORS was found" in the 2-year rat feeding study was reached only after extensive re-evaluation of the original liver slides as well as additional liver sections from all of the animals after the Kimbrough results on AROCLOR 1260 became known to us. The slides were read

independently by Dr. D. Gordon of Industrial BIO-TEST Laboratories, Professor W. Richter of the University of Chicago, and by Professor P. Pour of the Eppley Institute for Research in Cancer. In addition, Dr. Pour evaluated the Kimbrough slides and does not agree with the reported findings.

Barsotti and Allen have reported that 2.5 ppm of AROCLOR 1248 in the diet of rhesus monkeys adversely affected reproduction. This approximates a dosage of 100 µg/kg/day. It is higher than the safe human intake (1 µg/kg/day) estimated by FDA from human data when it promulgated its tolerances for PCBs in food.

OJL

3/1/78

PCB

1. Q. Do PCBs cause cancer?

   A. There are allegations that PCBs cause cancer in man, but we have no evidence to confirm this. (Toxicologist George Levinskas says that even if PCBs do cause cancer, it won't happen until after the liver has been virtually destroyed.)

2. Q. What did PCBs do to che workers who manufactured the material?

   A. Monsanto has had virtually no problems.
   Two incidents of chloro-acne among workera -- at a Swann Corporation plant in the 1930s and one on ships during World War II -- were both traced to impurities, and not to the PCBs themselves.

   Preaently, Monsanto is conducting an epidemiological study of 300 workers who were employed in the manufacture of PCBs at one time or another. We expect to have preliminary results within 6 months.

3. Q. How did the information about PCB skin problems among Swann employees become public in the 1930s?

   A. Two dermatologiats from Atlanta, Ga., who served as consultants during the plant investigation of employee skin problems, published their findings in "The Archivea of Dermatology and Syphilogy" (Vol. 33, pg. 1027; 1936).

4. Q. What kind of testing has Monsanto done on PCBs?
   What tests are underway at this time?

   A. In the past, when questions arose about worker safety, Monsanto conducted a number of subacute inhalation studies with rats. We used the data from these tests to set the threshold exposure for our workers.

   In the late 1960s, we initiated an extended series of studies on rats, dogs and chickens, and made our information available to the regulatory agencies.

   Because of growing evidence independent of these studies that PCBs were remaining in the environment, Monsanto took action in 1970 and 1971 to atop manufacture and sale of PCBs to uses in open applications. Results of our animal studies were later used by FDA to set acceptable levels for human ingestion.

   At present, Monsanto is sponaoring a long-term study of the effect of PCBs on monkeys -- looking at health and alao reproductive effecta.

5. Q. What do PCBs actually do to the environment?

   A. The original advantage of PCBs over other electrical insulating material has turned out to be the cause of present environmental problems. A heavy, oily liquid, PCB is almost inert, and will burn only under extremely high temperatures. The material is not soluble in water, which is why it persists in our waterways; it is soluble in fat, which is why fish in PCB-contaminated rivers and lakes have measurable amounts of PCB in their fatty tisaues.

   The FDA has set what it believed were safe limits for human ingestion of PCB over long periods. This amount -- 1 microgram of PCB per kilogram of body weight per day -- was then used to set acceptable tolerances in foods. The limit in fish, for example, is 5 ppm. The FDA monitors the levels of PCB in foods on a regular basis.

6. Q. When did Monsanto begin manufacturing PCBs? Why?

   A. PCBs were manufactured by Swann Corporation (purchased by Monsanto in 1935) in 1929 in response to the electrical industry's need for an explosion-proof insulating fluid for transformers. PCBs remained the "Cadillac" of the insulating materials, used in about 15 percent of electrical applications where special safety needs existed. Over the years, other applications were found for PCBs in heat-transfer systems, sealants, adhesives and printing inks.

