
Human Health Effects of Electrical-Grade PCB's

Corporate Health & Safety Operation

GENERAL  ELECTRIC

MONS 012009

HUMAN HEALTH EFFECTS
OF
ELECTRICAL-GRADE PCB's

J.F. Brown, Jr., Ph.D.
Manager - Life Sciences Branch
Corporate Research and Development Center
Schenectady, N.Y.

J.T. Coe
Staff Executive
Environmental Quality & Safety
Corporate Health & Safety Operation
Fairfield, Conn.

H.D. Pocock, Jr., M.D.
Associate Company Medical Director (retired)
Corporate Health & Safety Operation
Fairfield, Conn.

Corporate Health & Safety Operation
General Electric Company
3135 Easton Turnpike
Fairfield, Conn. 06431

August, 1981

INDEX

		Page
Section I	Introduction	2
Section II	PCB Composition and Terminology	4
Section III	History of PCB Use	7
Section IV	Health Effects of PCB and PCDF Mixtures	9
	A. Observations on Test Animals	
	1. General Bioeffects	
	2. Impurity Effects	
	3. Structure-Activity Relationships	
	4. Toxicity and Carcinogenicity Test Results	
	B. Human Health Effects Observations	11
	1. Early Occupational Chloracne	
	2. Yusho Episode	
	3. Effects of Eating Fish Containing PCB's	
	4. Clinical Studies of Capacitor Workers	
	5. NIOSH Mortality Study	
	C. Health Effects Summary	18
Section V	U. S. PCB Regulations	20
Section VI	On-going Research Programs	22
Section VII	References Cited	23

Abbreviations which may be unfamiliar to some readers include:

ppm	parts per million
ppb	parts per billion
kg	kilogram; 1000 grams
gm	gram (s)
mg	milligram(s); one thousandth of a gram
$\mu\text{g}/\text{m}^3$	micrograms (millionths of a gram) per cubic meter
$\mu\text{g}/\text{L}$	micrograms per liter (approx. = ppb)
LD ₅₀	an acute toxicity measurement meaning dose lethal for 50% of the test animals
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
GGTP	Liver serum enzyme gamma glutamyl transpeptidase
HEW	Health, Education and Welfare Department (now called Health and Human Resources Department)
NIOSH	National Institute for Occupational Safety and Health
OSHA	Occupational Safety and Health Administration
p,p'-DDE	Metabolite of DDT present as background in blood analyses
SGOT	Liver serum enzyme glutamic oxaloacetic transaminase
TLV	Threshold Limit Value: an exposure concentration representing conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effect.

Although the production of polychlorinated biphenyls (PCB's) in the U.S. has been banned, definition of the human health risks they may pose continues to be an important issue. The PCB's were widely used for nearly 50 years, chiefly as dielectric fluids and plasticizers, and large amounts are still present in electrical equipment that will require servicing and disposal. PCB's are also present in numerous environments that may, or may not, merit containment or restorative actions. Small, but measurable levels are found in some edible fish. Thus, the potential for human exposure to PCB's remains.

At present, Company managers, employees, physicians and public officials concerned with appropriate handling of these exposure situations face a contradictory array of information on the possible health hazards. On the one hand, the U. S. press and environmental literature (e.g., ref. 1) increasingly portray PCB's as very toxic materials, and situations resulting in human exposure at any level as hazardous and alarming. The Toxic Substances Control Act of 1976 (TSCA) and attendant regulations generally ban PCB manufacture, processing and distribution; severely limit use; and impose strict requirements for PCB labeling, disposal and storage for disposal.

On the other hand, many European countries have made a quite different risk/benefit assessment of PCB's since they continue to permit PCB manufacture and use in closed electrical equipment. More importantly, 40 years of U.S. occupational exposure in capacitor manufacturing has proven relatively uneventful, as judged by documented adverse health effects.

Many medical studies or observations of human populations that were heavily exposed to PCB's have been reported (2,3,4,5,6,7,8,9,10,11,12,13, 14,15,16,17,18,19,20,33,47,49,50,51,52,55,56,59,60,61,63). Some of these investigations are very recent and have only become available since the public image of PCB's was formed. Not all are yet reported in the published literature. The authors have undertaken this paper to provide perspective for General Electric managers and physicians, and to help identify situations of human exposure to PCB's that might present cause for concern. It draws on extensive GE experience in plants manufacturing PCB-filled capacitors, as well as on review of the scientific literature. The paper reflects today's knowledge and may be extended if significant new information becomes available. The concluding section describes on-going research that may provide additional information relevant to some present uncertainties.

This paper presents many quantitative observations because these are critically important to any health effects perspective. The fact that PCB's are persistent and readily detectable at low concentrations does not necessarily mean that they are toxicologically significant.

**As used throughout this paper "electrical-grade PCB's" describes various PCB's used in GE capacitors and transformers.*

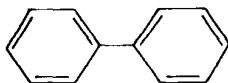
Section I

Introduction

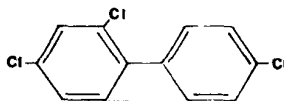
The PCB bioeffects literature is voluminous, comprising several hundred original articles. The present paper will not attempt to survey all aspects of this information, but will focus on those portions the authors judge most relevant to human health effects evaluation. In addition to literature citations the bibliography lists health-related conference reports (21,22,23,24,25) and several review books and documents (26,27,28,29,30).

PCB Composition and Terminology

In chemical terminology "phenyl" denotes a ring structure of six carbon atoms attached to something else; "biphenyl" results when two such rings are attached to each other; and a "polychlorinated biphenyl" (PCB) is any molecule having multiple chlorine atoms attached to the carbon atoms of a biphenyl nucleus. Biphenyl and a representative trichlorobiphenyl (PCB) are illustrated below:



Biphenyl



2,4,4'-Trichlorobiphenyl (a PCB)

There are 209 theoretically possible chlorinated biphenyl molecules, differing in the numbers (homologs) and positions (isomers) of the attached chlorines; of these 209 species, about half have been identified as being present among the complex mixtures that constitute commercial PCB products. These products range from light oily fluids (di-, tri-, and tetrachlorobiphenyls) to heavy, honey-like oils (penta-chlorobiphenyls) to greases and waxes (more highly chlorinated).

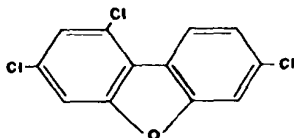
The manufacturers of PCB's sold them under trade names; e.g., "Aroclor" (Monsanto, USA), "Phenoclor" and "Pyralene" (Prodelec S.A., France), "Clophen" (Farbenfabriken Bayer AG, Germany), or "Kanechlor" (Kanegafuchi Chemical Industrial Co. Ltd., Japan). They also assigned product numbers that usually reflected either the average degree of chlorination or, what is equivalent, the weight-percent chlorine in the mixture. Thus, the American Aroclor 1242, its French equivalent, Phenoclor DP3, and its Japanese equivalent, Kanechlor 300, all contained 42% chlorine, or 3 chlorine atoms per biphenyl on the average. Likewise, Aroclor 1254 and its German equivalent, Clophen A50, contained 54% chlorine, or 5 chlorine atoms per biphenyl on the average. Aroclor 1016 designated a Monsanto PCB product similar to Aroclor 1242 with enhanced biodegradability, which was accomplished by removal of higher chlorinated homologs.

