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PCB GE Rebuttal

SUMMARY OF EVIDENCE THAT CAPACITOR GRADE PCB'S ARE NOT SIGNIFICANTLY TOXIC TO MAN OR MAMMALS

(Introductory Section)

In recent months there have been many allegations that all PCB's are highly toxic to fish, wildlife, and human beings, and hence that any exposure of any creature to a significant level of any PCB will result in serious injury. Such allegations are trumpeted forth almost daily in the popular press, and have been presented on several occasions during the proceedings of the present case. We feel compelled to point out that such allegations are becoming increasingly inconsistent with the available scientific information on PCB toxicity, and that the particular grades of PCB's and PCB handling procedures used in capacitor manufacture present a demonstrably low level of toxic hazard.

In rejecting the more general allegation that all PCB's are hazardous, we wish in no way to deny that some PCB-derived compositions are indeed highly toxic; have indeed caused serious injury to humans, mink, and laboratory rodents; and do indeed pose serious management problems for industry and for public health officials. Instead, we wish to demonstrate the growing weight of scientific evidence that different specimens of PCB products differ markedly in their toxicity to warm blooded animals; that the variations in toxicity can be related to variable levels of highly toxic contaminants, specifically, polychlorinated dibenzofurans (PCDF's) in the PCB's; that the PCDF's of greatest concern are the penta- and hexachlorinated homologs, which can be chronically accumulated in the body, particularly in the liver; that these PCDF contaminants originate primarily via oxidation of the corresponding

PCB's upon aging, particularly when heated; and hence that the real chronic toxicity hazard presented by PCB-derived compositions results not from an intrinsic toxicity of the PCB's themselves, but from the danger that they may have contained penta- or hexachlorobiphenyls that had at some time become oxidized to the corresponding penta- or hexachlorodibenzofurans. An obvious consequence of this conclusion is that a capacitor grade PCB, such as Aroclor 1221 or Aroclor 1016, which contains little or no penta- or hexachlorobiphenyl, and which is not subjected to heating in the presence of air during the course of capacitor manufacture, will not develop any significant level of the chronically toxic penta- and hexachlorodibenzofurans, and hence will not be capable of producing the chronic toxicities associated with other types of PCB's.

The idea that the toxicities associated with PCB-containing mixtures may arise from the presence of PCDF's therein is by no means unprecedented, original, or unique to us. Dr. Kimbrough, in her testimony, cited a lengthy review article that she wrote in 1972 tracing the historical ~~background to~~ development of the concept (NYS Exhibit 46, Subexhibit 2, p.364, footnote 13), and specifically recognized PCDF contaminants as possible sources of the toxic effects seen by Vos in chickens (loc. cit., p.355, col.1) or by herself in rats (ibid., p.363, col.2). Likewise, Dr. Kolbye testified that at the time of the FDA deliberations regarding the promulgation of the Final Order Regulations on polychlorinated biphenyls of July 6, 1973, there was general cognizance that there might have been PCDF's in the oil that caused the

Yusho incident, and that the Japanese disease may have been explained in part by the added contribution of these PCDF's (Transcript pp.1017-1019).

Although the idea that PCDF's may be responsible for some or all of the toxic effects exhibited by PCB's has thus been accepted for several years, the evidence required to convert this hypothesis from a possibility to a certainty is more recent. In part, this evidence has come from the work of Drs. Allen, Kimbrough, Ringer and their colleagues, which shows ever-increasing ranges of variation in the toxic activities of different specimens of PCB. In larger part, it has come from the continuing investigations of the Japanese Yusho poisoning incident, particularly as reported by Dr. Kuratsune in Chicago on November 21, 1975. (GE Exhibit 31). The key findings of these investigations were that the heat exchanger PCB that entered the rice bran oil eaten by the Yusho victims did indeed contain an entire homologous series of PCDF's, that these were present in massive amounts, and that they were chronically accumulated in the bodies of the victims. Even more significantly, it was found that some of the PCDF's were specifically concentrated in a known target organ of PCB intoxication, namely, the liver. (This finding represents the first demonstration of a specific localization of any PCB isomer, PCB contaminant, or PCB metabolite in a mammalian tissue; the PCB's themselves are non-specifically soluble in fats, and distribute themselves around the body in proportion to the fat content of its various parts.) Finally, it was shown that the specific PCDF's so concentrated in the target organ were the penta- and hexachlorinated homologs.

