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S-8A

SUPPLEMENT 1

STATUS REPORT ON

THE CHEMISTRY AND TOXICOLOGY

OF POLYCHLORINATED BIPHENYLS (PCB)

OR AROCHLORS

DECEMBER 1970

Bureau of Foods
Food and Drug Administration
Public Health Service
Department of Health, Education and Welfare

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I. Introduction

Residues of polychlorinated biphenyls (PCB) were first identified by Jensen (1966), in fish from various Swedish waters and in an eagle, and have since been reported in fish, bird, and animal specimen from different parts of the world; (Holden 1966), (Holmes et al. 1967), (Holden and Marsden 1967), (Koeman et al. 1967), (Risebrough et al. 1968), (Koeman et al. 1969), (Anderson et al. 1969), (Presst et al. 1969), (Risebrough at al. 1969), (Jensen at al. 1969), and (Westöö et al. 1970). Biros at al. (1970) reported residues of PCB in human adipose tissue.

Interest in residues of PCB has been in two broad areas: (1) their potential for interference in the determination of residues of organochlorine pesticides, particularly DDT and its analogs; (2) their significance as residues in animal tissues and foods. The second area of interest includes toxicology, analytical determination, and source of entry into the environment.

PCB, tradename Aroclor, are produced in the United States at plants in Anniston, Alabama and Sauget, Illinois, (Risebrough and Brodine 1970) by the Monsanto Company. PCB are also manufactured by Prodelec in France (Phenochlor) and Bayer in Germany (Clophen). It is reported (Peakall and Lincer 1970) that other manufacturers are located in Japan and the Soviet Union.

Uses of Aroclors, chemistry of PCB, and occurrence of PCB residues in foods will be covered in Section I, Chemistry and Surveillance, of this report. Toxicology will be covered in Section II.

A good, current review on PCB has been published by Peakall and Lincer (1970).

Previous reports on the Chemistry and Toxicology of PCB were issued on April 28 and June 1, 1970.

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II. Chemistry and Surveillance

a. Manufacture and Use

A series of Aroclors comprised of chlorinated biphenyls, chlorinated terphenyls, and mixtures of these are produced. Each Aroclor is a mixture of a number of individual chlorinated biphenyls (1200 series), chlorinated terphenyls (5400 series), or a combination of chlorinated biphenyls and terphenyls (4400 series). The last two digits of the identifying number indicate weight per cent chlorine. Chlorine content of individual Aroclors varies from about 10-70% by weight and the physical properties vary with chlorine content. Those with low percentage of chlorine are fluid liquids; as per cent chlorine increases the products become more viscous or become solids. General physical properties of the Aroclors are given in Table 1 (Monsanto Company).

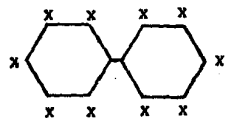
Aroclors have a variety of suggested uses (Monsanto Company). Although we do not have concrete information on specific applications, the more important seem to be in electrical capacitors and transformers, in heat transfer systems, as hydraulic fluids, flame retardants, plasticizers in chlorinated rubbers, and in caulking materials. Aroclors 1242, 1254, and 1260 account for the largest use (Papageorge 1970).

Aroclors have been included in certain pesticide products registered by the USDA Pesticide Regulations Division (PRD). The extent of use of formulations containing Aroclors is not known. PRD in PR Notice 70-25, October 29, 1970, stated that the use of PCB and polychlorinated terphenyls in economic poisons would be phased out over a six month period.

The Monsanto Company has stated in a letter to Congressman William F. Ryan of New York, that as of August 30, 1970, it would no longer sell PCB to customers for general plasticizer operations where end products cannot be controlled (Gustafson 1970). To our knowledge FDA has not validated this statement.

b. Properties and Analysis

PCB are not a single compound. The basic PCB structure is shown in Figure 1. Any or all positions marked X can be substituted by chlorine. A large number (approximately 200) of different compounds and isomeric configurations are possible.



MONS 051274

Figure 1. Basic Structure of PCB

PCB are stable, are not hydrolyzed by water, and are resistant to alkalis and acids. They are soluble in hydrocarbons and insoluble in water; exact figures are not available. Volatility is low and decreases with increasing chlorination. Experiments in Residue Chemistry Branch have shown, however, that lower chlorinated PCB (e.g., Aroclors 1221, 1232) readily volatilize from smooth surfaces at room temperature.

