Monsanto

Dept. of Medicine & Environmental Health [redacted]-8805

DATE December 30, 1980 cc J. H. Spraul

SUBJECT General Electric PCB Paper

REFERENCE

TO George Roush

I think this is an excellent paper for the purpose that Dr. Casey describes, i.e., for internal management consumption. For external publishing, more technical detail in certain areas would be desirable, particularly on page one (1) discussing the Japanese Yusho incident. The technical analysis concerning the presence of dibenzofurans should be specifically cited.

Jim Spraul's reference to Higuchi's book on PCB Poisoning and Pollution, particularly his reference to page 65, is a misquote. That particular reference stated that the specific materials that had been quoted in the test in that paragraph had been carefully examined to rule out contamination by chlorinated dibenzofurans or benzodioxins. It did not refer to the actual samples of Yusho Rice Oil that caused the outbreak in Japan.

I think that the table on page 12 should be looked at very carefully and conclusions drawn. Specifically, the three studies alleging to show liver cancers in animals, and in fact the only three studies that purport to show cancer as a result of PCB's, all have the same name on them, our friend Renate Kimbrough. I think that a rigid analysis of those three studies as published should be performed by the authors of this paper. This effort should show that these studies are overdrawn as to conclusions. Specifically, hepatomas of mice should be addressed as not representing carinomas but in fact are a benign process.

Furthermore, this study does not address at all the question of PCB contamination of mother's milk and the effects of this or lack of them on the new born. This is a natural area of inquiry as to the persistent effects and the bioconcentration effect of PCB's. The correlation of fat sample levels in humans to blood levels and mother's milk levels should also be addressed, as this has been written about in the literature.

Except for these three minor points which I feel would add to the paper, I feel it's an excellently condensed piece of work and either in present or modified form should be submitted for publication in the referenced press.

Don

Donald L. Coleman, M.D.

IN 10M (REV. 2/78)/ab

MONS 209667

Monsanto

FROM (NAME LOCATION PHONE) Dept. of Medicine & Environmental Health J. H. Spraul, M.D. -G2WF-8807

DATE December 23, 1980 cc D. L. Coleman, M.D.

SUBJECT General Electric PCB Paper

REFERENCE

TO George Roush, Jr., M.D.

I think this is an excellent article. It seems to have the qualities of a graduate school thesis. I feel it would be good to encourage rapid publication of this paper for several reasons, including the legal implications and the current controversies in science. It would clarify the issue for some physicians who are trying to deal with questionable medical problems related to this subject.

I have no serious misgivings about any section of the paper. There were merely a few editorial and typographical type of changes required.

Originally I had some concerns about the refuting of the Yusho studies on the basis of the dibenzofurans. This statement I make particularly in view of the dismissal of this concept in articles such as the book edited by Higuchi on PCB Poisoning and Pollution, which is published by Academic Press in which they state on Page 65 that the "contamination with dibenzofurans or benzodioxins has been ruled out by careful gas chromatographic examination". The refutation later in the paper, I think, covers this issue adequately, but does not address the fact specifically that some have said "yes" and others have said "no".

Overall, the paper is an excellent presentation of the history, uses, chemical structure, and health effects of PCB's. The extensive clinical studies of General Electric make an excellent case for confirming the lack of health hazards associated with this material.

Particularly, with the likelihood of small studies scattered in various locations that might come out in the future and might indicate an excess of one condition or another without a good, solid statistical base, the material in this particular paper ought to be widely disseminated as soon as possible.

Jim

James H. Spraul, M.D.

/ab

MONS 209668

IN-10M (REV. 2/78)

GENERAL ELECTRIC
GENERAL ELECTRIC COMPANY
3135 EASTON TPK., FAIRFIELD, CONN. 06431

THOMAS R. CASEY, M. D.
VICE PRESIDENT AND COMPANY MEDICAL DIRECTOR

December 15, 1980

George Roush, Jr., M. D.
Medical Director
Monsanto Company
800 N. Lindbergh Blvd.
St. Louis, MO 63166

Dear George:

First of all, thanks for agreeing to review and comment on the enclosed paper, "Human Health Effects of Electrical Grade PCBs". The document has had several internal reviews in GE and after a while, you feel like you're drinking your own bath water. That is why we have asked a few who are knowledgeable about PCBs to comment on the accuracy and content of the paper.

As for background, General Electric is frequently called upon to act or comment responsibly in PCB situations and, therefore, we have a need to inform our people and to establish a public posture on the question of human health effects. The authors of the enclosed draft were asked to review GE's experience and the scientific literature and to summarize the relevant health effects data. The paper is intended primarily to acquaint GE managers and Company physicians with appropriate perspectives on PCBs.