Electrical equipment manufacturers further purified these commercial PCB products to insure electrical performance; blended them with stabilizers and diluents; and then put the resultant PCB mixtures into capacitors and transformers under their own trade names and product numbers. GE's trade name for its PCB mixtures was "Pyranol." "Askarel" is a generic, industry-wide term for a PCB or other fire-resistant dielectric fluid.

PCB Composition and Terminology

In short, the materials now collectively referred to as "PCB's" are different complex mixtures of chlorinated biphenyls used under a variety of product names. These mixtures always contained several dozen individual PCB isomers and homologs clustered around some average degree of chlorination, frequently some trichlorobenzenes as diluents; often about 0.5% of an aliphatic epoxide as a stabilizer; and parts-per-million levels of trace impurities such as the polychlorinated derivatives of methylbiphenyls, terphenyls, naphthalene or dibenzofuran.

Returning to chemical terminology, "furan" denotes a ring structure of four carbon atoms and one oxygen atom; and "dibenzofuran" a tricyclic arrangement of two benzene rings and one furan ring fused together. This structure can result if an oxygen atom is added to a biphenyl system. If multiple chlorine atoms are attached to this nucleus, then a "polychlorinated dibenzofuran", or PCDF, results as illustrated below. There are 135 theoretically possible chlorinated dibenzofurans.

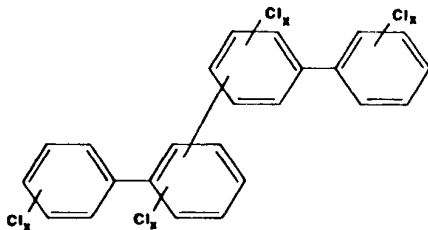


1,3,7-Trichlorodibenzofuran (a PCDF)

Trace levels of PCDF's have been detected in laboratory samples of U. S. PCB's, including specimens of both individually synthesized isomers and commercial mixtures (32,37). There are two plausible explanations for the presence of PCDF's in commercial PCB's: First, contamination may have occurred during manufacture, possibly as a result of oxygen in the benzene used to make the original biphenyl. Such contamination may have existed in French and Japanese PCB's, but apparently was not significantly present in American-made PCB's after one episode in 1933. Second, PCDF's may have been formed during usage as a result of high temperature oxidation. Oxidation experiments (31) report maximum conversion of Aroclor 1254 to total PCDF's as 2-3% at 550-600°C. Conditions suitable for significant conversion of PCB's to PCDF's did not exist in the normal manufacture of, and are not expected in the normal use of, capacitors and transformers, but may occur in high-temperature heat exchangers.

**PCB Composition
and Terminology**

A related group of molecular species mentioned in this paper are the polychlorinated quaterphenyls (PCQ's), which contain four phenyl units and a variable number of chlorine atoms as illustrated below:



Polychlorinated quaterphenyl (PCQ)

History of PCB Use

The Swann Chemical Co. began commercial U.S. production of PCB's in 1929. In 1935 Monsanto Industrial Chemicals Co. (Monsanto) purchased Swann and continued the manufacture of PCB's, initially at Anniston, Ala. and later at Sauget, Ill.

PCB's are excellent non-flammable, high-boiling, thermally and chemically stable dielectrics and solvents, and these properties led to a wide range of industrial applications. In addition to serving as dielectric fluids in capacitors and transformers, PCB's were used as plasticizers, hydraulic and heat exchange fluids, and were incorporated into such products as dust-settling agents, die-casting lubricants, inks, dyes, paints, pesticides and adhesives. PCB's were widely used in carbonless reproduction paper and entered paperboard production.

PCB's from such sources have entered into the environment. Slow biodegradability and bioaccumulation account for the presence of PCB's in sediments under rivers and lakes and in fish. Trace quantities have been found in some other food as well. As a result, PCB's are found in trace quantities in the blood and fatty tissue of the human populations of all industrial nations.

Concern over such accumulations in the environment led Monsanto in 1970 to begin voluntarily restricting PCB sales to manufacturers of sealed electrical equipment (33). In 1976 Congress enacted TSCA, which mandated a phaseout of PCB production and use. Although similar PCB phase-outs were instituted in Japan, Canada and Sweden, many other industrial nations (e.g., U.K., Germany, France, Spain and others) continue to permit PCB production and the manufacture of PCB-filled capacitors and transformers.

Estimates (34) for the cumulative total of U.S. industrial uses of PCB's from 1930 to 1975 and their service status in 1976 are noted in Table 1 below:

Table 1

Use	Millions of Pounds	
	Industrial PCB Purchases	PCB's Currently in Service
Capacitors	630	450
Transformers	335	300
Plasticizers	115	↑
Hydraulics and Lubricants	80	↑
Carbonless copy paper	45	8
Misc. industrial	28	↓
Heat transfer	20	↓
Total	1253	758

Section III

History of PCB Use

Estimates (34) of the status of these PCB's are shown in Table II below:

Table II

<u>Disposition</u>	<u>Millions of Pounds</u>
Environmentally biodegraded	30
Incinerated	25
Landfills and dumps	290
In soil, water, air and sediment	150
Currently in electrical service	750
In use other than electrical service	8
Total	1253

MONS 012018

Health Effects of PCB
and PCDF Mixtures

A. Observations on Test Animals

1. **General Bioeffects** PCB's resemble other fat-soluble chlorinated organic chemicals in biological uptake and internal transport. An animal can readily absorb PCB's through the lungs upon inhalation or through the intestines following ingestion, or less readily through the skin after physical contact. Fish can absorb PCB's through the food chain or through their gills, and the bioconcentration factors* can range between 10^3 and 10^6 . Once inside the body PCB's gradually distribute themselves equally among all fatty deposits present. Elimination processes are generally slow, especially for the more highly chlorinated homologs.

When increasing doses of PCB's are administered to animals the first observable effect is the induction, primarily in the liver, of the cellular enzymes variously known as "drug metabolizing" or "detoxification" enzymes, or as "mixed function" (i.e., chemically non-specific) oxidases. These enzymes catalyze chemical processes by which the animal's body seeks to convert lipid-soluble foreign chemicals into water-soluble substances excretable in the urine. Such effects are also produced by many other substances, and are generally regarded as physiological rather than pathological processes.

At high enough doses in animals, PCB's can induce many types of toxic effects and eventually death. The reported toxic effects with chronic exposure include chick edema disease and teratogenesis in chickens; liver hypertrophy, fibrosis, neoplasia and cancer in rodents; gastric and dermatological lesions in monkeys; and reproductive dysfunction in several species. An extensive literature on this subject is referenced in the bibliography (21-30).

There can be differences in toxicity between different PCB products, with the higher homologs generally being reported more toxic in chronic tests and the lower homologs more toxic in acute tests. There can also be large toxicity differences observed between different specimens of the same type of PCB, apparently caused by impurity-level variations.

2. **Impurity Effects** In 1970 a Dutch scientist, J.G. Vos, observed striking differences in chick embryotoxicity among three commercial PCB's that all contained 60% chlorine: Aroclor 1260 (which had virtually no effect), Clophen A60, and Phenoclor DP6. He then demonstrated that the variable toxic agent in the system was an impurity, polychlorinated dibenzofuran (PCDF) (35). He also showed that this impurity was responsible for chloracne in PCB dermal tests with rabbits (36).