7. Q. When did Monsanto stop making PCBs?

   A. In 1971 after scientific investigations had confirmed the presence of PCBs in the U.S. environment, Monsanto terminated sales of PCB to all non-electrical (open) applications. At the same time, we began publicizing potential environmental problems and the need to prevent entry of PCBs into the environment. /Note: the Anniston, Ala., PCB facility was shut down at that time. Presence (or absence) of this facility has not been emphasized in the press./ In July, 1977, the company ceased manufacturing PCBs altogether with all inventory distributed by October 31, 1977. Monsanto could not responsibly stop manufacture earlier. The product was in demand by our customers for a material which would prevent the possibility of electrical fires in apartment buildings and other high-population areas. Mineral oils -- used in most other applications -- have a stability problem that makes them potentially hazardous. In fact, fire insurance, building and electrical codes in many parts of the country have traditionally required use of PCBs in high density population applications. Monsanto's timetable for withdrawal from the PCB business had the endorsement of the federal government; in 1975 then-EPA Administrator Russell Train said he would not ask Monsanto to stop PCB production because that would shut down the electrical power industry and railroads in short order.

8. Q. Does anyone else still manufacture PCBs?

   A. PCBs are still being manufactured in Germany, France, Spain, Italy and certain eastern European countries. Monsanto ceased manufacturing PCBs in Newport, South Wales. Theoretically, the material could be imported into the U.S. market until 1/1/79 under TSCA.

9. Q. What is Monsanto doing to clean up the environment?

   A. There is no known technology that will guarantee 100% collection and disposal of PCBs from mud and silt bottoms of waterways. Dredging, for instance, doesn't do much but recirculate PCBs which have settled into the bottom of the waterway.

   Right now, incineration is the best known technology for destroying PCBs. A leading incineration service is developing equipment that will shred a PCB capacitor and then incinerate the liquid in one operation. For several years, Monsanto operated a small incinerator at our Krummrich plant to help customers destroy PCB waste liquids; a rag or other material contaminated by PCBs could not be incinerated there. The incinerator is being dismantled since more effective incineration capacity is available elsewhere. The incinerator will be disposed of in an approved landfill for hazardous waste.

10. Q. What else is being done to get rid of PCBs?

   A. The Ontario Foundation in Canada, General Electric's Schenectady Lab and the Institute of Fermentation in Japan are attempting to develop bacteria which will break down PCBs.

   Also, in November, 1977, MIT reported a new method of destroying PCBs in water by using high-energy electrons.

11. Q. Are there any lawsuits pending against Monsanto for producing PCBs? For how much?

   A. A number of lawsuits, including several class actions, have been filed against Monsanto, alleging damages and claiming that Monsanto failed to warn of the alleged dangers of PCBs. Altogether, those suits seek more than $2 billion.

12. Q. Did Monsanto fail to warn of PCB dangers?

   A. Absolutely not. From the time PCBs were first identified by the Swedish scientist in 1966-67, Monsanto has played a major role in the resolution of this environmental matter. For example, in the 1967-70 period, Monsanto refined test procedures for determining the presence of PCBs. It undertook animal feeding studies. Monsanto has made every effort to keep its customers and the public current on developments in the PCB environmental concern.

13. Q. What about nursing babies? What is the problem of PCBs in mothers' milk?

    A. There have been reports that in a few instances PCBs had been detected in human breast milk. We do not believe, however, that this is a serious problem. The concern, of course, is that breast milk might constitute the bulk of an infant's diet.

14. Q. Where are the most serious PCB pollution problems?

    A. PCBs have been found most heavily in Lake Michigan and the Hudson River. They seem to be located in the vicinity of former industrial users of the material.

15. Q. Are you working with your former customers to do anything about the PCB problem?

    A. We have been working closely with former customers as they phase out of the PCB business. We keep close watch of studies underway seeking to deal with PCBs in the environment.

16. Q. What happened at Yusho, Japan?

    A. In 1968 there was accidental poisoning of an unknown number of people in Japan by Kanemi rice oil contaminated with PCBs. The disease is now called "Yusho" or "Yusho oil" disease after the principal location involved.

    Approximately 1,300 patients were treated because of actual exposure.

    An unknown number of children, born up to three years after their mothers' initial exposure, also showed symptoms of the disease.

    There is much dispute about the level of PCBs the people ingested, but it is probably in the 800-1,000 ppm range.