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STATUS REPORT ON

THE CHEMISTRY AND TOXICOLOGY

OF POLYCHLORINATED BIPHENYLS (PCB)

OR AROCLORS

AS OF JUNE 1, 1970

'Bureau of Foods, Pesticides and Product Safety
Food and Drug Administration
Public Health Service
Department of Health, Education and Welfare
Washington, D.C.

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I. Introduction

In 1966 a Swedish scientist, Soren Jensen, revealed that the polychlorinated biphenyls (PCB) were dispersed widely in the environment, to the extent that he identified PCB in pike (in different parts of Sweden), in other fish and in an eagle (1). Further analyses for PCB were made in eagle feathers preserved in a museum, some of these dating back to 1880, but PCB was found in feathers which were collected in 1944. Within the same year of Jensen's observation, Widmark, a colleague of Jensen's, reported to an international commission studying pesticide analysis that a compound similar to DDT in identification and analysis, which contained chlorine, created a problem in isolation and identification of residues of DDT (2). Since that time PCB has been found in fish, sea birds, pine needles, rainwater (not detected as yet in airborne particulates), human body fat and mother's milk (3).

As indicated in the following section of this report on chemistry and surveillance (Section II), PCB is manufactured in USA by Monsanto Chemical Company (tradename Aroclor(R)) and in Europe and Japan by other manufacturers. Their industrial uses, as described later, are of a wide variety. Risebrough and Brodine (3) state that PCB's are recommended for mixing with chlorinated insecticides to suppress their vaporization and extend their "kill life." USDA advises us that as part of an inert ingredient PCB is in some pesticide formulations, especially such insecticides as DDVP, lindane and toxaphene. The addition is apparently for the purpose indicated above. This may be one source of environmental pollution by this extremely persistent fat-soluble compound. In this latter property it is like DDT in that is is not soluble in water.

The series of Aroclors are marketed under various numbers and consist of mixtures of chlorinated biphenyls and terphenyls. The 1200 series relates to the biphenyls, the 5400 series to the terphenyls and the 4400 series to a mixture of bi- and terphenyls. The physical properties of the compounds are related to the chlorine content with viscosity increasing in direct proportion to the chlorine content from very fluid liquids to viscous products and solids (see Table 3 in Section II).

Initially the concern about this synthetic chemical in terms of human health was limited to occupational exposure, at least prior to 1966. Since then, because of this series of compounds being to widely distributed in the environment and perhaps being as ubiquitous as DDT, their potential hazards to marine, avian, and mammalian species, including man, are being explored. In an investigation on the peregrin falcon (fast disappearing bird of prey), Risebrough et al (1968) showed the presence of some unknown compounds, along with DDT and DDE, in the eggs of a falcon nest which did not hatch. These hitherto unidentified compounds were later found to be polychlorinated biphenyls (4). In the North American peregrine

falcon PCB was found at level of 1.980 ppm and in a white tailed eagle in Sweden at level of 17,000 ppm (3). Apparently the greater the distance away from industrial centers the more the level of PCB decreases for various organisms. This is illustrated in Tables 1 and 2 for the peregrine falcon and the eggs of sea birds.

TABLE 1

DDT and PCB in Peregrine Falcons

	Total DDT[x] (ppm)	PCB (ppm)	Ratio of DDT to PCB
Immature Bird (California)			
breast muscle (wet)	14.4	9.4	1.5
liver (wet)	7.7	4.5	1.7
brain (wet)	2.8	1.5	1.9
brain lipid	36.0	19.3	1.8
carcass (wet)	20.2	19.8	1.9
carcass lipid	300.0	160.0	1.9
Adult Bird (California)			
breast muscle (wet)	127.0	98.0	1.3
liver (wet)	77.0	57.0	1.4
brain (wet)	49.5	34.6	1.4
brain lipid	595.0	415.0	1.4
carcass (wet)	85.0	65.0	1.3
carcass lipid	2600.0	1980.0	1.3
Immature Bird (Arctic)			
breast muscle (wet)	2.3	0.16	14.0
breast muscle (dry)	7.8	0.54	14.0
liver (wet)	1.0	0.10	10.0
brain (wet)	0.43	0.037	12.0
body fat	56.3	3.2	16.0
carcass (wet)	9.3	0.80	12.0
carcass (lipid)	63.7	5.5	12.0
Second Year Bird (Arctic)			
breast muscle (wet)	99.0	28.0	3.5
breast muscle (dry)	296.0	84.0	3.5
brain (wet)	85.0	21.0	4.7
carcass (wet)	70.0	19.7	3.5
carcass lipid	5000.0	1420.0	3.5