I believe I mentioned on the phone that according to your wishes, your comments can either be acknowledged in the paper or remain anonymous. Would you also indicate whether you care to be acknowledged as having reviewed the document.

Again, my thanks for your consideration and cooperation.

Sincerely,

Casey

TRC/je
Enclosure

HUMAN HEALTH EFFECTS

OF

ELECTRICAL GRADE PCB's

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DRAFT December 1, 1980

PLEASE DO NOT COPY

MONS 209670

Executive Summary

Definition of any actual human health hazard posed by the polychlorinated biphenyls (PCB's) continues to be an important issue, since their potential for human exposure cannot be eliminated completely.

PCB's were widely used in the United States for nearly 50 years chiefly as dielectric fluids and plasticizers. They are now controlled by law because they are a persistent environmental contaminant, and because they are popularly believed to be very toxic. Although PCB use in new products has been banned, 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; and small, but measureable levels are present in some fish available for consumption.

The available animal data show that PCB's, like many other substances, can produce toxic effects in animals under the conditions of toxicity testing. However, the doses required to produce such effects are usually large with respect to body weight. Toxicity in humans is not so readily demonstrated.

In the Japanese Yusho disease episode, which followed eating rice oil contaminated by a PCB fluid leakage, the key toxic agent is now thought to have been a PCDF contaminant, present at exceptionally high levels in the thermally decomposed heat exchange fluid. The presence of PCDF impurities also appears indicated in some incidents when PCB's were found to cause human chloracne.

The conditions required to convert PCB's to PCDF's may be encountered in high temperature heat exchangers or bake ovens, but not ordinarily in the manufacture or use of electrical equipment (the major past use of PCB's), nor that of plastioizers, oarbon paper, or printing inks (the main secondary uses). Available data indicates toxicologically insignificant (0-2 ppm) levels of PCDF's in U.S.-made electrical grade PCB's as manufactured, though additional research is needed to confirm the level in certain environments.

The most extensive data on PCB human health effects comes from an increasing number of occupational health studies of capacitor workers. Thousands of such individuals received heavy exposure to PCB's of Aroclor types 1254,1242, and 1016 over many years. While additional research may be needed to rigorously exclude all possibilities of subtle or infrequent health damage in such individuals, all common indicators, such as clinical examination findings, health complaints, or death rates due to cardiovascular disease, cancer, or nervous system disease indicate lack of serious health impairment. A recent study by NIOSH, which documents the long-term experience of a large group of such workers, found no excess of total mortality nor of overall cancer mortality.

In view of the paucity of evidence for health damage in people who had heavy PCB exposure in the past (daily skin contact and air inhalation levels from 100-1000 ug/m^3), there seems to be little basis for concern over the effects of occasional exposure to environments containing electrical grade PCB's at the levels which may typically be encountered today (e.g. 0.1-10 ug/m^3 in air or occasional skin contact).

HUMAN HEALTH EFFECTS OF ELECTRICAL GRADE PCB'S

I Introduction

At present, Company managers, employees, physicians, and public officials concerned with appropriate handling of situations involving human exposure to PCB's face a contradictory array of information on their 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 posing human exposure at any level as hazardous and alarming. This sentiment is also reflected in national bans on new PCB use and regulations for PCB control, transport, storage, and disposal in the U.S.

On the other hand, European countries have apparently made a different assessment, because new PCB usage in closed electrical equipment, with attendant occupational exposures during manufacture and service, continues as before. Moreover, an increasing number of medical studies of human populations which were heavily-exposed to PCB's continue to reveal absence of significant human health problems (2,3,4,5,6,7,8,9,10). Public statements by knowledgeable health authorities and scientists are sometimes so hedged as to make the authors' positions unclear.

In order to provide perspective for General Electric managers and physicians, to help identify situations of human exposure to PCB's which actually might present cause for concern, and to outline some future needed research, the writers have undertaken this paper. It draws on extensive GE experience in plants manufacturing PCB-filled capacitors, as well as on review and analysis of the scientific literature.

The PCB literature is voluminous, comprising several thousand original articles. The present paper will not attempt to survey all aspects of this information, but will focus on those portions most relevant to human health effects evaluation. Literature citations have been included in the bibliography, as have condensations of much of the health-related material in the form of conference reports (11,12,13,14,15) and several review articles (Kimbrough (16), Fishbein (17), NIOSH Criteria Document (18), and the IARC Monographs (19,37).