PCB are completely recovered and are detected by FDA methodology for multiple residues of organochlorine pesticides. That is, when a sample is examined for residues of organochlorine pesticides it is also being examined for residues of PCB. The sensitivity of electron capture gas chromatography to PCB is approximately one-tenth of its sensitivity to p,p'-DDT. For example, using FDA's standardized procedures, the limit of detectability for p,p'-DDT in butterfat is approximately 0.2 ppm, but for PCB it is approximately 2 ppm.

The presence of PCB in samples analyzed for organochlorine pesticides may complicate determination of the pesticides; this depends on the PCB/pesticide ratio and the pesticides in question. Similarly, the presence of organochlorine pesticides complicates the determination of PCB. A procedure is now available (Armour and Burke 1970) to separate PCB from organochlorine pesticides and permit separate determinations of the two groups of chemicals. If analyses are properly conducted, PCB interference with determination of pesticide residues is avoidable. Presence of PCB as a residue presents a difficult analytical problem; in the determination of pesticides and in the determination of PCB. Expertise and good judgement on the part of the analyst are necessary. FDA District chemists have been informed on the behavior of PCB in multi pesticide residue methods on the procedure to separate PCB from pesticides.

Determination of residues of PCB presents a problem in addition to separation from any pesticides present. Because the PCB (Aroclor) entering the environment is multi component, its composition is quite likely to be altered by effects of "weathering" and biological systems. Standards to exactly duplicate the residue composition for a comparative determination are not available. The current approach to PCB residue quantitation is to measure the residue versus a standard of the most similar Aroclor using gas chromatography with electron capture or halogen specific microcoulometric detection. Residue values less than 10 ppm should be rounded to the closest 0.1 ppm. Values 10 ppm and above should be rounded to the closest 1 ppm. At this time, we would expect interlaboratory reproducibility to be in the range of $\pm$10-20%.

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Chlorinated naphthalenes, tradename Halowax, Koppers Company, have suggested uses and properties similar to PCB. This group of chemicals is also recovered and detected by FDA methods for multiple residues of organochlorine pesticides. They also can be separated from pesticides by the same procedure used for separation of PCB (Armour and Burke 1971).

c. Residue Occurrence

As stated above, FDA methods for multiple residues of organochlorine pesticides also detect PCB. Therefore, every sample analyzed for organochlorine pesticide residues is also examined for PCB residues. In the examination for organochlorine pesticides, the limit of detectability for PCB in fatty foods is about 2 ppm and in non fatty foods about 0.3 ppm.

An addendum, issued November 10, 1970, to the current pesticide program calls attention to the PCB situation and directs Districts to make at least one (two in Atlanta and Minneapolis) "survey" of milk for residues of PCB. This program addendum lists manufactured dairy products, fish, animal feed, shell eggs, and any commodity potentially contaminated, as commodities for Districts to consider for survey. No guidelines have been given Districts on the course to be followed in the event PCB residues of a given level are found in a particular product. PCB are now given "visibility" in the pesticide program; however, the program addendum causes no significant change in surveillance coverage on this contaminant.

PCB residues have been quantitated and reported to Residue Chemistry Branch from mid 1969 until July 1970. Beginning July 1, PCB residue findings (code number 348) have been reported into the Program Orientated Data System (PODS). During the period July 1 - October 31, 1970, eleven Districts reported PCB residues in 205 samples. No residues of PCB were reported by Boston, Chicago, Dallas, Denver, and San Francisco. This should not be taken as an indication of absence of PCB in these areas. One hundred and twenty-one of these samples were fish of which 37 were marine species. Thirty-eight samples of milk, 26 samples of cheese, and 14 samples of eggs also were reported to contain PCB residues. Residues in cheese and eggs were at the limit of detectability of the method. Residues in milk ranged from the limit of detectability to 13 ppm (fat basis). Occurrence of residues in

fish appears to be widespread geographically. A cursory study of the levels reported in fish indicates that most residues are between 1 and 10 ppm. PCB residues in 23 samples of chubs from Lake Michigan ranged from 2.5 to 6.1 ppm and averaged 4.6 ppm. It appears that residue levels are related to the location of sampling and the species of fish (high or low fat). With the exception of PCB residues in waste potato products from four Idaho potato processors (discussed later), PCB residues have not been found in agricultural crops by FDA laboratories.

d. Source of Residues

We are not aware of adequate information on definite sources and routes of PCB entry into the environment and foods nor are we aware of concerted efforts to locate and eliminate the sources. As discussed above, residues of PCB have been found primarily in wildlife, especially fish and fish-eating birds. Residue findings, although widespread, appear to be associated to some extent with industrial locations. In addition to waste or loss from industries using PCB, it has been suggested that these chemicals may enter the environment via leaching from objects in waste disposal areas thus entering streams or may enter the atmosphere from incineration of waste. Examples below indicate some means by which PCB have or may have entered the environment or a food.