It is not possible to determine if the toxic response variabilities observed in other PCB animal tests should be ascribed to variations in PCDF levels because, unfortunately, few of the investigators reported impurity levels in the PCB specimens they tested. Chemical analyses have sub-

*A bioconcentration factor is defined as the ratio of the PCB concentration in a fish to that in its ambient water.

Health Effects of PCB and PCDF Mixtures

sequently reported that European and Japanese PCB's contained 5-20 ppm PCDF as manufactured, while the U.S.-made Aroclors had 0-2 ppm (37).

3. Structure-Activity Relationships Many recent animal studies have aimed at relating the molecular structures of individual PCB, PCDF or similar molecules to their biological activities. These studies have shown that chloracne-genic activity is specifically associated with molecules shaped like flat rectangles with chlorines at the corners (32). All such chloracne-genic species are also capable of inducing one specific type of mixed function oxidase, designated cytochrome P448 because of its spectral absorption band position.

Most lower homolog PCB molecules do not induce P448; however, some higher chlorinated PCB homologs, which constitute a few percent of the higher Aroclors and which are virtually absent from the lower Aroclors, do exhibit moderate P448-inducing activity. By comparison, 2,3,7,8 -tetra-chlorodibenzofuran is 700 times as potent a P448 inducer in rats as the active PCB isomers and is many orders of magnitude more biologically potent than most other PCB and PCDF molecules (26 chap. 6).

4. Toxicity and Carcinogenicity Test Results Toxicity testing of PCB's in experimental animals has produced a large body of experimental observations. Repeated short-term feeding tests have shown the acute toxicities of PCB's in animals to be low, with LD₅₀ values reported from 1,300 to 11,300 mg per kg of body weight (29).

Concerns over chronic human health effects of chlorinated aromatic hydrocarbons (including PCB's) led to a series of 3-4 month inhalation tests in animals at the Harvard School of Public Health in the 1930's (38) and confirmatory tests at the University of Cincinnati's Kettering Laboratory in the 1950's (39). From the observations in both test series the investigators recommended threshold limit values (TLV's) of 1000 µg/m³ for PCB's with 42% chlorine or less, and 500 µg/m³ for the more highly chlorinated PCB mixtures. These TLV's, used by industry during the remaining period of PCB use, were accepted as standards by the American Conference of Governmental Industrial Hygienists (ACGIH) in 1956, and by OSHA in 1971, and were adopted by many other countries as well.

When PCB's are chronically administered to rats in increasing doses, there is apparently a dose-related progression from "no-effect", to mild, reversible effects (40) to serious irreversible liver disease. The observed progression of effects on rodent livers includes cellular enzyme induction, microsomal proliferation, cellular hypertrophy, focal necrosis, fibrosis and eventually the development of increasingly abnormal types of tissue (41,42, 43). In some of these tests in rodents, PCB's have been judged to show carcinogenic activity, while in other tests the same materials (Aroclor 1254 and 1260) were judged not to have shown carcinogenic activity (33, 42,43, 44).

Health Effects of PCB and PCDF Mixtures

Reports of positive carcinogenic findings in long-term tests of substances in rodents at high dosage levels, while prompting caution with respect to human exposure, are not an uncommon observation. General Electric has noted that in HEW's "Survey of Compounds Which Have Been Tested for Carcinogenic Activity", PHS Document 149, Vols. 4,5,6, & 7, 70% to 80% of all substances tested from 1960 to 1973 were reported to produce excess tumors in animals (45,46).

B. Human Health Effects Observations

1. Early Occupational Chloracne Reports During the first 35 years that PCB's were in industrial use, three American medical reports described unambiguous episodes of PCB-linked occupational illness.* Two involved PCB vapors from high-temperature equipment, and the other was ascribed to an unidentified impurity.

The first episode occurred in 1933 at the Swann Chemical Co. when 23 of 24 men working on the manufacture of PCB's almost simultaneously developed skin eruptions diagnosed as "chloracne." The eruptions were similar to adolescent acne, i.e., a progression of blackheads and pustules that persisted several months before disappearing. Some of the men also complained of lassitude but showed no clinical signs of ill health other than the skin condition. In their report on this PCB episode, the investigators concluded that the toxic agent was probably an unidentified impurity that appeared in the PCB when a new source of crude benzene was used for making the biphenyl (47). When purchase from this benzene source was discontinued and the process equipment better enclosed, the problem disappeared.

Chloracne was known by this time to be induced by chlorinated coal tar products and by chlorinated naphthalenes (Halowaxes). Later, occupational chloracne was frequently observed among electrical workers who handled "cable wax" containing the latter materials. Chloracne was found to clear up some time after the contact was removed and improved hygiene instituted. Concerns about long-term effects of chloracne have been addressed by a recent study, in which a group of 121 male chemical workers who had experienced a chloracne attack in 1949 (unrelated to PCB's) showed no excess in total mortality nor in cancer mortality after 29 years (48). A background incidence of chloracne in children in Northern Italy has been reported as 0.1-0.5% (26, p.331).

The second episode involving PCB's occurred in 1950 and 1951, when 7 of 14 people exposed to vapors (reported at 100 $\mu\text{g}/\text{m}^3$) from a leaky PCB-containing heat exchanger developed chloracne (49). A third episode was noted in the early 1960's when 13 of 16 people exposed to vapors from an oven in which PCB-plasticized enamels were being baked were similarly affected (50).

**Some other early papers confusingly associated PCB's with the health effects of certain other chlorinated hydrocarbons.*

Health Effects of PCB
and PCDF Mixtures

2. Yusho Episode Despite the long and relatively uneventful PCB occupational exposure experience the Japanese "Yusho" (oil-disease) incident in 1968 created a wave of concern. In that episode some 1300 people in southwestern Japan developed a very severe and persistent form of chloracne after eating rice oil found to have been contaminated by fluid leakage from a heat exchanger originally filled with Kanechlor 400, a Japanese PCB (51).*

In addition to the acne-like eruptions and feelings of lassitude previously observed in chloracne outbreaks, the Yusho victims commonly exhibited swelling of the upper eyelids, increased eye discharge, hyperpigmentation of the nails and skin, sweating of the palms and a variety of other individual effects. Signs of the disease were also transmitted in some cases to newborn children. The brown dermal pigmentation of these children is reported to have diminished with time. (26 chap. 9B1). In the same period a chick edema epidemic that killed 400,000 chickens was traced to consumption of feed containing the same rice oil. The first contaminant to be identified in the rice oil was Kanechlor, and a widespread demand for controls or elimination of all PCB's resulted.

After the Vos identification of PCDF impurities as the active toxic agent in two PCB animal test systems, Japanese scientists reanalyzed some of the rice oil specimens that had caused Yusho illness (52). From 1975 to 1978 it became known that these rice oil samples contained about 1000 ppm PCB's, 5 ppm PCDF's and 1000 ppm of another chlorinated material, later identified as polychlorinated quaterphenyl (52,53,54). The PCDF's and PCQ's presumably were formed from PCB's by thermal oxidation and condensation in the heat exchanger at high temperature. The apparent PCDF content of the leaking heat exchanger fluid, calculated from the above analysis of rice oil contaminants, is 2500 ppm (0.25%), a very high level compared to PCDF levels in U.S. electrical-grade PCB's as manufactured (0-2 ppm).