Many quantitative observations are included in this paper because these are critically important to any health effects perspective. The fact that PCB's are detectable does not necessarily mean that they are toxicologically significant.

The paper's content is organized as follows:

I Introduction

II PCB Composition and Terminology

III History of PCB Use

IV Health Effects of PCB and PCDF Mixtures

A. Animal Test Results

1. General bioeffects
2. Tolerance levels
3. Impurity effects
4. Structure-activity relationships
5. Carcinogenicity test results

B. Human Health Effects Observations

1. Early occupational chloracne
2. Yusho episode
3. Effects of eating PCB-contaminated fish
4. Occupationally-exposed capacitor workers
5. NIOSH epidemiology study

V U.S. PCB Regulations

VI On-going Programs

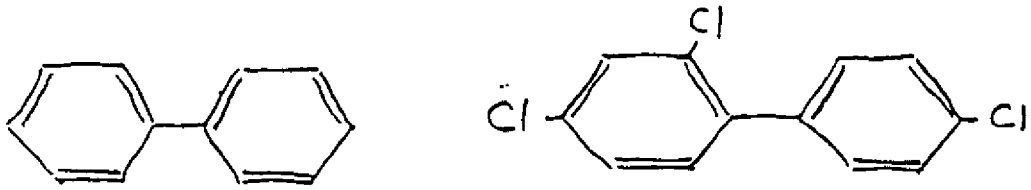
VII References Cited

Abbreviations which may be unfamiliar to some readers include:

ppm	parts per million
ppb	parts per billion
kg.	kilogram; 1000 grams or 2.2 pounds
gm.	gram (s) or 1/28 oz.
mg.	milligram; one thousandths of a gram
ug/m^3	micrograms (millionths of a gram) per cubic meter
LD_{50}	an acute toxicity measurement meaning lethal dose for 50% of the test species

II 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 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 (PCB)

Usually "PCB" is used as a generic term, not as the name of any one individual type of molecule.

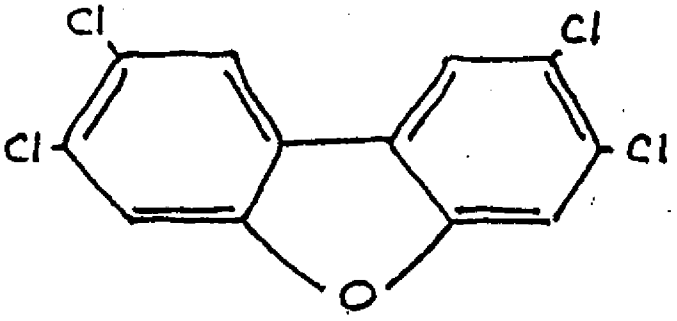
There are 209 theoretically-possible PCB molecules, differing in the numbers (homologs) and positions (isomers) of the attached chlorines; of these 209 species, about half have been actually identified among the complex PCB mixtures that constituted the commercial PCB products. These products ranged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

The manufacturers of the PCB's sold them under brand names, e.g., "Aroclor" (Monsanto, USA); "Phenoclor" (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.

The major electrical users of PCB's subjected these commercial products to further purification to insure electrical performance, blended them with stabilizers and diluents, and then put them into use under their own brand names and product numbers. General Electric's generic name was "Pyranol"; Westinghouse's was "Inerteen". "Askarel" is an industry term for a PCB or other fire-resistant dielectric fluid.

In short, the material that we now refer to as a "PCB" could have originally had a variety of brand and product names and it was a complex mixture of chemicals. It always contained several dozen individual PCB isomers and homologs clustered around some average degree of chlorination, not infrequently some trichlorobenzenes as diluents, often about 0.5% of an aliphatic epoxide as a stablizer, and parts-per-million levels of trace impurities, such as polychlorinated methylbiphenyls, polychlorinated terphenyls, polychlorinated naphthalenes, and sometimes polychlorinated dibenzofurans (PCDF's).

Returning to chemical terminology, "furan" denotes a structural arrangement comprising a ring of four carbon atoms and one oxygen; "benzo" an arrangement of four carbon atoms fused onto an adjacent pair in some other structure so as to form a six-membered ring; and hence "dibenzofuran" a tricyclic arrangement of two benzene rings and one furan ring fused together. This arrangement can result if an oxygen atom is added to a biphenyl system. If chlorine atoms are attached to this nucleus, then a "polychlorinated dibenzofuran", or PCDF, results.