Duke et al. (1970), detected PCB (Aroclor 1254) in the biota, sediment, and water of estuarine areas near Pensacola, Florida. One source of the Aroclor was determined to be the outfall of a local industry on the Escambia River. The Aroclor reportedly entered the industrial effluent through accidental leakage of a heat exchange fluid (Duke, 1970).

Baltimore District found that waste electrical insulator fluid containing PCB was used as solvent in herbicide treatment of power right-of-ways near Martinsburg, W. Va. This was presumed to be the source of PCB residues (up to 13 ppm) previously found in milk from several dairies in that area. We are not aware of what steps, if any, were taken to prevent this practice by this power company or by other power companies.

Atlanta District reported residues of PCB as high as 811 ppm in catfish from water near Anniston, Alabama. We can only speculate that the Anniston Monsanto Company PCB manufacturing

plant was somehow related to this residue. Eight additional samples of fish from different Alabama waters contained residues of PCB from 35-277 ppm. These findings were relayed by Atlanta District to the Alabama State Department of Conservation. Eiduson (CF-30) to Fischbach memorandum of August 25, 1970, indicated that BF-300 would advise as to how Alabama should approach the problem. We are not aware if the source of this PCB contamination has been found and/or eliminated.

Atlanta District also reported finding PCB residues in bread wrappers. Eiduson (CF-30 to MacMillin (ATL-DO) memorandum of September 9, 1970, advised Atlanta on follow-up procedure. We do not know how this matter, including its relationship to food additive regulations, has been disposed of.

PCB have been found by both FDA and State laboratories in certain preparations used for treatment of silos. There appears to be a relationship between cows fed from treated silos and residues of PCB in their milk. It is this situation which prompted the surveys of milk required by the addendum on PCB to the pesticide program. It is our understanding that Cincinnati District is assisting the State of Ohio in monitoring analysis of PCB contaminated milk.

In February 1970, Denver District found PCB in potato waste from four Idaho potato processers. Seattle District began follow-up sampling in August 1970. Reports to date from Seattle indicate only that PCB residues have been found in certain samples taken at four of eleven firms investigated. This matter is of interest for at least three reasons: (1) the waste product is likely used as animal feed and if contaminated would result in residues in meat or milk; (2) it is not known whether human food products produced at these locations also contain residues; (3) this is the first reported instance of an FDA labotatory detecting residues of PCB in an agricultural crop.

e. Chemistry and Surveillance Needs

A better knowledge of the accuracy and precision of the current approach to quantitation of PCB residues is needed. Residue Chemistry Branch is evaluating the use of the electron capture and halogen specific microcoulometric gas chromatographic in this measurement. Results from analysis of the current inter District

pesticide quality assurance sample, fish containing added pesticides and an Aroclor, should provide useful information on PCB determination. If results of these efforts are good, the method for determination of residues of PCB should be subjected to collaborative study with the objective of obtaining AOAC official status. As more information on the composition of residues of PCB becomes available, the development of a special technique for residue quantitation may be desirable.

Research is necessary to identify the primary constituents of residues of PCB. Attention should be directed to fish since this is the food in which these residues are prevalent. Knowledge of the important components of the residue is of concern in both the measurement of the residue and evaluation of its hazard to health.

Much needs to be known about sources of entry of PCB into the environment. A greater effort should be made to establish sources of entry and if sources of this pollutant are established, they should be eliminated. It would seem that timely and well planned follow through by FDA Districts on their findings, particularly those which are unusual, would be valuable in this regard. At this point, we are not assured that our current effort on PCB surveillance is offering the maximum benefit.

III. TOXICOLOGY

Despite the presence of PCBs in our environment in such quantity and in such conditions as to cause residues in food, the toxicology of these substances remains poorly defined as compared to that of the chlorinated phydrocarbon pesticides. Acne-like lesions have been reported to occur following industrial uses of the polychlorinated biphenyls (Schwartz (1936); Meigs, et al. (1954)). More recently an extensive poisoning among the general population of Western Japan resulted from the ingestion of rice bran oil contaminated with chlorinated biphenyl compound (Kuratsume, M., et al (1969)). However, these observations have not produced sufficient interest to stimulate satisfactory animal studies. Early animal studies of an acute or subacute nature were done on compounds of undefined specifications or in mixtures. The following summary brings the data on toxicology up to date.

a. Acute Studies

Early studies indicated that the acute lethal dose of chlorinated biphenyls was relatively low. Smyth and Smyth (1931) found that a chlorinated biphenyl was nontoxic when administered orally to guinea pigs and rabbits in doses of 4 gm/kg. Drinker, et al. (1937) reported that 0.05 gm of a chlorinated biphenyl fed to rats over a period of 6 days caused liver injury. These authors, likewise, found that hepatoxic action resulted in rats from inhalation of chlorinated biphenyls. Miller (1944) found that 2 oral doses of 69 mg of a 42% chlorinated biphenyl a week apart were fatal to guinea pigs and caused marked liver changes.