As the Yusho victims were estimated to have ingested an average of 2.0 gm of the heat exchanger fluid (51), this amount would have included about 1.0 gm each of PCB and PCQ, along with approximately 5 mg of PCDF. As will be noted later, 1.0 gm of PCB is less than the average body burden of heavily exposed capacitor workers; however, the Yusho victims apparently eliminated their PCB burdens more rapidly than capacitor workers, exhibiting nearly normal background levels of PCB's after 5 years. Nonetheless, many Yusho patients remained sick, and such autopsy liver samples as became available showed concentration of penta- and hexa-chlorinated PCDF's in that organ (52).

*A second episode, involving essentially identical circumstances and consequences, has just been reported from Taiwan (59).

Health Effects of PCB and PCDF Mixtures

These later Japanese investigations linked the disease to the PCDF content of the rice oil. This conclusion is consistent with PCDF activity in animal tests and with the observation that body burdens of electrical-grade PCB's (from inhalation and skin contact) larger than the PCB doses ingested by Yusho victims have not induced Yusho illness in capacitor workers.

The Japanese Yusho investigators also reported that the minimum dose for induction of the disease was about 0.5 gm of the thermally decomposed heat exchange fluid (the PCB-PCQ-PCDF mixture) (51). Using a range of reported PCDF analyses (52), the PCDF toxicity threshold dose might therefore be estimated at 1.0 - 1.5 mg.* A similar threshold dose (1.26 mg) has been estimated from data on the amount of PCDF consumed by patients before the onset of the symptoms in the recent episode in Taiwan (60).

3. Effects of Eating Fish Containing PCB's The Michigan Department of Public Health, under the sponsorship of FDA, conducted a study of 182 adults, 105 of whom consumed over 26 pounds of Great Lakes fish per year. A significant correlation between blood PCB levels and quantity of fish eaten was observed. The mean blood PCB value for the exposed group was 73 ppb, while that of the comparison group was 20 ppb. Individual blood PCB levels ranged from 7 ppb for a person who ate no fish to 366 ppb for one who ate 132 pounds per year (11,12).

Evaluation of health histories and current medical problems of the study subjects failed to identify a significant difference between the exposed and comparison groups. Symptoms characteristic of reported PCB toxicity (Yusho symptoms) were not found nor did those with the highest PCB levels have a consistent pattern of complaints or conditions. Although the data demonstrate an association between fish consumption and PCB levels in humans, no toxic manifestations from this exposure have been identified to date (12). The question of PCB accumulation over time and the effects of long-term exposure are being evaluated in a continuation of this study.

A recent study (61) of 458 persons who had significant exposure to DDT from eating fish also reported PCB blood levels (arithmetic mean, 22 µg/L; range 3.2 to 158 µg/L). The authors report that the following significant correlates of log diastolic blood pressure might account for 24.1% of its variation in this cohort: body mass index, 6.8%; sex, 8.3%; log PCB level, 6.3%; age, 1.5%; Hollingshead index, 1.1%.

4. Clinical Studies of Capacitor Workers The most extensive long-term exposure of humans to PCB's has probably occurred in capacitor plants around the world. (There were 17 capacitor plants using PCB's in

*A recent reanalysis of YUSHO patient data puts this figure at 0.6 mg (26 p. 291)

Health Effects of PCB
and PCDF Mixtures

the U.S.) Many employees in these plants had daily PCB skin contact for several years and inhaled PCB's at levels in the 100 to 1000 $\mu\text{g}/\text{m}^3$ range. General Electric's major capacitor fluid usage was originally Aroclor 1254, then changed to Aroclor 1242 around 1954, and subsequently to Aroclor 1016 (and some 1221) in 1971. This usage pattern was probably typical of the industry.

PCB blood tests of 174 heavily exposed GE capacitor workers have indicated a geometric mean* around 300 ppb and an arithmetic mean of about 500 ppb. Ten percent of the individuals' analyses were above 1000 ppb. A blood PCB value of 300 ppb roughly corresponds to a 100 ppm level in fatty tissue of the same individual, or a body content of about 1.5 gm (16). By comparison, mean serum PCB background levels for various groups of industrially unexposed persons in the U.S. range from 2-24 ppb (26 p.269).

In capacitor plants the most frequent PCB-related health effect observed was transient skin rashes affecting a small percentage of exposed employees. For example, analysis of GE medical records of the Ft. Edward and Hudson Falls, N.Y. plants for the 1960-1975 period showed a cumulative total of 49 contact and allergic dermatitis cases attributed to PCB's among an exposed employee group totalling about 1300 individuals (5). This condition responded to simple topical treatment and employee reassignment to other work areas. The medical records of this worker population have shown no obvious incidence of systemic disease attributable to PCB's. Additional studies (described below) are continuing.

Observations of high PCB blood levels, some dermal conditions and isolated cases of chloracne have been reported in the industrial hygiene literature of Japan, Finland, Australia and Italy (2,3,4,6,7,8). The reported biochemical examinations (2,3,4,6,7) identified scattered individual abnormalities in serum enzymes; however, on a group basis the various liver function tests were considered normal. The Italian chloracne cases of ref. 7 were observed in men who had worked where the level of Aroclor 1254 was measured at 5200-6800 $\mu\text{g}/\text{m}^3$ (10-14 times the U.S. TLV). Ref. 4 states that the Finnish capacitor workers are in good health and that, in spite of approximately 50 times larger PCB concentration in their blood compared with a control group, the researchers were unable to detect any biological effect caused by PCB in them.

In a 1977 U.S. study 32 capacitor workers were examined in a program sponsored by the South Carolina State Department of Health and Environmental Control (DHEC). Newspaper reports (January 1978) quote Dr. D.H. Robinson of the DHEC as saying that the study "clearly shows that at present there is no evidence of physical harm resulting from working with PCB's." Dr. Ira Rosenblum of Albany Medical College, who directed the study, is also quoted as stating, "it is exceedingly difficult

*The geometric mean of n numbers equals the n th root of their product.
For a log normally distributed population the geometric mean equals the median.

Health Effects of PCB and PCDF Mixtures

to establish a cause-effect relationship between exposure to PCB's in the workers' environment and any sign or symptom of acute disease of occupational origin (9)."

A study of occupationally exposed Bloomington, Ind. capacitor workers and other residents, reported in 1978, did not note liver injury, but found that levels of GGTP liver enzyme and plasma triglycerides were positively correlated with those of serum PCB's (10). No correlations were observed between serum PCB levels and five other liver function indicators. A letter to the study participants from the U.S. Center for Disease Control noted that human cancer risk would remain unknown until the extensive mortality study (reported below, ref. 15) then being conducted by NIOSH had been completed.

A broader clinical study of 224 Bloomington, Ind. capacitor workers was later conducted by NIOSH. The investigators reported in a preliminary draft (1981) that the plant employees' serum L-PCB levels* were 8 to 50 times, and their serum H-PCB levels* 2 to 4 times, the community background level (17). A parallel study was also conducted of 92 employees in two electric utilities, 39 of whom were active in the maintenance, repair and overhaul of transformers (18). A draft report covering both studies (63) stated that no clinical abnormalities directly attributable to PCB exposure were observed on physical examination. Serum SGOT, GGTP, triglycerides and HDL-cholesterol were within normal ranges. The first three of these parameters were correlated positively, and the last, negatively, with serum PCB levels.