x - includes p,p'-DDT, p,p'-DDE, p,p'-DDD, p,p'-DDMU, o,p'-DDT and o,p'-DDE

From Risebrough et al, reference 4

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TABLE 2

PCB Content of Eggs of Sea Birds

Species	Locality	No. of Samples	Average PCB Level* (ug)
Branat's Camorant	Farallon Islands	17	113
Pelagic Camorant	San Mateo County, California	2	62
Murre	Farallon Islands	6	558
Pigeon Guillemot	Farallon Islands	1	20
	San Mateo County, California	1	62
Cassins Auklet	Farallon Islands	2	15
Western Gull	Farallon Islands	1	118
	San Mateo County, California	1	118
	San Francisco County, California	1	480
Black-crowned night heron	San Francisco Bay	1	330
	"	1	24
Carpian Tern	"	2	805
	San Diego Bay	5	1010
Forsters Tern	"	2	114
Least Petrel	Boya, California	2	3.1
	"	1	471

*where more than one sample, value is average

From Risebrough and Bodine, Environment 12, No 1 16-27 (1970) Ref 3

Various speculations, alluded to later in this report, have been advanced as to the origin of these environmental pollutants but apparently these compounds, like DDT, are carried by global air currents from the Arctic circle to the southern hemisphere (3). More studies are needed to identify the routes of entry of PCB into the environment.

Since wide scale distribution of PCB is now recognized, the primary question relates to transmission of these compounds to man through the environment and the possible human health impact from such exposure. For occupational situations the American Conference of Governmental Industrial Hygienists (ACGIH) have set a "threshold limit value" for PCB (containing 42 percent chlorine) of one mg/m^3 of air which happens to be the same as "threshold" for DDT (5). For more heavily chlorinated biphenyls the ACGIH threshold limit is decreased.

One important observation is that the more lightly chlorinated PCB's are somewhat less persistent and accordingly more readily metabolized and excreted, whereas the highly chlorinated compounds are more persistent and by inference, no doubt, less easily degraded in the body. There is little known about the metabolites of PCB. (6)

Sax (5) in his description of dangerous properties of industrial materials includes PCB as a toxic agent affecting human skin and liver at high concentrations. He describes the lesion produced in the liver as an acute yellow atrophy. Carbon tetrachloride exposure potentiates the toxicity of PCB. It would appear that in rats the acute toxicity of polychlorbiphenyls (LD_{50} values) decreases with increase in chlorine content (Table 3). However, in the rabbit, on skin testing, there is a trend toward increased toxicity with an increase in chlorine content up to 54% where there is a decrease in toxicity (Table 3). With respect to hepatotoxic action of chlorinated diphenyls, Risebrough and Brodine (3) and Sax (5) claim that the higher the chlorine content of the diphenyl compound, the more toxic it is likely to be. Oxides of chlorinated diphenyls are more toxic than the unoxidized materials. Like the skin lesion produced by 2,4,5-T and 2,4-D and the dioxins, the clinical observations in occupational exposure are that of chloracne. From systemic intoxication the usual symptoms are nausea, vomiting, weight loss, jaundice, edema and abdominal pain. If there is extensive liver pathology, the highly exposed individual may become comatose and die.

Risebrough and Brodine (3) have the view that PCB in the environment may not attain those concentrations where severe injury or death from short term exposure would occur. However, they feel that the greatest hazard in continuous low level exposure to PCB may be the chronic effects either from this compound or combinations of and interaction with other environmental toxicants. They further indicate there may be a danger in destroying other forms of life which are part of the food chain (3).