Studies in the FDA Laboratories have shown that the oral LD_{50} of Aroclor 1254 was 5 gm/kg in female rats and considerably higher for males. That for Aroclor 1260 was 10 gm/kg. Consulting Laboratories for the Monsanto Chemical Company reported the oral LD_{50} in rats for Aroclor 1254 and 1260 to be in the neighborhood of 10 gm/kg. The oral LD_{50} of DDT for female rats is 118 mg/kg (Hayes (1967).

Japanese workers have reported the oral LD_{50} of an undefined PCB as approximately 2 gm/kg in mice (Tanaka, et al. (1969)).

Tucker (1970) found that a single oral dose of 500 mg/kg Aroclor 1254 caused regular egg laying of Japanese quail to turn first to scattered egg production and then to stop completely for a week. The scattered eggs had shells 9% thinner than normal, but thickness returned to control values when regular laying was resumed. Mallard ducks dosed with 1000 mg/kg of the Aroclor laid one or no eggs before stopping for 1 - 2 weeks. The few eggs laid after the single large dose of Aroclor had shells 18% thinner than normal controls.

McLaughlin, et al. (1963) reported that 25 mg Aroclor 1242 injected into the yolk sac of hen eggs caused 100% mortality and 10 mg caused 95% mortality from 20 eggs. One chick hatched but died 2 days later. Some embryos, which were examined after they died, showed beak deformities, edema and growth retardation. In additional studies, Verrett and Associates have tested Aroclors 1221, 1232, 1242, 1254, 1268, 2565, and 5460 by injections into the air cells or yolk sacs of fertilized eggs. In general the lethal effects of the Aroclors decreased with increase in the chlorine content. All compounds produced some type of terata. Beak defects, cleft pellets, abnormal eyes, edema, deformed legs, and unsymmetrical development of brain hemispheres occurred in various degrees; however, with the limited number of observations no correlation of these deformities could be made with chlorine content of the PCBs.

Walker (1970) found that in 8°C spring water the 96 hr TL 50 value for Aroclor 1221 (tolerance limit at which 50% of the fish survive 96 hours exposure) in cutthroat trout was 1.2 mg/l and for Aroclor 1260 it was 60.9 mg/l. For channel catfish in 18°C water similar TL 50 value were 7.0 mg/l for Aroclor 1254 and slightly less for 1248. Tests with Aroclors 1254 and 1248 with bluegills gave 96-hour TL 50 values of 2.7 and 0.3 mg/l, respectively. In general, the data indicated that the toxicity of the Aroclors to fish was inversely proportional to the percentage chlorination and directly related to their solubilities.

In studies with fruit and house flies, Lichtensten, et al. (1969) found that the Aroclors were 40-300 times less toxic than DDT. However, these authors reported that an interaction occurred between each of 11 different Aroclors and dieldrin or DDT in which the toxicities of the pesticides were significantly increased. The toxicity of the PCBs to the flies decreased as the chlorine control increased.

In behavioral and physiological studies using single doses of Aroclors 1254 and 1260 in mice (1 and 10 mg/kg, p.o.), it has been found in FDA Laboratories that (1) anticonvulsant properties were exhibited with respect to maximum electroshock seizure (i.e. increased ratio of tonic flexion/tonic extension and increased duration of clonus); (2) Aroclor administration prolonged the latency of mice to enter a shock-stress chamber. All of these effects are in direct contrast to those noted when DDT was given.

b. Short-term Studies

The experiments of Bennett, et al. (1938) showed that an aroclor containing 65% chlorine was highly toxic and lethal when fed to rats at a dosage level of 300 mg/day for 6 days. At a dosage level of 50 mg/day some animals survived for 6 months; however, all animals had enlarged and damaged livers. In Food Additive Petition, 8B-2106 a subacute study in rats was reported in support for the use of Aroclor 5460 as a plasticizer component of adhesive formulations. This Aroclor is a chlorinated terphenyl with less than 0.05% biphenyls. Rats were fed diets containing 100, 300, or 1,000 ppm for 90 days. Growth depression and increase in liver size occurred at the 1000 ppm dosage. The "no effect" level was 100 ppm with only a slight increase in liver to body weight ratio of males in the 300 ppm group.