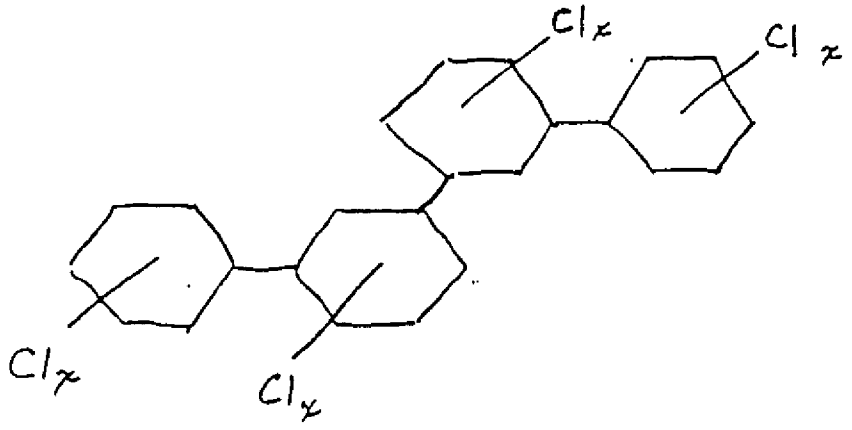


2,3,7,8 tetrachlorodibenzofuran (PCDF)

Trace levels of PCDF (or other species giving PCDF color tests) have been detected in laboratory samples of U.S. PCB's, including specimens of individually synthesized isomers as well as those of commercial mixtures (20,21).

We know of two ways that PCDF's get into commercial PCB's; first, contamination may occur during manufacture, possibly as a result of oxygen in the benzene used to make the original biphenyl. Such contamination may have been present in French and Japanese PCB's, but apparently not significantly in American-made PCB after one episode in 1933. Second, the PCDFs may be formed as a result of high temperature oxidation (e.g., a week above 500°F, or a few seconds at 900°F). Such conditions are not expected in the normal manufacture or use of capacitors and transformers, but may occur in high temperature heat exchangers.

Another related molecular species are the polychlorinated quaterphenyls, (PCQ's) which contain four phenyl units and a variable number of chlorine atoms:



Polychlorinated quaterphenyl (PCQ)

III History of PCB Use

PCB materials have had a long history of use in the U.S. and throughout the world. Monsanto (and the Swann chemical predecessor plant) was the sole U.S. producer, manufacturing PCB's from 1929 to 1977, initially at Anniston, Alabama, and later at Sauget, Illinois.

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 fluids, heat exchange fluids, dust-settling agents, die-casting lubricants, and in paints. They were widely used in printing ink formulas and in carbonless reproduction paper, and they entered paperboard production. Transport of PCB's from these products into the environment, combined with their slow biodegradability and high bioaccumulation factors, resulted in their persistence in sediments under rivers and lakes, accumulations in fish, and entry, in trace quantities, into human food. As a result, PCB's are found (in trace quantities) in the blood and fatty tissue of almost all human populations.

Concern over such accumulations in the environment led Monsanto in 1970 to begin restricting PCB sales voluntarily to manufacturers of sealed electrical equipment (27). A phaseout of PCB use in the U.S. was mandated by Congress in the Toxic Substances Control Act of 1976, and specific regulations to achieve this purpose were completed by EPA in 1979. Although similar PCB phaseouts were instituted in Japan, Canada, and Sweden, other industrial nations (e.g., U.K., Germany, France, Italy, Spain and others) continue to permit new PCB use in closed electrical applications.

Estimates for the cumulative total of U.S. industrial uses (1930-1975) and their service status are noted below (22).

Table I

Millions of Pounds

Use	Industrial PCB Purchases	PCB's Currently in Service
Capacitors	630	450
Transformers	335	300
Plasticizer uses	115	n.a.(but small)
Hydraulics and Lubricants	80	↓
Carbonless copy paper	45	
Misc. industrial	28	
Heat transfer	20	↓
Total	1253	750

The same study made rough estimates of degradation and of other environmental distribution as follows:

Table II

Disposition	Millions of Pounds
Environmentally biodegraded	30
Incinerated	25
Landfills and dumps	290
In soil, water, air and sediment	150
Currently in electrical service	750
Other	8
Total	1253

General Electric manufactured capacitors containing PCB's at the Hudson Falls and Ft. Edward, New York plants from 1946 until 1977. Pyranol-filled transformers, which comprised a portion of the plants' transformer production, were manufactured at Pittsfield, MA from the 1930's until 1977, at Rome, GA from 1954 until 1977, and at Oakland, CA from 1938 to 1968. GE apparatus service shops have repaired Askarel-filled transformers for many years.