Another aspect of this pollution problem is the necessity of viewing not just the impact on local ecosystems but the global system. If future planning based on exploiting sea resources to feed the increasing population is maximized, then this problem of accumulation of PCB as well as other contaminants in marine organisms and other species closely related becomes a critical matter for resolution. Considering this problem in terms of exposure to PCB of many forms of life and of human populations of varying age and states of health demands a re-evaluation of "threshold limit values" regarding safety in terms of inhalation and ingestion. Subsequent reference to the toxicology of PCB in Section III of this report also emphasizes the effect of PCB on liver enzymes which, in turn, may relate to hormonal controls and the influence of physiological processes, including reproduction. The fact that PCB has been identified in human fat and in human milk in a series of tests at a level of 0.06 ppm of the whole milk suggests the need for assessment of the hazard of these compounds to mammalian systems is clearly indicated.

Since speculations have been made as to sources of environmental residues of PCB, more definitive information is required to trace the paths by which these compounds move through the environment. There is an important difference between DDT and PCB as environmental contaminants in that the former has been intentionally introduced into the environment while the latter escapes into the environment by accident.

II. Chemistry and Surveillance

Polychlorinated biphenyls (PCB) are industrial chemicals with a variety of uses. These compounds are quite stable and have important applications as plasticizers in plastics, as modifiers in many paints and other products, lubricants, electrical insulators, and fire retardants. We understand that they are also used in printing inks, textile dyes, heat transfer fluids, and many other products.

In the United States PCB are manufactured by the Monsanto Chemical Company with the tradename Aroclor(R). 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 biphenyl or terphenyl components. 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 very fluid liquids; as percent chlorine increases the products become more viscous or become solids, (See Table 3)

There is a food additive regulation permitting the use of polychlorinated terphenyls in adhesives for food packaging. No regulation has issued for polychlorinated biphenyls.

We do not know the exact route by which PCB enters food products. Residues of PCB have been found primarily in wildlife. European and U.S. investigators have reported residues in fish, fish-eating birds, and some wild animals. The first literature reports of PCB residues were in 1967 by European workers. Residue findings although widespread appear to be associated to some extent with industrial locations. Literature in the early 1950's reported increased effectiveness of some chlorinated pesticides when formulated with PCB. There has been some speculation that PCB may be entering the environment via this route; however, we are aware of no substantiation of this. In addition to waste from manufacturing plants using PCB, it has been suggested that these chemicals may enter the environment via leaching of plasticizer from plastic objects in waste disposal areas and thus enter streams or may enter the atmosphere from the burning of plastics at waste incineration plants.

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TABLE 3

l Physical Properties of the r® Chlorinated Compounds

	Aroclor 1221 Colorless mobile oil	Aroclor 1232 Practically colorless mobile oil	Aroclor 1242 Practically colorless mobile oil	Aroclor 1248 Colorless to light yellow-green, clear, mobile oil	Aroclor 12[illegible] Light yell[illegible] viscous oil
	50 Max. (APHA)	50 Max. (APHA)	50 Max. (APHA)	50 Max. (APHA)	50 Max. (APHA)
Maximum (Mgm. KOH per Gm.)...	0.014	0.014	0.010	0.010	0.010
efficient 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)	0.00065 (25°-65°C)
ensity Gravity..... per gallon — 25°C(77°F).....	1.182-1.192 (25°/15.5°C) 9.85	1.270-1.280 (25°/15.5°C) 10.55	1.381-1.392 (25°/15.5°C) 11.50	1.405-1.415 (65°/15.5°C) 12.04	1.495-1.5[illegible] (65°/15.5[illegible] 12.82
on Range — ASTM D-20 (Mod.) °C.....	275°-320°	290°-325°	325°-366°	340°-375°	365°-390°
tion Loss — % — ASTM D-6 Mod. .....5 hrs. C.....6 hrs.	— 1.0 to 1.5	— 1.0 to 1.5	3.0 to 3.6 0.0 to 0.4	3.0 to 4.0 0.0 to 0.3	1.1 to 1.3 0.0 to 0.2
Point — Cleveland Open Cup.....°C °F	141°-150° 286°-302°	152°-154° 305°-310°	176°-180° 348°-356°	193°-196° 379°-384°	None
Point — Cleveland Open Cup.....°C °F	176° 349°	238° 460°	None*	None	None
our Point — ASTM D-97.....°C °F	Crystals at 1°C Crystals at 34°F	−35.5° −32°	−19° 2°	−7° 19.4°	10° 50°
Softening Point — ASTM E-28.....°C °F	— —	— —	— —	— —	— —
Refractive Index — D-line — 20°C.....	1.617-1.618	1.620-1.622	1.627-1.629	1.630-1.631	1.639-1.6[illegible]
Viscosity — Saybolt Universal Sec. (ASTM — D-88) 210°F (98.9°C)	30-31	31-32	34-35	36-37	44-48
130°F (54.4°C)	35-37	39-41	49-56	73-80	260-340
100°F (37.8°C)	38-41	44-51	82-92	185-240	1800-25[illegible]
*None indicates — "No fire point up to boiling temperature" mg/kg					
Oral LD_{50}-rats (approx.)	3980*	4470*	8650*	11,000*	11,9[illegible]
Skin MLD-rabbits-mg/kg	>2000*	>1260*	>794*	>794*	>126[illegible]
~~administered~~	~~<3160*~~	~~<2000*~~	~~<1260*~~	~~<1260*~~	~~<2[illegible]~~