In a preliminary study at FDA, groups of 6 rats were fed diets containing Aroclor 1254 or 1260 at levels of 500, 1000, or 2000 ppm for 7 weeks. Surviving animals were sacrificed at the end of this period. At the dietary level of 2,000 ppm, none survived. At the dietary level of 1,000 ppm, one of the 6 fed Aroclor 1254 and one of those fed Aroclor 1260 survived. All rats survived on the 500 ppm diet. Liver enlargement occurred in the survivors at all dosage levels.

A subacute feeding study in rats lasting up to 90-days and including sacrifices at 5, 15, 30, 60, and 90 days has been conducted at FDA on Aroclors 1254 and 1260. Dosage levels were 25, 75, 150, 300, and 500 ppm. Liver weight to body weight ratios increased at all levels. Also, there were dose-related increases in liver aniline hydroxylase and nitroreductase activity at all levels. The magnitude of the increases was approximately the same at all time intervals for both aroclors. In contrast to many chlorinated hydrocarbon pesticides, these aroclors did not stimulate liver aliesterase activity. Examination of some of the livers by light microscopy gave equivocal results and the tissues are being examined by electron microscopy.

Nishizumi (1970) gave groups of 30 female mice a dosage level of 0.2 ml rice bran oil containing chlorinated biphenyl (48% chlorine) at 1600 ppm or a 0.5% PCB in olive oil by stomach tube each day for 4 to 26 weeks. Marked liver enlargement occurred. Light microscopy revealed only slight liver changes, however, electron microscopy revealed marked alterations in the liver cells. A similar study with eight monkeys given PCB in dosage levels of 1.4 to 16 mg/day in their diet for 40 to 48 days showed liver cell enlargement and fatty degeneration. The outstanding abnormality reported from the administration of PCB to both mice and monkey was an increase in the smooth endoplasmic reticulum in the liver cells.

Street and coworkers (1969) fed diets containing 50 to 100 ppm aroclors ranging in chlorine content from 31% to 68% to rats for 15 days and studies their effects on sleeping time induced by hexobarbital, in vitro rates of aniline hydroxylation and demethylation of p-nitroanisole, and the rate of excretion of dieldrin. All effects increased with increasing chlorine content. For example, 50 ppm of Aroclor 1221 reduced hexobarbital sleeping time by 11%, whereas for Aroclor 1248 and 1268, the figures were 35% and 48%, respectively. Liver weights increased with increasing chlorine content When 50 ppm of the Aroclors were incorporated in the diet with 1 ppm dieldrin, the storage of dieldrin was decreased in relationship to the chlorine content. With the Aroclors containing 60% chlorine, or more, the storage of dieldrin in adipose tissue was reduced to the levels found in untreated control animals. Induction of hepatic hydroxylating enzymes has been demonstrated also in pigeons (Risebrough, et al. (1968)) and the American kestrel (Peakall and Lincer (1970)).

McCune, et al. (1962) fed chickens diets containing 100 or 200 ppm Aroclor 1242 for four weeks without observing any mortality. On diets of 400 ppm or 800 ppm, the mortalities within four weeks were 50% and 90%, respectively. In a study at FDA, Flick, et al. (1965) reported a study in white leghorn cockerels. The chicks were fed diets containing 200 or 400 ppm chlorinated biphenyls for three weeks. Edema formation in the pericardial sac and in the abdominal and subcutaneous areas was pronounced at the 400 ppm level. Other gross effects were in decreasing order of incidence, as follows: cream colored spleens; enlarged hemorrhagic kidneys; enlarged adrenals; small spleens; dermatitis and defeathering. Koeman et al. (1969) reported pericardial edema in Japanese quail at a dosage level of 1000 ppm. More recently Vos and Koeman (1970) fed Penoclor DP 6, Clopen A60, and Aroclor 1260 to chickens at a dosage level of 400 ppm up to 60 days. They reported that hydropericardium was common with the first two compounds but rare with the Aroclor 1260. Likewise, the mortality rate of the birds with the first two compounds was much greater than with the Aroclor 1260. This difference could not be explained on the basis of chlorine content since all three compounds contain 60% chlorine. A recent report (B.I.B.R.A. (1970) 9; 377)) by the same authors states that the two compounds manufactured in Europe contain chlorinated dibenzofurans which apparently account for the increased toxicity. Data presented in Food Additive Petition 8B-2306 did not indicate any "chick edema factor" in chicks fed diets containing either 50, 200, or 400 ppm of Aroclor 5460. In an 18-week study with chickens, the "no-effect" level for this aroclor was 500 ppm.

c. Long-Term Studies

On September 15, 1970, Dr. Elmer Wheeler of the Monsanto Chemical Co. presented to FDA the following reports on Aroclors 1242, 1254, and 1260.