Although the fuller results of the Yusho investigation reported by Dr. Kuratsune in November 1975 thus strongly implicated PCDF's as the actual toxic agents, the incomplete investigations reported by him in April 1972 did not; they showed only that leakage of a PCB heat exchanger fluid, Kanechlor 400, was responsible for this most massive and unfortunate poisoning of some 1200 people. Likewise, the incomplete investigations of Dr. Allen showed only that these toxic effects of Kanechlor 400 on people could be simulated in monkeys dosed with Aroclor 1248. An understandable conclusion to be drawn from the results of these and other incomplete investigations was that PCB's were intrinsically toxic, and hence that all usages of all PCB's should be rigidly controlled. It is thus also understandable, although regrettable, that advocacy of this latter conclusion has forced many public officials, science writers, and scientists themselves into fixed public positions on this issue, which they are understandably reluctant to modify in light of the results of more complete scientific investigations.

In developing what we believe to be the most rational interpretation of the entire body of available scientific data, we shall review first, the ~~information~~ evidence relating to the chemical composition of the various PCB products in question; second, that relating to their general chemical, physical, and biological properties; third, that relating to the nature of toxicity in general; and fourth, that relating to the toxicity of PCB's themselves in man and other mammals. We shall argue only from the testimony and documents that have been admitted into evidence. We must emphasize, however, that during the course of these proceedings approximately 50 other scientific documents relating to PCB toxicity were exchanged among the parties concerned, and that

MDNS 089584

some 100-200 additional documents on this subject are currently residing in the respondent's files. To the best of our knowledge, the interpretations and conclusion that we shall set forth are consistent with all of this body of data, not just those portions that have been formally admitted into evidence.

1. Evidence Relating the Chemical Composition of Commercial PCB Products and General Biological Properties of PCB Product Constituents

The highly concordant testimony of Dr. Veith (NYS Exhibit 14, pp 4-5; NYS Exhibit 15, subexhibits 1-7) and of Dr. Simons (Transcript pp. 1118-1127) described the major constituents of PCB products as complex mixtures of molecules containing a biphenyl nucleus to which chlorine atoms are attached in various numbers and locations. Species differing in numbers of chlorine atoms per biphenyl nucleus were termed homologs; those having the same empirical composition but differing in the locations of the chlorine atoms were termed isomers. In all, there are 10 possible families of homologs (e.g., groups of isomers containing 1-10 chlorines per molecule) and 209 possible isomers. A table giving the average compositions of the PCB mixtures in commercial Aroclors was presented by Dr. Veith (NYS Exhibit 15, sub. 8). Adaptations of two frequently published tables giving the approximate distributions of PCB homologs in the commoner Aroclor products were given by Dr. Kolbye (NYS Exhibit 39, p.7) and by Dr. Simons (GE Exhibit 13). These tables show that each of the commercial PCB products is a mixture of PCB isomers and homologs representing several of the 10 possible levels of chlorination; however, the relative proportions of the different homologs may differ grossly as one ascends the series from one Aroclor to another.

Corresponding to these large differences in homolog distributions are associated large differences in gross physical and biological properties. Dr. Veith reported (NYS Exhibit 15, subexhibit 9) that between Aroclor 1242 and 1260 there was an increase in boiling point of 60°C, implying a large change in room temperature volatility, and a

decrease in water solubility from 240 ppb to 2.7 ppb, implying large changes in water/lipid distribution coefficients and bioaccumulation factors. The above Tables I and II show that upon proceeding from Aroclor 1016/1242 to 1248 to 1254 to 1260 there were sizeable increases in chronic toxicities to fish and water-to-fish bioaccumulation factors, respectively.