[illegible] in corn oil # 33/36 in corn oil

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	Aroclor 1262 Light yellow sticky clear resin	Aroclor 1268 White to off-white powder	Aroclor 4465 Light-yellow, clear, brittle resin	Aroclor 5442 Yellow trans-parent sticky resin	Aroclor 5460 Clear, yellow-to-amber, brittle resin	Aroclor 2565 Black, opaque brittle resin
[illegible] (ASTM)	50 Max. (APHA)	1.5 Max. NPA (molten)	2 Max. NPA (molten)	2 Max. NPA (molten)	2 Max. NPA (molten)	—
[illegible]	0.014	0.05	0.05	0.05	0.05	1.4
0.00067 (70°-100°C)	0.00064 (25°-65°C)	0.00067 (20°-100°C)	0.00061 (25°-65°C)	0.00123 (25°-99°C)	0.00179 (25°-124°C)	0.00066 (25°-65°C)
1.555-1.566 (90°/15.5°C) 13.50	1.572-1.583 (90°/15.5°C) 13.72	1.804-1.811 (25°/25°C) 15.09	1.670 (25°/25°C) 13.91	1.470 (25°/25°C) 12.24	1.670 (25°/25°C) 13.91	1.734 (25°/25°C) 14.44
385°-470°	395°-425°	435°-450°	230°-320° at 4 mm. Hg.	215°-300° at 4 mm. Hg.	280°-335° at 5 mm. Hg.	—
0.5 to 0.8 0.0 to 0.1	0.5 to 0.6 0.0 to 0.1	0.1 to 0.2 0.0 to 0.06	0.2 to 0.3 0.0 to 0.02	0.2 0.01	0.03 1.5 to 1.7 (at 260°, 5 hrs.)	0.2 to 0.3 —
None	None	None	None	247° 477°	None	None
None	None	None	None	> 350° > 662°	None	None
31°	35°-38°	—	—	46°	—	—
88°	99°	—	—	115°	—	—
—	—	150° to 170° (hold pt.)	60° to 66°	46° to 52°	98° to 105.5	66° to 72°
—	—	302° to 338° (hold pt.)	140° to 151°	115° to 126°	208° to 222	149° to 162°
1.647-1.649	1.6501-1.6517	—	1.664-1.667	—	1.660-1.665	—
72-78	86-100	—	90-150 (266°F or 130°C)	300-400	—	—
3200-4500	600-850 (150°F or 71°C)	—	—	—	—	—
—	—	—	—	—	—	—
9,900**	11,300**	10,900**	16,000**	10,600**	19,200//	6,310///
1260**	>1260**	>2510///	>2000**	>1260**	>7940//	>2000///
3160**	<3160**		<3160**	<2000**		<3160

** 10% soln. in corn oil /// 10% soln. in corn oil

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Aroclors at relatively high concentrations (about 2000 ppm) have been shown by FDA and others to produce hydropericardium in chicks (chick edema effect). We do not know whether the effect is from Aroclors or impurities.