One report at variance with this pattern of clinical studies describes a recently published study of 80 Italian capacitor workers who were chronically exposed to French and Italian PCB's containing 42% chlorine. PCB concentrations in air were reported from 48-275 $\mu\text{g}/\text{m}^3$, and skin absorption was noted. Fifteen of the 80 exhibited skin abnormalities, including 4 diagnosed as chloracne. Sixteen other workers were judged to show more or less pronounced hepatic involvement, as deduced from symptoms, clinical examination of the liver, and serum enzymes (19,20).

In 1976 Dr. Irving Selikoff of Mt. Sinai School of Medicine began a study of the health status of capacitor workers in the GE plants at Hudson Falls/Ft. Edward, N.Y. Three hundred twenty-six volunteers, some of whom had a long history of occupational exposure to PCB's, were given extensive medical examinations. In one paper the investigators reported average PCB blood levels of 124 ppb (lower homologs) plus 48 ppb (higher homologs) and noted a correlation between individual values and the estimated job exposure. A number of dermatological findings were reported, some of which showed an association with blood PCB levels of the higher

*L-PCB (lower homologs) and H-PCB (higher homologs) are defined as species having respectively shorter and longer gas chromatographic retention times than p,p'-DDE.

Health Effects of PCB and PCDF Mixtures

homologs. The authors noted a paucity of other abnormal findings on physical examination, including a very low prevalence of abnormal liver findings (13). In another 1979 paper the Mt. Sinai group reported that 14% of the workers examined had abnormal vital (lung) capacity, compared with 5.6% cited for Morris' non-smoking normal population (14, 62). We believe the significance of this observation is uncertain.

Medical surveillance by General Electric of a group of 174 heavily exposed capacitor workers has consisted of multiple examinations over the last four years. The GE service of this group averages over 15 years, and ranges from 1 to 35 years. About 20% of this study population is overweight, shows elevated serum triglycerides and periodic, mild elevations of fasting blood sugar. However, the medical examinations have not revealed serious health problems related to PCB exposure. The pulmonary function tests of the non-smokers in this heavily exposed population were in the normal range.

As previously noted, the serum PCB levels in this group are high (1979 arithmetic mean of 500 ppb with 10% of the individual analyses above 1000 ppb) and persistent. The only clinical parameter thus far found to be statistically correlated with the serum PCB level is that of serum triglycerides. The interpretation of this correlation is confounded by the fact that PCB's distribute equally among all lipid pools in the body, including those in the blood; and hence for any given PCB body burden the serum PCB level must vary directly as the level of serum lipids.

A rough correlation which is emerging from this study of GE capacitor workers is that people who are exposed to airborne PCB's for long periods may show an increase of about 0.5 ppb in their blood for each 1 $\mu\text{g}/\text{m}^3$ present. Thus long-term environmental exposure to air containing 2 $\mu\text{g}/\text{m}^3$ PCB might be expected to add about 1 ppb to an average person's 2-24 ppb PCB background level, a small amount compared with the normal background, and insignificant compared to levels reported in heavily exposed capacitor workers (30-3000 ppb ref. 17).

5. NIOSH Mortality Study. Three preliminary reports have suggested a possible epidemiological association between PCB exposure and human cancer (33,55,56). All of these have been regarded as inconclusive because they involved small groups of people, few deaths, uncertain levels of exposure to PCB's and to other chemicals, short latency intervals, and lack of consistency in cancer site. The International Agency for Research on Cancer evaluated the evidence available through 1979 for PCB's causing cancer in humans as "inadequate", meaning "insufficient to allow any conclusion regarding carcinogenicity for humans" (30). The FDA's assessment in 1979, based on review of both animal tests and the human reports, was that the question of carcinogenicity of PCB's was unresolved, though a matter worthy of further inquiry (57). Shortly thereafter, more definitive evidence became available from a long-term NIOSH study of two PCB-exposed capacitor worker populations.

Health Effects of PCB and PCDF Mixtures

A report of this NIOSH mortality study (15), by far the most comprehensive ever conducted concerning human PCB exposure, provides the best current data on mortality experience. This retrospective cohort, standardized mortality study includes 2567 PCB-exposed hourly capacitor workers in two plants, one of which was the GE Hudson Falls/Ft. Edward, N.Y. complex. The cohort was defined as all workers who accumulated at least three months employment in areas of the plant where there was potential for exposure to PCB's. Exposure in one plant began as early as 1938, in the other by 1946. A total of 39,018 person-years had been accumulated by the January 1, 1976 study cutoff. Personal air samples in the plants in April, 1977 ranged from 24 to 1260 $\mu\text{g}/\text{m}^3$ and area air samples from 3 to 810 $\mu\text{g}/\text{m}^3$ PCB's.

The NIOSH study reported that the incidence of all cancer mortality for these plant populations was slightly lower than that of the general U.S. population, or 39 deaths due to malignant neoplasms vs. 43.79 expected based on national norms adjusted for age and sex. For other causes of death the findings were as follows: from cardiovascular disease, 60 vs. 62.93 expected; from nervous system disease, 11 vs. 12.55 expected; from accidents, 13 vs. 18.29 expected; and from all other causes, 40 vs. 44.79 expected. Deaths from all causes were 163 vs. 182.35 expected.

No statistically significant excesses of specific cancer types were observed, though the authors called attention to four rectal and three liver cancer cases (5 of 7 in one plant). We believe this observation should be followed up by extension of the study time span, because these reported rectal and liver cancer cases are too few to be statistically meaningful. Liver cirrhosis deaths were higher than normal in one plant (with the possibility of some alcohol association noted) and lower in the other, with the total cohort experience about equal to national norms. None of the causes of death analyzed demonstrated a clear association with latency. There was no clear relationship between increasing lengths of employment in PCB-exposed jobs and the risk of mortality due to cancer or cirrhosis of the liver.

While the mortality experience reported in this paper is reassuring, it should be recognized that even this large study does not yet encompass enough person-years of experience to exclude the possibility that there might have been increased risk of some uncommon type of disease. Further, the plant populations described were not segregated between those in lightly vs. those in more heavily exposed jobs, which might have provided more data concerning dose-related differences.

Health Effects of PCB and PCDF Mixtures

C. Health Effects Summary

To summarize, there is now available a scientific literature of several hundred papers describing many facets of the biological behavior of PCB's in animals: routes and rates of uptake and elimination; bioaccumulation and persistence; enzyme induction; other pharmacological effects; and the effects of molecular structures of individual PCB molecules or impurities on biological activity. This literature includes early toxicological studies that led to recommendations to limit continuous occupational PCB exposure to 500 or 1000 $\mu\text{g}/\text{m}^3$ (depending on the degree of chlorination).

Nearly 50 years of experience has shown that electrical-grade PCB's, at industrial occupational exposure levels, are not acutely toxic to humans. A continuing concern about these materials has been potential chronic effects, since exposure to PCB's leads to accumulation in the body and retention for long time periods. The largest available source of data on such effects is presented by capacitor worker populations.

Thousands of such individuals received light to heavy exposures to PCB's of Aroclor types 1254, 1242, and 1016 over many years, and elevated levels of PCB's in their blood and fatty tissues continue to be observed. A number of clinical studies of such exposed worker groups have now been completed (2,3,4,5,6,7,8,9,10,13,14,16,17,19,20,63). Dermal reactions were noted in some cases. These included some rare observations of chloracne, especially in plants outside the U.S. Some studies report correlation of serum enzymes and triglycerides with serum PCB levels. In sum, the preponderance of these studies neither identify significant clinical disease associated with electrical-grade PCB exposure, nor provide persuasive evidence of health impairment. In addition, the NIOSH study of the long-term mortality experience of a large group of hourly capacitor workers at two plants showed no excess in total mortality, nor in mortality due to cancer, to cardiovascular disease or to nervous system disease.