IV 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 adsorb PCB's through the lungs upon inhalation, through the intestines following ingestion, or through the skin after physical contact. Fish can absorb them through their gills and the bioconcentration factors can be large (10^3-10^5). Once inside the body they 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 of the microsomal enzymes variously known as "drug metabolizing" or "detoxification" enzymes, or as "mixed function" (i.e., chemically non-specific) oxidases. Such effects may also be induced by many other substances, and are generally regarded as physiological rather than pathological processes.

At high enough doses PCB's can produce many types of toxic effects and eventually death. The reported toxic effects include edema disease and teratogenesis in chickens; liver hypertrophy, fibrosis, and neoplasia in rodents; gastric and dermatological lesions in monkeys; and reproductive disfunction in rats and monkeys. An extensive literature on this subject is referenced in the bibliography (12-18). There can be substantial differences between different PCB products in chronic toxicity, with the higher homologs generally being the more toxic. There can also be large differences observed in toxicity between different specimens of the same type of PCB.

2. Tolerance Levels Early concerns over possible human health effects of chlorinated aromatic hydrocarbons (including PCB's) led to a series of long-term inhalation tests in animals at the Harvard School of Public Health in the 1930's (26) and confirmatory tests at the University of Cincinnati's Kettering Laboratory in the 1950's (27). Both test series showed cumulative, but reversible, effects on rat livers at high doses, and also identified threshold levels for such effects. From these levels were established the threshold limit values (TLV's) of 1000 ug/m^3 for PCB's with 42% chlorine or less, and 500 ug/m^3 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.

Repeated short-term feeding tests have shown the acute toxicities of PCB's in animals to be low, with LD_{50} values ranging from 1 to 10 gms. per kg. of body weight.

3. Impurity Effects The association of human chloracne (see below) with an unidentified PCB impurity was reported in 1936 (23) but was apparently forgotten. Then, 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 the impurity, polychlorinated dibenzofuran (PCDF) (30), and that this impurity was also responsible for chloracne in PCB dermal tests with rabbits (31). Chemical analyses subsequently showed that European and Japanese PCB's contained 5-20 ppm PCDF as manufactured, while the US-made Aroclors had 0-2 ppm.

It is not possible to also ascribe the toxic response variabilities observed in other animal tests to variations in PCDF because, unfortunately, few of the investigators reported impurity levels in the PCB specimens they tested.

4. 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 chloracnegenic activity is specifically associated with molecules shaped like flat rectangles with chlorines at the corner (21). All such chloracnegenic species are also capable of inducing one specific type of oxidase enzyme, designated P448 because of its spectral band position.

Three rare PCB isomers, which constitute less than one percent of the higher Aroclors, and which are virtually absent from the lower Aroclors, have approximately the right shape and exhibit detectable P448-inducing activity. The really strong P448 inducers, however, are the PCDF's, which are typically 1000 times as active as these three PCB isomers .

5. Carcinogenicity Test Results The American PCB's (Aroclors) have been tested for carcinogenicity in animals in many ways, with results listed in Table III below. Similar tests with the Japanese PCB's (Kanechlors 300, 400, and 500), which presumably contained 5-20 ppm PCDF's, have also produced positive, negative, and anticarcinogenic findings.

The reports of some positive findings in lifetime rodent tests at maximum tolerated dosage levels (e.g., 100 ppm in the diet), while prompting caution, represent a common observation. Examinations of HEW's "Survey of Compounds Which Have Been Tested for Carcinogenic Activity," PHS Document 149, Vols. 4,5,6, and 7, shows that a substantial majority of all substances tested since 1960 (3233 out of the 4233 PHS-149 substance listings) have been reported to produce excess tumors in animals.

TABLE III
U.S. PCB CARCINOGENICITY TESTS

Aroclor No.	Route	Species Result	Author	Date
1221	rabbit-oral	No cancer	Koller, Zinkl	1973
1016	rat-oral	No cancer	Burse, Kimbrough et al	1974
1242	rat-oral	No cancer	Monsanto Contractors *	1971
1242	rabbit-oral	No cancer	Koller, Zinkl	1973
1242	rat-oral	No cancer	Burse, Kimbrough et al	1974
1254	rat-oral	No cancer	Monsanto Contractors *	1971
1254	rat-oral	Liver cancer	Kimbrough et al	1972
1254	mouse-oral	Liver cancer	Kimbrough and Lindner	1975
1254	rat-oral	No cancer	NCI Carcin. Program	1978
1254	mouse-skin	Not tumor-initiating	DiGiovanni et al	1977
1254	mouse-skin	Not tumor-promoting	Berry et al	1978
1254	mouse-skin	Anticarcinogenic	Berry et al	1978
1260	rat-oral	No cancer	Monsanto Contractors *	1971
1260	rat-oral	Liver cancer	Kimbrough et al	1975