There may also be very large changes in persistence within the organism, because of decreased rates of biodegradation. Dr. Kolbye pointed out that there is a general tendency for the biological half-life to increase with the degree of chlorination (Transcript p. 1025). Several studies have shown that the di-, tri-, and tetrachlorinated homologs are readily metabolized in mammals (NYS Exhibits 60, 61, and 62), but have pointed out that metabolism of the higher homologs is more difficult (NYS Exhibit 61, p. 476). More specifically, Dr. Kuratsune showed that the PCB's recovered from the tissues of people who had consumed Kanechlor 400 (similar in homolog distribution to Aroclor 1248) exhibited gas chromatograph patterns (GE Exhibit 31, p.6) resembling those of a mixture of Kanechlors 500 and 600 (similar in homolog distributions to Aroclors 1254 and 1260, respectively). Comparison of his chromatograms with the reference standards provided by Dr. Stalling (NYS Exhibit 19, Sub. 3, p. 804) shows total removal of the tri- and tetrachlorinated homologs in the PCB subjected to human metabolism. Similar observation for Aroclor 1248 metabolism in the monkey have been reported by Dr. Allen (NYS Exhibit 42, Sub 3, p. 448).

The chromatograms of the PCB recovered from the muscle or liver of mink fed Aroclor 1254 (NYS Exhibit 44, Sub 4, p.395) showed a pattern like that of Aroclor 1260 (NYS Exhibit 19, Sub. 3, p. 804) and indicated that total removal of tetrachlorobiphenyls and substantial metabolism of pentachlorobiphenyls had occurred in these tissues.

Because of this tendency for the more highly chlorinated homologs to be more slowly biodegraded by individual organisms, such homologs have tended to be more persistent in the environment as a whole, as pointed out by Dr. Kimbrough (NYS Exhibit 46, Subexhibit 6, p. 391). Concern over the environmental accumulation of the penta-, hexa-, and other highly chlorinated PCB homologs was what originally led to the development of a PCB product depleted in such species, namely Aroclor 1016; the discoveries of its reduced toxicity did not come until much later. As Dr. Papageorge testified, Monsanto has not claimed that Aroclor 1016 was less toxic, only that it was more biodegradable (Transcript p. 1231).

As for the actual content of penta- and hexachlorobiphenyls in Aroclor 1016, the tables of approximate homolog distribution presented by Drs. Kolbye and Simons (NYS Exhibit 39, p. 7; GE Exhibit 13) indicate the "nominal" contents of these two homologs to be 1% and 0.1% respectively. The tables of manufacturer's specifications, presented by Dr. Stalling (NYS Exhibit 18, Subexhibit 2, pp. 2,4) indicate that the specified content of penta- and hexachlorobiphenyls, also collectively termed "higher boiling homologs" is 0.4% max. The product quality

control sheet for the lot of Aroclor 1016 shipped from Monsanto to General Electric on 10/1/75 (NYS Exhibit 7, Subexhibit 5) indicates that the actual level of penta- and hexachlorobiphenyls in recent production of Aroclor 1016 has been 0.07%. The corresponding figure for Aroclor 1242 is 6-7% (NYS Exhibit 18, Sub 2, p.2). Thus, Aroclor 1016 contains only about 1% as much of the higher homologs as does Aroclor 1242, or about 0.1% as much as does Aroclor 1254.

In addition to the individual PCB isomers, which make up the great bulk of the material in the commercial PCB products, other types of chemical species, generally referred to as "contaminants" may also be present. Dr. Kimbrough called attention to the presence of polychlorinated naphthalenes and polychlorinated dibenzofurans (PCDF's) in specimens of PCB that had been found toxic to chickens (NYS Exhibit 46, Sub 2, pp. 354-355; p. 364 footnotes 11-13) and the possible presence of PCDF's in the specimen of Aroclor 1254 that caused adenofibrosis in rats (ibid., p. 363). Very recently, Kuratsune reported finding PCDF's in all specimens of Japanese PCB's examined. For Kanechlors 300, 400, 500, and 600 (corresponding in PCB homolog distribution to Aroclors 1242, 1248, 1254 and 1260, respectively), the PCDF contents, as determined by the perchlorination method, were 1.5, 16.6, 2.5, and 2.7 ppm, respectively (GE Exhibit 31, p. 6). He also noted a later report of a Kanechlor 400 specimen containing 33 ppm PCDF (ibid., p.9). More significantly, he reported that Kanechlor 400 that had been "used" as a heat transfer medium and thence passed into the Yusho oil contained