A human hazard that was not recognized early was the possibility that PCB's used in high temperature environments, such as heat exchangers or baking operations at 270°C and higher, could be partially oxidized to PCDF's with a consequent increase in toxicity. This factor makes the YUSHO episode not directly relevant to the usual U.S. occupational or environmental exposure. Even in such special cases the health risk appears to be finite. The Japanese and Taiwanese Yusho investigations both provide evidence that the PCDF threshold dose for inducing Yusho illness is 0.6-1.5 mg. This may provide a benchmark for evaluating PCDF risk and for considering whether protective measures are needed when a PCDF level is identified in an environment (as, for example, in air with PCB's which have been overheated, or as trace quantities in the edible portion of fish). The available analyses indicate that U.S. electrical-grade PCB's contained 0-2 ppm PCDF's as manufactured. Such levels may be consider-

Health Effects of PCB and PCDF Mixtures

ed toxicologically insignificant since intake of about a kilogram of such PCB would be needed to acquire a threshold dose of PCDF. However, additional measurements are needed to check the PCDF levels in used PCB's.

In view of the lack of evidence for health damage in people with heavy PCB exposure in the past (daily skin contact and inhalation of air containing 100-1000 $\mu\text{g}/\text{m}^3$), there does not presently seem to be a substantial basis for concern about the effects of exposure to environments containing electrical-grade PCB's at the greatly reduced levels typically encountered today. Accordingly, while a confirmed blood or fat tissue PCB analysis* significantly higher than the local average may indicate exposure, there is little reason to believe that significant adverse health effects will occur. In the light of our present knowledge there is no further examination procedure or therapy which is likely to be meaningful.

While the lack of evidence for serious effects of electrical-grade PCB exposure on capacitor workers is encouraging, the studies available today do not completely rule out the possibility of subtle or infrequent effects in some individuals who were heavily exposed in the past, and more observation time is needed to reduce uncertainty about the very long-term experience of these people. Concerns about the reproductive experience of heavily exposed individuals also need to be addressed. The concluding section of this paper describes some on-going research programs that may resolve some of these uncertainties.

**Any unconfirmed single PCB analysis should be regarded cautiously: a recent round-robin study by the N.Y. State Department of Health showed at least one case where 2 out of 10 commercial analyses of the same sample reported PCB values that were 20-fold different from the median.*

U.S. PCB Regulations

The concern about environmental accumulation of PCB's and about possible human health effects led in 1976 to the enactment of Section 6(e) of TSCA. Section 6(e) directs EPA to prescribe PCB marking and disposal requirements; generally bans continued PCB use except in a "totally enclosed manner;" and generally bans PCB manufacture, processing and distribution. The PCB Disposal and Marking Rule and the PCB Ban Rule promulgated by EPA to implement Section 6(e) contain the following major features (58):

- Most items that contain 50 ppm (0.005%) or greater PCB must be labeled.
- All liquids that contain 500 ppm (0.05%) or greater PCB and PCB-containing capacitors with 3 lbs. or more dielectric fluid must be disposed of in an EPA-approved high temperature incinerator.
- All liquids that contain between 50 ppm and 500 ppm PCB must be disposed of in an EPA-approved high temperature incinerator, in a high efficiency boiler or in an EPA-approved chemical waste landfill.
- PCB-containing capacitors with less than 3 lbs. of dielectric fluid may be disposed of as municipal solid waste unless owned by a capacitor manufacturer or manufacturer of items that contain such capacitors (e.g., microwave ovens, electronic equipment and fluorescent light ballasts and fixtures). These manufacturers must dispose of their PCB-containing capacitors in an EPA-approved high-temperature incinerator.
- Waste oil that contains any detectable concentration of PCB's cannot be used as a sealant, coating or dust control agent.
- Most items and liquids that contain 50 ppm or greater PCB and that have been designated for disposal must be stored in compliance with specific requirements.
- PCB's contained in intact, non-leaking capacitors, transformers and electromagnets are being used in a "totally enclosed manner;"* therefore, such capacitors, transformers and electromagnets may remain in service.
- The manufacture, processing, distribution and use of PCB's in concentrations below 50 ppm may continue without restriction*.

*A recent court decision requires EPA to re-examine this determination.

U.S. PCB Regulations

- Eleven uses of PCB's in other than a "totally enclosed manner" (including servicing transformers and electromagnets and PCB use in existing stocks of carbonless copy paper, in pigments and in heat transfer and hydraulic systems) may continue subject to certain conditions and time limits.

The FDA has established tolerances for unavoidable residues of PCB's in several classes of food. Present tolerances are given below (57):

Milk and dairy products	1.5 ppm (fat basis)
Poultry	3 ppm
Eggs	0.3 ppm
Fish and shellfish (edible portion)	5 ppm *

**In 1979 the FDA reduced the tolerance for fish and shellfish to 2 ppm, but stayed the effective date of the 2 ppm tolerance pending resolution of objections.*

On-Going Research
Programs

Notwithstanding the experience of 50 years usage and the extensive research which has been completed, some questions and uncertainties remain. General Electric and others are continuing research on some of these issues.

The actual PCDF content of PCB's in existing capacitors and transformers as well as in various environmental samples needs to be determined. Based on the reported PCDF content of Aroclors (0-2 ppm), one may postulate that PCDF's will be detected in such minute quantities that they should not be of concern. This postulate needs to be validated by analysis and evaluation, and GE is conducting an analytical research program to make such data available.

A number of medical research programs that will further clarify the possible PCB health effects are continuing. With the cooperation of General Electric, New York State's Department of Health (Dr. Philip R. Taylor) is analyzing further the epidemiology of the GE capacitor worker population, and is extending the research to include reproductive experience. General Electric is continuing medical research with a group of heavily exposed capacitor workers; and some additional observations may become available from the Mt. Sinai School of Medicine's studies of other workers at the same location. The Michigan State Department of Health (Dr. H.E.B. Humphrey) is extending and broadening its study of individuals who have ingested PCB's by eating fish.

Another question concerns industrial exposures of transformer workers. Transformer plants typically used Aroclor 1254 and 1260, usually mixed with chlorobenzenes, for a portion of their production, whereas Aroclor 1260 was not used in capacitors. Few epidemiological studies of transformer workers exposed to PCB's are available. The capacitor worker experience may be relevant, however, as Aroclors 1254 and 1260 contain substantially overlapping though not identical populations of PCB molecules. In addition, capacitor worker blood analyses show retention of the molecules contained in Aroclor 1260.

Lastly, some research programs are being directed at economically effective PCB containment and destruction processes in order to respond more effectively to Federal and State requirements. General Electric is active in some of these programs.