* Testing by Industrial Biotest; 1975 data review by D. Gordon (Industrial Biotest), W. Richter (U. of Chicago) and P. Pour (Eppley Institute for Research in Cancer). (27)

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 which had caused Yusho illness (32). By 1975 it was known that these rice oil samples contained about 1000 ppm PCB's, 5 ppm of PCDF's and 1000 ppm of another chlorinated material, later identified as polychlorinated quaterphenyls (33). The PCDF's and PCQ's presumably were formed from PCB's by thermal oxidation and condensation in the heat exchanger at high temperature. This analysis would imply that the leaking heat exchange fluid itself contained PCDF's at the extraordinary level of 2500 ppm.

As the Yusho victims were estimated to have ingested an average of 2.0 gms. of the heat exchanger fluid, this amount would have included about 1.0 gm. each of PCB and PCQ, along with 5 mg. of PCDF. As will be noted later, 1.0 gm. of PCB is less than is detected in heavily-exposed capacitor workers. Unlike capacitor workers, the Yusho victims rapidly eliminated their PCB burdens and showed normal background levels of PCB's in about a year. However, the patients remained sick, and such autopsy liver samples as became available showed that significant levels of PCDF's were retained in that organ.

Since doses of electrical-grade PCB's, absorbed by inhalation and skin contact, larger than the Yusho ingestion have not induced the Yusho illness, these later Japanese investigations link the disease to the PCDF content of the rice oil, a hypothesis which is consistent with PCDF activity in animal tests.

3. Effects of Eating Fish Containing PCB's The Michigan Department of Public Health conducted an FDA-sponsored study (38) of 182 adults, 105 of whom consumed over 26 pounds of Great Lakes fish year 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. Blood PCB levels ranged from 7 ppb for a person who ate no fish to 366 ppb for an individual who ate 132 pounds per year.

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 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 of this exposure have been identified to date. The question of PCB accumulation over time and the impact of long-term exposure are being evaluated in a continuation of this study. (39)

4. Occupationally-exposed Capacitor Workers The most extensive and severe 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 the U.S.). Many employees in these plants had daily PCB skin contact for several years and the inhalation levels have been measured in the 100 to 1000 ug/m3 range. General Electric's major capacitor fluid useage was

originally Aroclor 1254, then changed to Aroclor 1242 around 1952, and subsequently transitioned to Aroclor 1016 (and some 1221) around 1971. This useage pattern was probably typical of the industry. PCB blood tests of heavily-exposed GE capacitor workers have indicated a log normal distribution whose geometric mean was around 330 ppb. Ten percent of the individuals' analyses were above 1000 ppb. (41)

A blood PCB value of 330 ppb roughly corresponds to a 130 ppm level in fatty tissue of the same individual, or a body content of about 1.5-2.0 grams. By comparison, background PCB blood levels for industrially unexposed persons in the U.S. range from 5-25 ppb (13).

In capacitor plants the most frequent health effect observed has been 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 allergic dermatitis cases, but none of chloracne, attributed to PCB's among an exposed employee group which totalled about 1300 individuals (28). The condition responded to simple topical treatment and employee reassignment to other work areas. Only 16 other GE clinical cases of possible PCB health effects were noted in this 15-year period. Of significance is the fact that the medical records of this worker population showed no obvious incidence of systemic disease attributable to PCB exposure.

Observations of high PCB blood levels, some dermal conditions and isolated cases of chloracne are reported in the industrial hygiene literature of Sweden, Australia and Japan (2,3,9,10), but other causally-related adverse health effects have not been shown in heavily-exposed capacitor workers.

Public concern about Yusho and inferences drawn from animal tests have stimulated many other clinical investigations of human health effects in addition to those cited above. In one study, 32 capacitor workers were examined in a program sponsored by the South Carolina State Department of Health and Environmental Control. 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 from working with PCB's (4).

A study of occupationally-exposed Bloomington, Indiana capacitor workers and other residents, reported in 1978, did not note liver disease, but found that levels of a liver enzyme increased with increases in serum PCB levels and that plasma triglyceride levels were higher than normal in capacitor workers (5). A letter to the Bloomington study participants from the U.S. Center for Disease Control noted that human cancer risk would remain unknown until the extensive study (reported below) then being conducted by NIOSH had been completed.