5,000-12,000 ppm PCDF's (ibid., p. 10-11). (We are informed that Dr. Kuratsune reported orally on other Japanese investigations of elevated PCDF levels in "used" PCB heat transfer oils at the National Conference on PCB's in Chicago on 11/19/75, but that no other written reports of these current investigations are yet available.) The PCDF's detected in either "unused" Kanechlor 400, "Yusho oil," or the tissues of people who had consumed the "Yusho oil" included the entire homologous series from the di- to the hexachlorinated homologs. In the "Yusho oil," the major constituents were the tetra- and pentachlordibenzofurans; in the livers of Yusho victims, the PCDF's were mainly the penta- and hexachlorinated PCDF's, with only a trace of the tetrachloro isomers. (ibid., p. 7, 15).

Since the chlorine contents of the PCDF's in the "used" heat transfer oils correspond to those of the PCB's in the Kanechlor 400 used, it must be concluded that they are formed from the PCB's by oxidation:

$C_{12}H_6Cl_4 + O_2 \rightarrow C_{12}H_4OCl_4 + H_2O$

Tetrachlorobiphenyl — Tetrachlorodibenzofuran

If they were formed instead by hydrolysis of the PCB's, much less chlorine would be found in the PCDF's:

$C_{12}H_6Cl_4 + H_2O \rightarrow C_{12}H_6OCl_2 + 2HCl$

Tetrachlorobiphenyl — Dichlorodibenzofuran

The source of the oxidant for converting the PCB's to PCDF's was probably atmospheric oxygen, but the possibility that peroxides from the cooking oils could also contribute has been suggested (Kuratsune, ibid., p. 31.)

In addition to thermal oxidation as a mechanism for the conversion of PCB's to PCDF's, other forms of oxidation (e.g., slow autoxidation upon aging at ambient temperatures) may also occur for some isomers. Dr. Kuratsune's data showed wide variations in the PCDF contents of even the "unused" Kanechlors (ibid., pp. 7,8). Since the biphenyl used to manufacture the different grades of PCB was undoubtedly the same in all cases, whatever PCDF was initially present in the PCB's as a result of the chlorination of a dibenzofuran impurity in the biphenyl used must also have been the same, and could not have amounted to more than 1-3 ppm. This suggests that the additional PCDF found in the "unused" but aged samples of Kanechlor 400 came from some form of slow oxidation on aging. The apparent proneness of this particular grade of Kanechlor to form PCDF's on aging suggests that particular attention should be given to the question of PCDF's in old samples of the U.S. equivalent, namely Aroclor 1248. Since this grade of Aroclor has not been manufactured for several years (GE Exhibit 19) all available samples must be presumed to be old.

The biological implications of PCDF's in PCB samples are profound. The PCDF's are very similar to the polychlorinated dibenzodioxins (PCDD's) in structure, mode of toxicological action, and level of toxicity, being among the most toxic substances known. (Goldberg Testimony, Transcript pp. 1793-1797; Kuratsune, GE Exhibit 31, p.25). Dr. Goldberg

stated that he was unaware of data indicating that the chronic as well as the acute toxicities of PCDF's had yet been tested; however, in view of the generally close chemical and biological similarities between the PCDF's and the PCDD's, where such chronic toxicities have been studied extensively, he would presume severe chronic, as well as acute toxicity, to be a legitimate extrapolation (Transcript p. 1795-1796). (Dr. Goldberg was apparently unaware of Dr. Kuratsune's report of the prior week showing chronic persistence of PCDF's in the human.) As pointed out earlier, Dr. Kimbrough's and Dr. Kolbye's testimonies both indicated that they were concerned over the role of PCDF's in PCB toxicity even back in 1972-73, long before there was adequate analytical data available to indicate just how much PCDF could be present in some specimens of PCB. Since Dr. Kuratsune's has now shown that the Japanese PCB's, at least, may contain anywhere between 1 ppm and 12,000 ppm PCDF, and since the PCDF's may be a million times as toxic as the PCB's (or even more, for all we know, in chronic tests), it is evident that PCDF "contaminants" in PCB's could easily dominate their patterns of toxic activities.

2. General Nature of Toxicity

Before proceeding to a detailed examination of the evidence pertinent to the toxicities of PCB-containing mixtures in man, monkey, mink, and rats, it may be helpful to review some of the general concepts and terminology used in toxicology. We shall do this mainly by quoting from Dr. Goldberg's testimony.