1. A 12-month status summary of a two-year chronic toxicity study on beagle dogs.

2. A 15-month status report of a two-year chronic toxicity study in albino rats.

3. Results of the first generation reproduction study of a three-generation study.

4. Results of toxicity, reproduction, and residue study in white leghorn chickens.

In all these studies the levels of administration were 1, 10, and 100 ppm of the individual Aroclors in the diet. Four dogs of each sex and 50 rats of each sex were started on each dosage level.

In the dog study Aroclors 1242 and 1254 produced no compound related changes in any of the parameters measures. With Aroclor 1260 the male dogs receiving 100 ppm and the females receiving 10 or 100 ppm displayed lower weight gains than the untreated controls. The 12-month clinical

terminations revealed a moderate increase in serum alkaline activity among five of the six animals receiving 100 ppm.

In the report of the 15-month period of the two year rat toxicity study, there were no significant difference between the control and test rats on the parameters measured with Aroclor 1242 or Aroclor 1254. With Aroclor 1260 significantly elevated liver and kidney weights were noted among the rats fed 100 ppm. No other differences were found.

In the rat reproduction study, the data from the first generation were normal for Aroclor 1242. However, new data on the second generation showed that the mating indices at 100 ppm were low and that there were only two females left to continue the reproduction study. This part of the experiment was discontinued since there were insufficient females for a statistically significant group. With Aroclor 1254, the progeny of the females fed either 1 or 10 ppm were normal in all respects. With the females fed 100 ppm, the number of pups delivered and weaned from the second litter was significantly lower than normal. The survival of the pups delivered was also significantly lower. In view of these findings, the females fed 100 ppm were remated for a third litter. The data from this litter substantiated the findings noted in the second litter. The organ weight data showed that there were significantly higher liver to body weight ratios recorded for all the rats fed 100 ppm of Aroclor 1254, but the absolute weights were significantly higher only in the males. The males fed 1 or 10 ppm exhibited significantly lower liver weights and liver to body weight ratios. An elevation of thyroid weights was noted for both males and females fed 100 ppm. In the second litter, Aroclor 1260 at 100 ppm appeared to increase the number of stillborn.

At the Atlanta Laboratories of FDA, weanling male and female rats were fed diets containing Aroclor 1254 at dosage levels of 0, 100, or 500 ppm for 67 days and then pair-mated. Only 2 of 10 females fed 500 ppm of Aroclor 1254 had litters (1 and 7 pups, respectively) and these pups died within 3 days after birth. The rats fed 100 ppm were comparable with the controls in number of litters and pups per litter, however, 76.8% of the pups in the 100 ppm group survived to weaning compared with 95.5% of the controls. The mean body weight of the 100 ppm group at weaning were 31.4 gm and that of the controls was 39.2 gm. A similar study was made with Aroclor 1260 in which there was no difference in reproduction between the controls and the 100 ppm group. However, the mean number of pups per litter in the 500 ppm was reduced (8.5 vs 11.4 for the controls) and only 38.2% of the pups survived to weanling compared with 99.1% of the controls.

In a study with white leghorn chickens, the body weights of the males fed Aroclor 1242 at 10 or 100 ppm and the body weights of males and females fed Aroclor 1254 at 100 ppm were slightly lower than the weights of control chickens. The chickens fed Aroclor 1242 or Aroclor 1254 ate less at 100 ppm than those fed the control diet. Egg production in hens fed Aroclor 1242 at 100 ppm or Aroclor 1254 at 100 ppm was much lower than egg production of the control group. There was poor hatchability of eggs from hens fed Aroclor 1242 at 10 ppm.

None of the eggs from the hens fed Aroclor 1242 at 100 ppm or Aroclor 1254 at 100 ppm hatched. Eggs from hens fed Aroclor 1242 at 10 or 100 ppm that did not hatch had a large number of embryos from one to three centimeters in size. The egg shells from hens fed Aroclor 1242 at 10 or 100 ppm or fed Aroclor 1254 at 100 ppm were not as thick as the shells of eggs from hens fed the control diet. Aroclor 1260 at 1, 10, or 100 ppm caused no apparent effects on the mature chickens or on their eggs including hatchability and physical appearance of the eggs.