PCB residues are detected by the FDA multi-pesticide residue analytical methods if the amount present in relation to the amount of pesticide present is great enough. Their presence in samples analyzed for pesticides complicates the analysis for chlorinated pesticides. Mrs. Judith Armour, Division of Pesticide Chemistry and Toxicology, has developed a method for separating PCB from chlorinated pesticides. Separation permits measurement of either the pesticide or PCB residue without cross interference. The separation method, information on the behavior of PCB in FDA's multiresidue analytical methods, and background on the problem have been made available to all FDA District laboratories through Laboratory Information Bulletins. District laboratories have been given guidelines on the determination and reporting of PCB residues. They have been asked to report to Washington any findings of PCB. Special emphasis has been placed on fish since this appears to be the most likely product to contain residues of both PCB and the DDT group. District laboratories have reported residues of PCB in Great Lakes and certain other fish, fishmeal for animal food, crabmeat, and milk from one location in West Virginia. The identity of PCB in the milk sample was verified by mass spectrometry. Dr. Francis Biros, Division of Pesticide Chemistry and Toxicology, has used mass spectrometry to confirm the finding of PCB in a few samples of human adipose tissue. To our knowledge there has been no evidence of PCB residues in any field or orchard crop analyzed by FDA laboratories.

Present and future plans include: discussion was held on the analytical aspects of PCB and PCB-pesticide combination residues at the FDA Pesticide Analytical Workshop in March; accumulation of data on PCB occurrence through analyses by District laboratories; improvement of the measurement of PCB residues at low levels; investigation of the analytical characteristics of other organohalogens which may be similar to PCB in use and behavior. Chlorinated naphthalenes and chlorinated paraffins are being studied.

III. Toxicology

The toxicological information on commercially used Aroclors is rather limited and incomplete. Early studies were done on compounds of undefined specifications or on mixtures. However, the following summary brings the data on toxicity up to date.

a. Early Studies

Smyth and Smyth (7) 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) (8) found that 0.05 gm of a chlorinated biphenyl fed to rats over a period of 6 days caused liver injury to rats. Miller (1944) (9) found that 2 doses of an Aroclor fed to guinea pigs one week apart was fatal in 11 to 29 days and marked liver changes were present. The toxicity to rats of chlorobiphenyl by inhalation was also investigated by Drinker et al (1937) (8) and some hepatotoxic action was found. In 1953 the American Conference of Government Hygienists (10) set 1.0 to 0.5 mg of polychlorinated biphenyl compounds/M^3 of air as the threshold limits.

In Food Additive Petition 8B-2306, two short-term studies were reported in support of the use of Aroclor 5460 as a plasticizer component of adhesive formulations. This aroclor is a chlorinated terphenyl with less than 0.05% biphenyls. In a 90 day study in rats with dosage levels of 100, 300, and 1,000 ppm, the "no effect" level was 100 ppm with only a slight increase of liver to body weight ratio of males in the 300 ppm group. A similar 18 week study in chickens demonstrated a "no effect" level at 500 ppm. A specific study (as outlined in J.A.O.A.C. 44, 142, (1961) for the "chick edema factor" was conducted with 12 chicks at dosage levels of 50, 200, and 400 ppm. No significant increase in edema was noted.

b. More recent studies

(1) The findings of Street et al (1969) (11) that feeding of a number of PCB materials to rats for 15 days resulted in induction of liver microsomal enzymes, and the degree of induction increased with increasing chlorine content. Those PCB containing over 60% chlorine were more potent inducers than DDT.

Street also reported that when a series of polychlorinated biphenyls were incorporated at 50 ppm together with 1 ppm dieldrin into the diets of rats for 15 days, those biphenyls containing 60% chlorine or more reduced the dieldrin storate in adipose tissue to the levels found in untreated control animals.

(2) Consulting laboratories for Monsanto Company (12) found the oral LD_{50} in rats for Arocior 1254 and 1260 to be in the neighborhood of 10 gm/kg. Monsanto is also conducting a 2-year chronic oral

toxicity study of Aroclor 1254 and 1260 in beagle dogs and a three generation reproduction study in rats of Aroclor 1242, 1254 and 1260. The 90-day interim results of the dog study revealed no significant findings for body weights, food consumption, mortality, hematology, blood chemistry, or urine analysis.