First, the term "toxicity" was defined as "a manifestation of the injurious effect of a chemical or physical agent on a living organism as manifested in a variety of possible ways, such as structurally, functionally, or in regard to the response of the organs, for instance, behavior." (Transcript, p. 1768).

Second, he pointed out that neither PCB's nor any other chemical substances could be generically termed either toxic or non-toxic in absolute terms. Instead, "essentially every compound has the capacity to bring about an injurious effect, so when we use the term toxic or non-toxic, we do so in a relative sense, in that some substances are injurious at a lower dose than others, and this is a question of degree, but essentially every common chemical by which we are surrounded, or that we ingest or inhale, is capable of causing injury (e.g., at sufficiently high dose)." Thus, in order to determine whether any particular chemical, for example, be toxic, one would have to know the quantity or dosage of the chemical that was brought into contact with the living matter. (Transcript, pp. 1769-1770).

Third, a distinction is made between "acute" and "chronic" toxicity. "Essentially, acute is an injurious effect that manifests

itself over a short period of time, let's say up to two weeks. Then we have what one might call short-term toxicity, which is observed over a period up to one year, (speaking mainly as regards rodents), and long term is everything over a year." Thus, the term "chronic" includes both the effects defined as "short term" and "long term" and indicates an effect requiring more than two weeks to develop. (Transcript p. 1792-1793).

Fourth, it is recognized that any test of a substance for toxicity, and particularly a chronic toxicity assay, tests not only the substance administered to the animal, but also any contaminants that may have been present, and any metabolites of the substance that may have been formed in the animal. In most cases, metabolites are less toxic than the substances administered, since the metabolism generally detoxifies toxicants by converting them into more soluble species that can be more readily excreted from the body; but this is by no means universally true (Transcript, pp. 1770; 1780-1786; 1805). Nevertheless, the possible formation of a toxic metabolite (e.g., a phenol, arene oxide, or dibenzofuran from a PCB) can in no way be used as an argument that the substance tested may be actually more toxic than shown by the bioassay test result; any chronic bioassay tests the total effects of administered toxicant and <u>all</u> metabolites thereof simultaneously.

3. Recent Observations of the Effects of PCB's and Associated Contaminants on Men and Mammals

In examining the evidence relating to toxic effects produced by PCB-containing mixtures, we shall review the effects observed in man, monkeys, mink, and rodents, and discuss each in turn.

In the U.S. PCB's have been used on a wide scale for a broad variety of applications. Monsanto figures show domestic sales of 26-73 million pounds per year during the period 1957-1975. (GE Exhibit 19). Despite this widescale use, no clinical reports of human poisoning by PCB's in the U.S. during this period have been alluded to or introduced into evidence, and we must turn to Japanese data for clinical information.

In October, 1968 an epidemic of a peculiar skin disease similar to chloracne was reported in Fukuoka-Ken (Fukuoka prefecture) in the extreme western part of Japan. Over 1200 people were eventually found to be afflicted. Soon after the epidemic was announced, an interdisciplinary research team from the faculties of medicine, pharmaceutical sciences, agriculture, and engineering of Kyishu University was assembled to investigate the incident. These investigations have continued ever since, and have so far produced about 50 technical publications, mostly in Japanese. On two occasions Dr. Masamori Kuratsune, the senior medical investigator, has presented detailed English language summaries of this massive investigation; the first in April, 1972 (now NYS Exhibit 42, Subexhibit 5); the second in November, 1975 (now GE Exhibit 31).

To summarize briefly, in the April 1972 report, it was established (a) that the disease could be related to the consumption of an edible oil, "Yusho," that had become contaminated with 2000-3000 ppm of a Japanese PCB, Kanechlor 400, from a leaky heat exchanger in the K Company; (b) that the symptoms produced were primarily dermatological, consisting of acne-like skin eruptions, pigmentation of the skin and nails, distinctive hair follices, swelling of the upper eyelids, increased eye discharge, and a variety of non-specific manifestations of general malaise; and (c) that the symptoms were highly persistent, and even transmissible to babies born to afflicted mothers.