With the incomplete date on long-term toxicity and reproduction studies, it is not possible at this time to compare the toxicity of the PCBs with that of other chlorinated hydrocarbon pesticides, especially with DDT.

IV. Occurrence in Biological Tissues

Although residues of PCB have been reported to occur in animal tissues in the United States (Anderson, et al. (1969); Risebrough (1969)), Canada (Holden and Marsden (1967); Anderson, et al. (1969); Germany (Koeman et al. (1967); Great Britian (Holmes, et al. (1967); Presst, et al. (1969); Holden and Marsden (1967); The Netherlands, Koeman, et al. (1967); and Sweden (Jensen, et al. (1969); Westöö, et al. (1970), no extensive data are available in the literature on the biological magnification of the substances. The most detailed studies are those of Jensen, et al. (1969) in Sweden. The figures (with mean, range of values, and sample size) given in their study were as follows in ppm for extractable fat.

Animal Source	Region in Sweden: Baltic		Stockholm Archipelago	
Mussel	4.3(1.9-8.6)	(40)	5.2(3.4-7.0)	(15)
Herring	6.8(0.5-23)	(18)	5.1(3.3-8.5)	(4)
Seal	34 (16-44)	(3)	30 (18-56)	3
Guillemont eggs	250 (140-360)	(9)		
White Tail Eagle				
Petoral Muscle	- -		14000 (8,400-17,000)	(4)
Brain	- -		910 (490 - 1500)	(3)
Eggs	- -		540 (250 - 800)	(5)
Heron			9400	(1)

The recent report of Westöö, et al. (1970) showed that the PCBs in about 1400 samples of margarine, vegetable oils, and foods of animal origin were in almost all cases below 1 ppm. A few samples of marine fish were above 1 ppm, however, the highest reported figure was 3 ppm. The number of fish samples with higher values for DDT plus its metabolites is greater than that for PCB. Unfortunately, no mean values are given. Preset, Jefferies, and Moore (1970) found that the livers of fish-eating birds in the British Isles ranged up to a maximum 900 ppm PCBs (wet weight), bird feeders up to 70 ppm, mammal eaters to 50 ppm and insectivores to 1 ppm.

V. Investigations in Progress or Proposed

At FDA additional hepatic enzymes studies are in progress on Aroclor 1254 at SPAL with rats. Dr. Van Loon stated that these would be extended to pigs and dogs. Combination studies with drugs will be done. Likewise, other Aroclors will be used. Also, short-term reproduction studies will be undertaken to determine the effect on the fetus.

A study on mortality and enzyme induction in rats will be made after feeding combinations of Aroclors and various classes of pesticides.

VI. Additional Studies Required for a Complete Evaluation of the Safety on the PCBs

(1) A brief report in the literature (Jensen, 1969) indicates that there is no substantial metabolism by living organisms, but that they can be stored in mammalian tissues. Investigations into the storage of Aroclors in animals are necessary, particularly since the toxicological hazards of these compounds to mammals have not been adequately evaluated.

(2) Special studies on the effects of the Aroclors on the young should be done. This need is emphasized by the observations that the reproduction experiments in rodents and chickens do not follow the pattern of the chronic studies. Aroclors appear to be more toxic than DDT in these studies.

(3) The observations that Aroclors produce abnormalities in chicken embryos require further studies on the teratogenic potential of these compounds.

(4) One rodent species (rat) is now under study for the carcinogenic potential of 3 aroclors. Since it is the recommendation of the Panel of Carcinogenesis of Advisory Committee on Protocols for Safety Evaluation for a second species to be used, another species, either mice or hamsters, should be used for studies on at least 3 important Aroclors.

(5) Mutagenic studies are needed on these compounds. Since DDT has been indicated to be a possible mutagen, a comparison is needed for the Aroclors which similarly contaminate the ecology.

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Submitted by Jerry Burke
and O. Garth Fitzhugh

December 1970

TABLE I - Properties of Aroclors
(Monsanto Company)