References Cited

1. J.H. Highland, et al, "Malignant Neglect", Alfred A. Knopf, New York, 1979, Chapter 3.
2. Hasegawa, H., Sato, M., and Tsuruta, H., PCB Concentration in the Blood of Workers Handling PCB, *Occup. Health*, 10, 50 (1972). (In Japanese).
3. Kitamura, M., Tsukamoto, T., Sumino, K., Hayakawa, K., Shibata, T., and Hirano, I., The PCB Levels in the Blood of Workers Employed in a Condenser Factory, Japan *J. Ind. Health*, 47, 354 (1973). (In Japanese).
4. Karppanen, E. and Kolho, L., The Concentration of PCB in Human Blood and Adipose Tissue in Three Different Research Groups, *Proceedings of PCB Conference II*, Solna, Sweden, 1972, National Swedish Environmental Protection Board, Stockholm, 1973, pp. 124-8.
5. General Electric response to interrogatory #17, N.Y. State Dept. of Environmental Conservation Proceeding, File No. 2833, Dec. 1, 1975.
6. Ouw, H. K., Simpson, G.R., and Siyali, D.S., Use and Health Effects of Aroclor 1242, a Polychlorinated Biphenyl, in an Electrical Industry, *Arch. Environ. Health*, 31, 189 (1976).
7. Puccinelli, V., On Chloracne, *Med. d. Lavoro*, 45, 131 (1954) (In Italian).
8. Hofman, M.F., and Meneghini, C.L., Concerning Folliculosis Caused by Chlorosubstituted Hydrocarbons, *G. Ital. Dermatol. Sifilol*, 103, 427 (1962) (In Italian).
9. South Carolina Dept. of Health and Environmental Control, Study of Sangamo Capacitor Division Workers, (Press Report). Jan. 1978.
10. Polychlorinated Biphenyl Exposure - Indiana, Center for Disease Control, Morbidity and Mortality Weekly Report, Mar. 24, 1978.
11. Michigan Dept. of Public Health, Final Report on FDA Contract 223-73-2209, Evaluation of Changes in the Level of Polychlorinated Biphenyls (PCB's) in Human Tissue, 1975.
12. Humphrey, H.E.B., Evaluation of Humans Exposed to Halogenated Biphenyls, *Am. Chem. Soc. Div. Environ. Chem. Preprints*, 20 No. 2, 272 (1980).

-
13. Fischbein, A., Wolff, M.S., Lillis, R., Thornton, J., and Seli-koff, I.J., Clinical Findings among PCB-Exposed Capacitor Manu-facturing Workers, *Ann., N.Y. Acad. Sci.*, 320, 703 (1979).
 14. Warshaw, R. Fischbein, A., Thornton, J., Miller, A., and Seli-koff, I.J., Decrease in Vital Capacity in PCB-Exposed Workers in a Capacitor Manufacturing Facility, *Ann. N.Y. Acad. Sci.*, 320, 277 (1979).
 15. Brown, D.P., and Jones, M., Mortality and Industrial Hygiene Study of Workers Exposed to Polychlorinated Biphenyls, *Arch. Env. Health*, 36, 120 (1981).
 16. Lawton, R.W., Ross, M. R., and Feingold, J., GE Draft Report (1981).
 17. Smith, A.B., Schloemer, J., Lowry, L.K., Smallwood, A.W., Ligo, R.N., Tanaka, S., Stringer, W., Jones, M., and Glueck, C.J., Draft report: Cross-Sectional Medical Survey of a Group of Workers Occupationally Exposed to Polychlorinated Biphenyls (PCB's) at an Electrical Equipment Manufacturing Plant, National Institute for Occupational Safety and Health, Division of Sur-veillance, Hazard Evaluations and Field Studies, Cincinnati, OH 45226, and Lipid Research Center, University of Cincinnati Medical Center. Cincinnati, OH 45267, 1981.
 18. Smith, A.B., Schloemer, J., Lowry, L.K., Smallwood, A.W., Ligo, R.N., Tanaka, S., Stringer, W., Jones, M., Herven, R., and Glueck, C.J., Draft report: Cross-Sectional Medical Survey of Two Groups of Workers Occupationally Exposed to Polychlorinated Biphenyls (PCB's) in the Maintenance, Repair, and Over-haul of Electrical Transformers, *Ibid.*, 1981.
 19. Maroni, M., Colombi, A., Cantoni, S., Ferioli, E., and Foa, V., Occupational Exposure to Polychlorinated Biphenyls in Electrical Workers. I Environmental and Blood Polychlorinated Biphenyls Concentrations, *Brit. J. Ind. Med.*, 38, 49 (1981).
 20. Maroni, M., Colombi, A., Cantoni, S., Ferioli, E., and Foa, V., Occupational Exposure to Polychlorinated Biphenyls in Electrical Workers. II Health Effects, *Ibid.*, 38, 55 (1981).
 21. NIEHS Conference on Polychlorinated Biphenyls ,*Environ. Health Perspec.*, 1, (1972).
 22. NIEHS Conference on Chlorinated Dibenzodioxins and Dibenzo-furans, *Environ. Health Perspec.*, 5, (1973).
 23. Proceedings of the National Conference on Polychlorinated Biphenyls, November 19-21, 1975, Chicago, Ill., EPA - 560/6-75-004, March, 1976.
-

-
24. Health Effects of Halogenated Aromatic Hydrocarbons, Ann. N.Y. Acad. of Sci., 320, (1979).
 25. Proceedings of the Conference "PCB's Impacts on Health," September 12, 1979, Hartford, Conn. Transcript by Conn. Dept. of Environmental Protection, Oct. 1, 1979.
 26. "Halogenated Biphenyls, Terphenyls, Naphthalenes, Dibenzodioxins and Related Products", Kimbrough, R.D., Ed., Elsevier/North Holland Biomedical Press, Amsterdam, 1980.
 27. Fishbein, L., Toxicity of Chlorinated Biphenyls, Ann. Rev. Pharmacol., 14, 139 (1974).
 28. Criteria for a Recommended Standard: Occupational Exposure to Polychlorinated Biphenyls (PCB's), DHEW (NIOSH) Publ. 77-225, Sept., 1977.
 29. Polychlorinated Biphenyls and Polybrominated Biphenyls, International Agency for Research on Cancer Monographs, 18, (1978).
 30. International Agency for Research on Cancer Monographs, Supplement 1 to Vols. 1-20, (1979).
 31. Buser, H.R., Bosshardt, H.P., and Rappe, C., Formation of Polychlorinated Dibenzofurans (PCDF's) from the Pyrolysis of PCB's, Chemosphere, 1, 109 (1978).
 32. Goldstein, J.A., The Structure-Activity Relationships of Halogenated Biphenyls as Enzyme Inducers, Ann. N.Y. Acad. Sci., 320, 164 (1979).
 33. Monsanto Co., Submission to the Subcommittee on Oversight and Investigations of the Committee on Interstate and Foreign Commerce, U.S. House of Representatives, Nov. 16, 1979.
 34. "PCB's in the United States; Industrial Use and Environmental Distribution", Versar, Inc. EPA Contract No. 68013259. U.S. Dept. of Commerce, NTIS PB 252012, Feb. 25, 1976.
 35. Vos, J.G., Koeman, J.H., van der Maas, H.L., ten Noeverde de Brauw, M.C. and de Vos, R.H., Identification and Toxicological Evaluation of Chlorinated Dibenzofuran and Chlorinated Naphthalene in Two Commercial Polychlorinated Biphenyls, Fd. Cosmet. Toxicol., 8, 625 (1970).
 36. Vos, J.G., and Beems, R.B., Dermal Toxicity Studies of Technical Polychlorinated Biphenyls and Fraction Thereof in Rabbits. Toxicol. Appl. Pharmacol., 19 617 (1971).
-