The findings reported in November, 1975, were (a) many of the Yusho victims were still showing the symptoms of the disease; (b) the Yusho oil consumed by the victims was found to have contained about 900 ppm PCB's and about 4-5 ppm PCDF's, i.e., in a PCB/PCDF ratio of about 200; (c) the adipose tissue of the victims, examined in late 1968, showed 13-76 ppm PCB; after 1968 it contained near-normal levels of PCB's (1-4 ppm) and sufficient PCDF's for a PCB/PCDF ratio of about 157; (d) the livers of the victims (after 1968) contained near-normal levels of PCB's (0.05 ppm on a whole tissue basis; 4.6 ppm, the same as for adipose tissue, on a fat content basis) but enough PCDF's to bring the PCB/PCDF ratio down to 4; (e) the PCDF's thus indicated as being specifically bound to liver tissue were the penta- and hexachlorinated homologs; (f) there were no PCDF's present in the livers of the control population, although comparable amounts of PCB's

were detected; (g) 1972-73 analyses for PCB's in the blood showed about 1-7 (av. 3) ppb in "normal persons," 1-26 (av. 6) ppb in Yusho patients; and 60-920 (av. 364) ppb in workers engaged in Kanechlor production, of whom only 2 out of 23 shows any dermal signs.

The most significant aspects of these findings, we submit, are (a) the striking lack of correlation between the level of PCB found in the blood, adipose tissue, or liver and the presence of disease, (b) the observed correlation between the level of PCDF in the PCB involved (e.g., 5,000-12,000 ppm in the Yusho oil PCB; 1-33 ppm in the "unused" Kanechlor 400) and the development of symptoms in those exposed to that PCB, (c) the long term chronic persistence of PCDF's in the human body, and (d) the specific concentration of the penta- and hexachlorodibenzofurans in a known target organ of "PCB" poisoning, namely, the liver.

The investigations of the effects of PCB's on laboratory monkeys have understandably been far less extensive and complete than those of the human victims of Yusho. The informaton in evidence comes from the work of Dr. J.R. Allen and his associates, who have been studying the effects of Aroclor 1248 on rhesus monkeys from 1967 to date (NYS Exhibit 41, p. 1; Exhibit 42, Subexhibit 4). In these studies they observed signs and lesions that were generally similar (NYS Exhibit 41, pp 2-6; Exhibit 42, Subexhibit 2, p. 489; subexhibit 3, p. 449) though not identical (Transcript pp. 1053-1058) to those reported for the human victims of Yusho.

Attempts to establish dose/response relationships for these effects led to a most extraordinary series of observations. In successive studies over the 8 year interval 1967-1975 they examined the chronic effects on adult monkeys of dietary Aroclor 1248 given first at a level of 300 ppm (NYS Exhibit 42, Sub. 2, p. 498; Exhibit 42, Sub 10a, p. 344; Sub. 10d, p. 1675); then at 100 ppm (NYS Exhibit 41, p. 3; Exhibit 42, Sub. 10d); then at 25 ppm (NYS Exhibit 41, p. 3; Exhibit 42, Sub. 3, p. 440; Exhibit 42, Sub. 10d, p. 1676); and finally at 5. and 2.5 ppm (NYS Exhibit 41, p. 4; Exhibit 42, Sub. 4, Abstract; Exhibit 42, Sub. 6, Abstract; Exhibit 42, Sub. 10d, p. 1676). The dermatological symptoms developed at about the same rate and to the same degree in all of these cases. According to Dr. Allen, they even "appeared in animals receiving 2.5 or 5 ppm PCB as rapidly as in animals which were fed the larger doses." (NYS Exhibit 42, Sub 4, p. 8).

Equally remarkable observations were made on infant monkeys. In one of the earlier studies, one month old infants were fed 300 ppm Aroclor 1248 for a month and observed to be free of the acne, alopecia, and sub-cutaneous edena noted in the adult. (NYS Exhibit 42, Subexhibit 10e, p. 83). Later, however, it was found that the characteristic signs did appear in infants ingesting milk from the mothers who had received 2.5 and 5 ppm Aroclor 1248 in their diets (NYS Exhibit 41, p.5; Exhibit 42, Subexhibit 6).