TABLE 14

CHEMICAL AND PHYSICAL PROPERTIES OF REPRESENTATIVE AROCLOR® PLASTICIZERS AND RESINS

Property	Aroclor 1221	Aroclor 1232	Aroclor 1242	Aroclor 1248	Aroclor 1254	Aroclor 1260	Aroclor 1262	Aroclor 5442	Aroclor 4465	Aroclor 2505	Aroclor 5460	Aroclor 12-[illegible]
Appearance	Clear, mobile oil	Clear, mobile oil	Clear, mobile oil	Clear, mobile oil	Light-yellow viscous liquid	Light-yellow, soft, sticky resin	Light-yellow sticky, viscous resin	Clear yellow sticky resin	Clear, light-yellow, resin	Black, opaque, brittle resin	Clear, yellow-to-amber, brittle resin or flakes	White [illegible] off-wh[illegible] powder
Color, maximum	*100 APHA	*100 APHA	*100 APHA	*100 APHA	*100 APHA	*150 APHA	*150 APHA	*2 NPA (molten)	*2 NPA (molten)	—	*2 NPA (molten)	*1.5 NP[illegible] (molten)
Chlorine, percent	20.5-21.5	31.5-32.5	42	48	54	60	61.5-62.5	42	65	65	58.5-60.5	68
Acidity, mg KOH/g, maximum	*0.014	*0.014	*0.015	*0.010	*0.010	*0.014	*0.014	0.05	0.05	1.4	0.05	0.05
Moisture, ppm, maximum	—	—	*50	*50	*50	*50	—	—	—	—	—	—
Ave. Coefficient of Expansion, cc/cc/°C	0.00071 (15°-40°C)	0.00073 (25°-100°C)	0.00068 (25°-65°C)	0.00070 (25°-65°C)	0.00066 (25°-65°C)	0.00067 (25°-100°C)	0.00064 (25°-65°C)	0.00123 (25°-99°C)	0.00061 (25°-65°C)	0.00066 (25°-65°C)	0.00179 (25°-124°C)	0.0001[illegible] (20°-1[illegible]
Specific Gravity	*1.182-1.192 (25°/15.5°C)	*1.270-1.280 (25°/15.5°C)	*1.301-1.392 (25°/15.5°C)	*1.405-1.415 (65°/15.5°C)	*1.495-1.505 (65°/15.5°C)	*1.555-1.566 (25°/15.5°C)	*1.572-1.583 (90°/15.5°C)	1.470 (25°/25°C)	1.670 (25°/25°C)	1.734 (25°/25°C)	1.670 (25°/25°C)	1.804-1[illegible] (25°/2[illegible]
Density, pounds per gallon, 25°C	9.85	10.55	11.50	12.04	12.82	13.50	13.72	12.24	13.91	14.44	13.91	15.00
Distillation Range, °C, corrected (ASTM D-20, modified)	275-320	290-325	325-360	340-375	365-390	385-420	390-425	215-300 (4 mm. Hg)	230-320 (4 mm. Hg)	—	280-335 (5 mm. Hg)	430-4[illegible]
Evaporation Loss, %, 100°C, 6 hours (ASTM D-6, mod.) 163°C, 5 hours	1.0-1.5	1.0-1.5	0-0.4 3.0-3.6	0-0.3 3.0-4.0	0-0.2 1.1-1.3	0-0.1 0.5-0.6	0-0.1 0.5-0.6	0.01 0.2	0-0.02 0.2-0.3	0.2-0.3	0.03	0-0.00 0.1-0.[illegible]
Flash Point (Cleveland Open Cup), °C °F	141-150 286-302	152-154 305-310	176-180 348-356	193-198 379-384	None to boiling point	None to boiling point	None to boiling point	241 477	None to boiling point	—	None to boiling point	None [illegible] boiling
Fire Point (Cleveland Open Cup), °C °F	176 349	238 460	None to boiling point	None to boiling point	None to boiling point	None to boiling point	None to boiling point	>350 >662	None to boiling point	—	None to boiling point	None [illegible] boiling
Pour Point (ASTM E-97), °C °F	1 (crystals) 34 (crystals)	−35.5 −32	−19 2	−7 19.4	10 50	31 88	35-38 99	46 115	—	—	—	—
Softening Point (ASTM E-28), °C °F	—	—	—	—	—	—	—	*46-52 115-126	*60-66 140-151	*66-72 140-162	*96-105 200-222	*150-[illegible] 302-3[illegible]
Refractive Index, n D-20 20°C	1.617-1.618	1.620-1.622	1.627-1.629	1.630-1.631	1.639-1.641	1.647-1.648	1.6501-1.6517	—	1.664-1.667	—	1.660-1.666	—
Viscosity, Seconds Saybolt Universal (ASTM D-88) 100°F (37.8°C) 130°F (54.4°C) 210°F (98.9°C)	*38-41 35-37 30-31	*44-51 39-41 31-32	*62-92 49-56 34-35	185-240 *73-80 36-37	1800-2500 260-340 *44-48	3200-4500 *72-78	600-850 (160°F, 71°C) *86-100	300-400	90-150 (266°F, 130°C)	—	—	—

*Remote Specification

MONS 051290