In 1976 Dr. Irving Selikoff, of Mt. Sinai School of Medicine was asked to check on the health status of capacitor workers in the GE plants at Hudson Falls and Ft. Edward, N.Y. Three hundred

twenty-six volunteers who generally had a long history of some 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 (6). Some dermatological findings were reported to correlate with blood PCB levels of the higher homologs. The authors noted a paucity of other abnormal findings on physical examination, including a very low prevalence of abnormal liver findings.

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 in this paper for Morris' normal population (7). The significance of this observation is uncertain and requires further study.

Medical surveillance by General Electric of 193 heavily-exposed capacitor workers has consisted of multiple examinations over the last four years. As previously noted, persistent high PCB blood levels have been found; but there has been a general absence of serious health problems. There are elevations of blood lipids in some males. Pulmonary function tests of vital capacity in non-smokers have been in the normal range. Statistical analysis of this examination data is continuing (41).

A rough correlation which is emerging from this study of GE capacitor workers is that people who are regularly exposed to PCB's may eventually accumulate about 1 ppb in their blood for each 1 ug/m^3 present in the air. Thus, long-term environmental exposure to air containing 2 ug/m^3 PCB might be expected to add about 2 ppb to an average person's 5-25 ppb PCB background level, a small amount compared with the normal background, or with the levels observed in heavily-exposed capacitor workers (200-1000 ppb).

5. NIOSH Epidemiology Study With respect to human carcinogenic effects, three reports of possible cancer association with PCB-exposure (27,34,35) have been regarded as inconclusive, as they involved small groups of people, few deaths, uncertain levels of exposure to PCB's and to other chemicals, generally short latency intervals, and lack of a consistent cancer site incidence.

After reviewing both the animal tests and the above human reports, the FDA assessment in 1979 (36) was that the question of carcinogenicity of PCB's was unresolved though a matter worthy of further serious inquiry. The International Agency for Research on Cancer has evaluated the degree of evidence for PCB's causing cancer in humans as "inadequate" (37). Neither of these 1979 evaluations had yet received a report of NIOSH's long-term mortality study of a PCB-exposed capacitor worker population, which showed no excess in overall cancer mortality.

A report of this NIOSH epidemiology study, by far the most comprehensive ever conducted concerning human PCB exposure, has recently beoome available (8), and it provides the best data available on mortality experience. The retrospective cohort standardized mortality study includes 2349 PCB-exposed capacitor workers in two plants. One of these plants was the GE Hudson Falls and 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, and a total of 38,890 person-years had been accumulated by the January 1, 1976 study cutoff.

The NIOSH study reports that the incidence of all cancer mortality for these plant populations has been slightly lower than that of the general U.S. population, 39 deaths due to malignant neoplasms vs. 40.62 expected based on national norms adjusted for age and sex. For other causes of death the findings were: from cardiovascular disease, 60 vs. 61.86 expected; from nervous system diseases, 11 vs. 12.3 expected; from accidents, 13 vs. 17.64 expected; and from all other causes, 40 vs. 41.62 expected. Deaths from all causes were 163 vs. 174.04 expected.

No statistically significant excesses of specific cancer types were observed, though the authors called attention to four rectal and three liver oancer cases. This should be followed up by extension of the study, although these present mortality numbers are too small to be meaningful. There was no latency relationship demonstrated with total cancer mortality, nor was there an increase in mortality with increasing lengths of occupational exposure. Liver oirrhosis deaths were higher than normal in one plant (with some alcohol association possibility noted) and lower in the other, the total cohort experience being about equal to the national norms.

C. Summary

To summarize, there have been many PCB toxicological studies, of both animal and human subjects, dating back to the 1930's. These led to the establishment of PCB exposure guidelines (later, standards) that were apparently quite successful in preventing serious injury to heavily-exposed American capacitor workers. A human hazard that was not recognized early was the possibility that PCB's used in very high temperature environments, such as heat exchangers or baking operations, could be partially oxidized to PCDF's, with consequent increase in toxicity. Even in such cases, the health hazard is finite. The Japanese Yusho disease investigations reported that the threshold dose may have been about 0.5 gms. for ingestion of the thermally-decomposed heat exchange fluid that was involved. (PCB-PCQ-PCDF mixture containing about 2500 ppm PCDF).