It would appear to us that the only simple explanation for Dr. Allen's findings is that the poisoning of his monkeys is being caused by some variable constituent of his Aroclor 1248 that is increasing

with time. In view of (a) the similarity between the effects observed in the monkeys and those seen in the human victims of Yusho, (b) the chemical resemblance between Aroclor 1248 and Kanechlor 400, and (c) the nature of Dr. Kuratsune's findings regarding both Kanechlor 400 and Yusho disease it would seem most likely that this variable constituent is a mixture of PCDF's. Dr. Allen himself now recognizes this possibility, and stated that he has submitted a sample of his Aroclor 1248 for PCDF analysis (Transcript p. 1050-1051).

The studies of the effects of PCB's on mink reported by Dr. Ringer also reflect sizeable variations in dose-response relationships. Thus, his Table 5 on p. 155 of Subexhibit 3 of NYS Exhibit 44 shows that the effect on whelping was 3 times greater for the "PCB's" derived from Coho salmon than for added Aroclor 1254, even when this was supplemented by pesticides. When Ringer fed his mink a salmon-based diet containing 30 ppm PCB, he observed a pattern of toxic responses that were essentially identical to those observed by Platanow upon feeding a diet containing 3.57 ppm PCB. (NYS Exhibit 43, pp. 3-4; Exhibit 44, Subexhibit 4, p. 392). Similarly, when he fed his diet with PCB at the 5 ppm level, he observed essentially the same results as seen by Platonow upon feeding at the 0.64 ppm level. (NYS Exhibit 44, Subexhibit 3, p. 153, Table 5; Subexhibit 4, p. 392-393). Thus, in both cases, the PCB in Platonow's experiments appeared to be 8 times as toxic as Ringer's. Platonow's PCB consisted of Aroclor 1254 that had been fed to a Jersey cow that was then slaughtered so that the muscle, fat, liver, and kidneys could be fed to the mink. No analyses for

PCDF's in any of the PCB's were performed; however, the unusual tendency of PCDF's to concentrate in the liver now provides an obvious ~~might be offered as an~~ explanation for the difference between Ringer's results and Platonow's.

Dr. Kimbrough and her colleagues have studied the effects of a variety of Aroclors on the livers of Sherman rats, and examined the action of Aroclor 1254 on Balb/cj mice. A wide variety of effects were observed, ranging from mild, reversible changes to the development of hepatic tumors. Two of the studies offer particular insight into the nature of the toxic agent involved.

In the first of these (NYS Exhibit 46, Subexhibit 2) the investigators fed Sherman rats large daily doses of either Aroclor 1254 or 1260 over an 8 month period and examined for liver adenofibrosis. Dietary levels of 100 ppm Aroclor 1254 produced 10% and 70% adenofibrosis in male and female rats respectively. With 100 ppm Aroclor 1260, only 10% of the female rats developed adenofibrosis in their livers while no males were affected. Because the less chlorinated Aroclor 1254 was significantly more effective than the more chlorinated Aroclor 1260, it was considered that the causative agent might be an impurity: "Contamination of PCB's with traces of other chemicals such as chlorinated dibenzodioxins, chlorinated dibenzofurans, or chlorinated naphthalenes may also be responsible. Vos and Koeman [11] checked Aroclor 1260 of the same lot and also did not demonstrate any contaminants. However, preliminary chemical analyses of this lot of Aroclor 1254 suggest possible contamination with a chlorinated dibenzofuran. This is

still under investigation.[27]" (NYS Exhibit 47, Subexhibit 2, p. 363)