-
37. Bowes, G.W., Mulvihill, M.J., Simoneit, B.R.T., Burlingame, A.L., and Risebrough, R.W., Identification of Chlorinated Dibenzofurans in American Polychlorinated Biphenyls, *Nature*, 256, 305 (1975.)
 38. Drinker, C.K., Warren, M.F., Bennett, G.A., The Problem of Possible Systemic Effects from Certain Chlorinated Hydrocarbons, *J. Ind. Hyg. Toxicol.* 19, 283 (1937).
 39. Treon, J.F., Cleveland, F.P., Cappel, J.W. and Atchley, R.W., The Toxicity of the Vapors of Aroclor 1242 and Aroclor 1254, *Am. Ind. Hyg. Assoc. Quart.* 17, 204 (1956).
 40. Burse, V.W., Kimbrough, R.D., Villanueva, E.C., Jennings, R.W., Linder, R.E., and Sorocool, G., Polychlorinated Biphenyls, Storage, Distribution, Excretion, and Recovery: Liver Morphology After Prolonged Dietary Ingestion, *Arch. Environ. Health*, 29, 301 (1974).
 41. Kimbrough, R.D., Linder, R.E. and Gaines, T.B., Morphological Changes in Livers of Rats Fed Polychlorinated Biphenyls, Light Microscopy and Ultrastructure, *Arch. Ind. Health*, 25 354 (1972).
 42. Kimbrough, R.D. and Linder, R.E., Induction of Adenofibrosis and Hepatomas of the Liver in BALB/CJ Mice by Polychlorinated Biphenyls (Aroclor 1254), *J. Natl. Cancer Inst.*, 53, 547 (1974).
 43. Kimbrough, R.D., Squire, R.A., Linder, R.E., Strandberg, J.D., Montali, R.J. and Burse, V.W., Induction of Liver Tumors in Sherman Strain Female Rats by Polychlorinated Biphenyl Aroclor 1260, *J. Natl. Cancer Inst.*, 55, 1453 (1975).
 44. "Bioassay of Aroclor 1254 for Possible Carcinogenicity." Carcinogenesis Program, Div. of Cancer Cause and Prevention, Nat'l. Cancer Inst., Report No. (NIH) 78-838, (1978).
 45. Testimony of the General Electric Company, OSHA Carcinogen Policy Hearing, Wash., D.C., Dr. T.R. Casey, Vice-President. Cancer Policy OSHA Docket H-090, Ex. 152. July 20, 1978.
 46. General Electric Co. comments re Regulatory Council statement on Regulation of Carcinogens (44 FR 60038), Nov. 13, 1979, J.F. Young, Vice-President; and similar comment addressed to the Interagency Research Liaison Group, Nov. 28, 1979, and to the EPA, Feb. 21, 1980.
 47. Jones, J.W., and Alden, H.S., An Acneform Dermatogosis, *Arch. Dermat. Syphilol*, 33, 1022 (1936).
 48. Zack, J.A. and Suskind, R.R., The Mortality Experience of Workers Exposed to Tetrachlorodibenzodioxin in a Trichlorophenol Process Accident, *J. Occupat. Med.*, 22, 11 (1980).
-

-
49. Meigs, J.W., Albom, J.J., and Kartin, B.L., Chloracne from an Unusual Exposure to Aroclor, *J. Am. Med. Assoc.*, 154: 1417 (1954).
 50. Birmingham, D.J., *Occupational Dermatology: Current Problems, Skin*, 38 (Feb. 1964).
 51. Kuratsune, M., Yoshimura, T., Matsuzaka, J., and Yamaguchi, A., Epidemiologic Study on Yusho, A Poisoning Caused by Ingestion of Rice Oil Contaminated with a Commercial Brand of Polychlorinated Biphenyls, *Environ. Health Perspec.*, 1, 119 (1972).
 52. Kuratsune, M., Masuda, Y., and Nagayama, J., Some of the Recent Findings Concerning Yusho, *Proceedings of the National Conference on Polychlorinated Biphenyls, November 19-21, 1975, Chicago, Ill.* EPA-560/675-004, March, 1976, p. 14.
 53. Food and Drug Administration, "Polychlorinated Biphenyls (PCB's); Unavoidable Contaminants in Food and Food Packaging Materials; Reduction of Temporary Tolerances," *Fed. Register* 42, 17488 (1977).
 54. Kamps, L.R., Trotter, W.J., Young, S.J., Carson, L.J., Roach, J.A.G., Sphon, J.A., Tanner, J.T., and McMahon, B., Polychlorinated Quaterphenyls Identified in Rice Oil Associated with Japanese "Yusho" Poisoning, *Bull. Environ. Contam. Toxicol.*, 20 589 (1978).
 55. Bahn, A.K., Rosenwaite, I., Herrmann, N., Grover, P., Stellman, J., and O'Leary, K., letter, "Melanoma After Exposure to PCB's", *New Eng. J. Med.*, Aug. 19, 1976; Lawrence, C., Comment, "PCB? and Melanoma"; Bahn, A.K. et al., reply, *ibid.*, Jan. 13, 1977.
 56. Urabe, H., Koda, H., and Asahi, M., Present State of Yusho Patients, *N.Y. Acad. of Sci. Ann.*, 320, 273 (1979).
 57. Food and Drug Administration, "Polychlorinated Biphenyls (PCB's); Reduction of Tolerances, *Fed. Register*, 44, 38330, June 29, 1979.
 58. Environmental Protection Agency, "Polychlorinated Biphenyls (PCB's) Manufacturing, Processing, Distribution in Commerce, and Use Prohibitions, *Fed. Register*, 44, 31514, May 31, 1979.
 59. Lan, C., Shieh, L., Chen, P.H., Chen, Y., An Epidemiological Study on Polychlorinated Biphenyls Poisoning in Taichung Area, *Clin. Med. (Taipei)*, 1, 96 (1981).
 60. Chen, P.H., Chang, K.T., and Lu, Y.D., Toxic Compounds in the Cooking Oil which Caused PCB Poisoning in Taiwan. I. Levels of Polychlorinated Biphenyls and Polychlorinated Dibenzofurans, *ibid.*, 1, 71 (1981).
-

-
61. Kreiss, K., Zack, M.M., Kimbrough R.D., Needham, L.L., Smrek, A.L. and Jones, B.T., Association of Blood Pressure and Polychlorinated Biphenyl Levels, J.Am. Med. Assoc., 245, 2505 (1981).
 62. Morris, J.F., Kolski, A. and Johnson, L.C., Spirometric Standards for Healthy Nonsmoking Adults, Am. Rev. Respirat. Dis., 103, 57 (1971).
 63. Smith, A.B., Schloemer, J., Lowry, L.K., Smallwood, A.W., Ligo, R.N., Tanaka, S., Stringer, W., Jones, M., Hervin, R. and Glueck, C.J., Metabolic and Health Consequences of Occupational Exposure to Polychlorinated Biphenyls (PCB's), NIOSH, Div. of Surveillance, Hazard Evaluations and Field Studies 4676 Columbia Pkwy., Cincinnati, OH 45226, and Lipid Research Center, Univ. of Cincinnati Medical Center, Cincinnati, OH 45267 (1981).

This paper has been prepared for use within the General Electric Company.

Corporate Health and Safety Operation

GENERAL  ELECTRIC

MONS 012039