Data were recently obtained from Dr. Emmet Kelly, Medical Director of the Monsanto Chemical Company, St. Louis, Mo., by telephone on three polychlor biphenyls (13). These data were obtained with the promise from Dr. Kelly that he would send the interim report as soon as he obtained it. These were 90-day results on a two-year experiment. Some rats were sacrificed and microscopic examinations of tissues were done on the sacrificed animals.

Rats were fed diets containing 1, 10, or 100 ppm for the 90-day period. Dogs were fed diets containing 1, 10, or 100 ppm for the 90-day period. Reproduction studies in rats are in progress at dosage levels of 1, 10, and 100 ppm.

Aroclor 1242 - Liver enlargement occurred in rats at 100 ppm. No microscopic change was seen. Dogs showed no gross effect at any dosage. In the first mating of the reproduction study 100 ppm retarded growth of pups.

Aroclor 1254 - Liver enlargement occurred in rats at 100 ppm but no microscopic change was seen in the tissues. The dosage of 100 ppm decreased growth in the dogs. In the first mating of the reproduction study 100 ppm caused death of many of the pups.

Aroclor 1260 - Liver enlargement occurred in rats at 100 ppm but no microscopic change was noted in the tissues. Dogs on 100 ppm refused to eat the diet and two died. No effect was noted at the dosages of 1 and 10 ppm. Reproduction in rats appears normal at all dosage levels.

The status after 9 months of study is covered in the attached Table 4.

(3) In studies of the toxicological interaction between dieldrin, DDT and 11 different Aroclors in flies, Lichtenstein et al (1969) (14) found that the Aroclors significantly increased the toxic effects of the pesticides.

TABLE 4

SUMMARY--INTERIM STATUS

OF

CHRONIC TOXICITY STUDIES

	Aroclor 1242	Aroclor 1254	Aroclor 1260
ar chronic--rats , 10, 100 ppm in diet			
us-- 9 months	no effect clinically	Lowered weight gain at 100 ppm	No effect (see below)
us--6months sacri- including micro- ology	No effect clinically	Increased liver wt in males at 100 ppm Negative path- ology--all levels	Increased liver wt in males at 10 & 100 ppm. Negative path- thology--all levels
ar chronic--dogs , 10, 100 ppm in diet			
us--10 months	No effect clinically	Lowered wt gains* all females at 1, 10 & 100 ppm Lowered wt gains males at 100 ppm	Lowered wt gains** females at 10 and 100 ppm Lowered wt gains at 100 ppm
tus--6 months including od & urine chem.	Negative	Negative	Negative**

See report for details relative to "Mortality"
See report for details relative to "Mortality" and "Blood Chemistry"

santo Comapny, Interim Reports, Chronic Toxicity Studies on Aroclor 1242, 1254 and 1260

(4) A report by Risebrough et al (1968) (4) states that polychlorinated biphenyls are inducers of hepatic enzymes and together with other chlorinated compounds may be responsible for aberration in calcium metabolism observed in certain species of birds.

(5) The polychlorinated biphenyls have also been reported to produce hydropericardium in chicks (chick edema) (15, 16).

(6) In a petition for the use of Aroclor 5460 as a plasticizer component of adhesives (FAP 8B-2306) there is a report of a feeding study in rats. Rats were fed diets containing 100, 300, or 1,000 ppm for 90 days. Growth repression occurred at the 1,000 ppm. Liver to body weight ratios were increased at levels of 300 and 1,000 ppm. Likewise, young adults (12 weeks old) white leghorn chickens were fed diets containing 500, 1,000, or 2,000 ppm Aroclor 4560 for 18 weeks. The dosages of 1,000 and 2,000 increased mortality. Average body weights of the male birds at all dosage levels were slightly less than the controls. In a chick edema study 21-day old white leghorn chicks were fed 50, 200, and 400 ppm Aroclor 5460 for 21 days. There was a slight but not a significant average increase in pericardial edema fluid at all dosage levels.

c. Studies in FDA laboratories

(1) The single oral dose LD_{50} of Aroclor 1254 in female rats was 4 gm/kg and it was considerably higher for males. The oral LD_{50} of Aroclor 1260 was 10 gm/kg.