As regards the ordinary, unpyrolysed, U.S.-made electrical grade PCB's which may be involved in some industrial or environmental exposure situations, the hazard potential can be evaluated from the occupational health experience of capacitor workers, who had many years of heavy exposure (regular skin contact plus 100-1000 ug/m^3 in air). The paucity of evidence for health damage in these individuals, combined with the finding of normal long-term mortality experience, indicates that there is little basis for concern over the effects of occasional environmental exposure to such PCB's at the levels typically encountered (0.1-10 ug/m^3 and/or occasional skin contact).

There are some unanswered questions regarding possible low level or subtle effects in very heavily-exposed individuals, and there are on-going programs to attempt to resolve them. These are discussed in this paper's concluding section. But the extensive human health experience cited in this paper and the low future exposure potential do not indicate that typical environmental levels of electrical grade PCB's present a significant human health hazard.

V U.S. PCB Regulations

Early fire protection regulations covering confined-space electrical equipment essentially mandated the use of PCB-filled transformers. However, the subsequent concern about environmental accumulation and about possible human health effects led in 1976 to a national prohibition (TSCA, Section 6e) of new production and continued manufacturing use of PCB's. This prohibition is embodied in EPA phaseout rules which define" PCB" capacitors and transformers as those containing "PCB liquids", defined in turn as any liquid in which PCB concentration is greater than 0.05% (500 ppm). "PCB-contaminated" transformer oils (and the corresponding transformer) are defined as those containing 0.005%* to 0.05% of PCB material. The regulations contain the following major requirements: (40)

- PCB capacitors and transformers and PCB-contaminated transformers may be used for the remainder of their useful life.
- Most PCB equipment remaining in use is subject to marking requirements.
- Small PCB capacitors may be disposed of without restriction in municipal landfills (except by equipment manufacturers).
- Large PCB capacitors which are taken out of service must be drained and may be shipped (temporarily) to an approved chemical landfill. After high temperature incinerators are approved, these must be used for the future disposal of large PCB capacitors.
- Any PCB waste fluids ($>$ 0.05%) must be disposed of by high temperature incineration in EPA-approved incinerators. (No commercial incinerators have yet received approval at this writing).
- PCB-contaminated waste fluids (0.005%-0.05%) must be disposed of in high efficiency boilers, in approved chemical waste landfills, or by high temperature incinerators.
- Waste oil containing any detectable level of PCB's cannot be used as a dust control agent.
- PCB liquids and equipment awaiting final disposal are subject to marking and storage requirements.

* A recent court case requires EPA to reexamine this definition.

The Food and Drug Administration noted the presence of PCB's in food and established regulations in 1973 for certain foods in interstate commerce. Present tolerance limits for various food items were adjusted downward effective August 28, 1979 to the following levels: (29)

Milk and dairy products	1.5 ppm (fat basis)
Poultry	3 ppm "
Eggs	0.3 ppm "
Fish and Shellfish	2 ppm *(currently 5 ppm)

* The proposed 2 ppm tolerance limit for fish and shellfish has been stayed, pending resolution of objections raised concerning the final rule.

VI On-going Programs

Notwithstanding the experience of 50 years PCB useage and the extensive research which has been completed, some questions and uncertainties remain. General Electric and others are continuing research on a 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 only in such minute quantities that they should not be of concern. This question needs to be resolved by analysis and evaluation, and GE is continuing an analytical research program to make some of this data available.

A number of medical research programs are continuing which will further clarify the PCB health effects understanding. New York State's Department of Health (Dr. Phillip 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 surveillance of previously exposed capacitor workers to further characterize their health status. And some additional observations may become available from the Mt. Sinai School of Medicine work. The Michigan State Department of Health is extending and broadening their study of individuals who have ingested PCB's by eating fish.

These on-going studies may indicate if medical surveillance is appropriate for individuals exposed to PCB's in the past. While a confirmed* blood or fat tissue PCB analysis significantly higher than the local average can indicate exposure, on the basis of present knowledge there is apparently no further examination procedure which is meaningful. Nor is there any therapy or medical advice that can properly be given such an individual other than to reassure him or her that, on the basis of capacitor workers' experience, there is no reason to believe that significant adverse health effects will occur.

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

Lastly, many research programs are being directed at economically effective containment and conversion processes for PCB's in order to respond to Federal and State requirements. General Electric research is active in some of these programs.

* An unconfirmed individual PCB measurement should be regarded cautiously: a recent round-robin study by the N.Y. State Health Dept. showed at least one case where 2 out of 10 commercial analyses of the same biological sample reported PCB values that were 20-fold different from the average.

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