(2) In a preliminary study, rats fed diets containing Aroclor 1254 or 1260 were sacrificed after 7 weeks of feeding. At a dietary level of 2,000 ppm none survived. At a dietary level of 1,000 ppm one of six fed Aroclor 1254 and none of the six fed Aroclor 1260 survived. All rats fed 500 ppm survived. Liver enlargement appeared in the survivors at all dosages fed.

(3) In behavioral and physiological studies using single doses of Aroclor 1260 in mice (1 and 10 mg/kg, p.o.) it was found 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) the Aroclor exerted little effect on open-field exploration and (3) 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.

(4) A 30-, 60- and 90-day feeding study is underway in rats of Aroclors 1254 and 1260 at levels of 0, 25, 75, 150, 300 and 500 ppm. After each interval, body weight, liver weights, and the microsomal enzyme aliesterase, β-glucuronidase, and nitroreductase will be measured.

(5) In a study at FDA, Flick et al (Poultry Science 44, 1460, 1965) (17) reported a study in white leghorn cockerels. The chicks were fed diets containing 200 or 400 ppm chlorinated biphenyls for 3 weeks. Both dosages produced toxic effects which partially simulated those seen with the chick edema factor. Edema formation in the pericardial sac and in the abdominal and subcutaneous areas was pronounced only at the 400 ppm level. Other gross effects were in decreasing order of incidence as follows: cream colored pancreas, enlarged hemorrhagic kidneys, enlarged adrenals, small spleens, dermatitis and defeathering. Koeman et al (Nature 221, 1128, 1969) (18) reported pericardial edema in Japanese quail at a dosage level of 1,000 ppm. No lower dosage was used.

(6) Other teratological data

Results of various studies follow, keyed to the specific Aroclor.

Aroclor 1242

FDA test (1963) for chick edema factor (AOAC bioassay method) (19)

No. of Chicks	Diet Level (ppm)	Heart Fluid (ml) or Incidence of hydropericardium	Early Death	Remarks
10	100	2/9	1	Enlarged Heart Group Score 2+
6	349	1/12	4	Group Score 3+ (toxic)

Aroclor 1242 was distilled in a spinning band column; 28 fractions were more toxic than the early fractions. Some of the results of chick bioassay on these follow:

Sample	No. of Chicks	Diet Level (ppm)	Hydropericardium Incidence	Group Score	Remarks
Fraction 1	6	100	0	0	1 early death no edema
Fraction 21	6	100	0	0	no edema
Fraction 25	6	100	2	2+	Toxic
Fraction 28	6	100	3	5+	6 early deaths Toxic
Residue	6	100	5	5+	"
Fraction 25	10	50	0	0	2 early deaths no edema
Fraction 28	7	10	0	0	no edema
Fraction 28	10	50	7/7	15+	3 early deaths 5 hemorrhages

Aroclor 1242 was injected into fertile eggs, 0.01 ml of 10% solution in dioxane: 0/20 hatched, with short upper beak in most of the embryos that failed to hatch, edema, weight retardation.

Aroclor 1268 was used in a chick edema list 91963) with following results:

No. of chicks	Level in Diet ppm	Heart Fluid (ml) or Incidence of Hydropericardium	Early Results	Remarks
12	200	0.25 (1/12)	5	4/12 hemorrhage
12	400	7.21 (3/12)	3	6/12 "

d. Proposed Investigations:

(1) When the levels (see (4) above) producing enzyme induction are determined, then a study of mortality and enzyme induction after feeding combinations of Aroclors and various classes of pesticides will be made.

The study is prompted by the fact that although the toxicological data available at the present time is spotty the indications are that the toxicity of pesticides may be increased in the presence of the Aroclors. This interaction becomes increasingly important as the Aroclors become more widespread as contaminants in the global ecosystem.

(2) A brief report in the literature (1) indicates that there is no substantial metabolism of Aroclors 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 hazard of these compounds to mammals has not been adequately evaluated.

Studies should include administration of Aroclors to rats for short periods (30, 60, 90 days) and to pregnant rats so that transmission to the fetus could be determined.

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