In the other comparative study Burse et al. (NYS Exhibit 45, Subexhibit 6) fed Sherman rats either 100 ppm Aroclor 1242 or 100 ppm Aroclor 1016 over a six month period. Only mild alterations of liver morphology were observed. Light microscopic examination showed enlargement of some hepatocytes (liver cells). The cytoplasm of some hepatocytes was finely vacuolated, while occasional hepatocytes had coarsely vacuolated cytoplasm. These microscopic changes were found to gradually disappear after the Aroclor feeding was stopped; there was no evidence of serious or permanent liver damage. As stated by the authors in the concluding paragraph of this paper: "The morphological changes observed in the liver are similar to those observed with other chlorinated hydrocarbons.[15] They were generally mild, particularly when compared with findings made earlier with Aroclor 1254 and 1260.[8,9] Neither the pronounced lipid accumulation nor the adenofibrosis was observed in this study. However, some brown pigment was observed in the macrophages of the livers of some rats fed Aroclor 1242 but not Aroclor 1016. It was not determined whether the pigment represented ceroid or whether part of it was caused by an accumulation of hemosiderin and porphyrin in the liver. After feeding rats Aroclor 1242 and 1016 for six months, Goldstein et al [16] found an increase in liver uroporphyrin for Aroclor 1242 at this dietary level, but not Aroclor 1016 at the same dietary level. Unfortunately, the number of rats was not large enough to determine if the occasional liver cell necrosis and hemorrhage that was seen was related to the exposure to Aroclor 1242. From this study it may be concluded that both Aroclor 1242 as well as Aroclor 1016 are less persistent in the rat and have also less of an effect on the liver than either Aroclor 1254 or 1260."

4. Implications for Public Health

To summarize the evidence just examined, we may note the following key points: First, that observations on humans, monkeys, mink, and rats dosed with different specimens of PCB products have all revealed wide variations in the provoked response. Second, that the available analytical data show that widely varying levels of the extremely toxic contaminant, PCDF, may be present in PCB products. Third, that in cases where comparison is possible, the toxic effects exhibited by a PCB sample have been found to correlate with the PCDF content. Fourth, that PCDF's may be formed from at least some isomers of PCB's by oxidation, either upon aging or, more markedly, upon heating. Fifth,that certain of the PCDF's, namely, the penta- and hexachlorinated homolog , have been found to be specifically and chronically accumulated in a known target organ of "PCB" poisoning, the liver, and hence must be suspected as the primary causative agents of the chronic toxicity effects seen therein.

Identification of the higher PCDF's as the key agents of "PCB" poisoning immediately puts the higher PCB products under increased suspicion, since they would be capable of yielding such PCDF's by oxidation either upon aging, heating, or conceivably even as a result of metabolic action. Correspondingly, it removes most cause for concern from the lower PCB products, such as Aroclor 1221 and Aroclor 1016, that do not contain significant quantities of the penta- and hexachlorinated homologs needed for conversion to the chronically toxic PCDF's.

The available test data are in accord with this interpretation. The experiments in which rats were fed massive doses of Aroclor 1016 revealed that the serious liver damage provoked by Aroclors 1254 and 1260 simply did not occur. The medical records of the GE Hudson Falls and Fort Edwards plants (response to Interrogatory 17; NYS Exhibit 00), where hundreds of employees have been exposed to Aroclors 1242 and 1016 during the past 15 years, showed not one case of the unmistakable dermatological symptoms of "PCB" poisoning. We must conclude that Aroclor 1016 is indeed a

relatively non-toxic material; certainly far less toxic than that specimen of Kanechlor 400 containing 5,000-12,000 ppm PCDF's that the present FDA temporary tolerance limit is specifically based on. (NYS Exhibit 39, p. 6-7)

In pointing out that Aroclor 1016 is less toxic than some other PCB's, we wish in no way to criticize the idea of a strict FDA tolerance limit for its intended purpose, which is to regulate the shipment of foods in interstate commerce. We recognize that an FDA inspector standing at a State line with his gas chromatograph, and trying to make confiscatory decisions on the basis of PCB analyses alone may not be able to tell whether he is seeing a toxic PCB that is loaded with PCDF's or an innocent one. In such cases, sound public health policy obviously requires that he err on the side of safety, and he needs a strict law to back up his actions.

However, in the present case we are not talking of certifying fish data for interstate commerce, but only of regulating a discharge of known composition and toxicity in order to protect the health of Hudson River fishermen. What we need is some form of a public health guideline that distinguishes between Aroclor 1016 on the one hand and, say, Aroclor 1254, on the other, as the DEC already does in its own water quality analyses.

The testimony already offered in this case shows how one might go ahead devising such a guidelines. Dr. Kolbye showed two alternative ways of calculating the present FDA temporary tolerance limit, which happened to lead to exactly the same answer (NYS Exhibit 39, p. 4,5). One of these was based on the human data taken from the Yusho incident, the other from animal data on dogs and rats that included the studies offered in evidence here by Dr. Kimbrough. In comparing the effects seen for Aroclor 1016 referred to in NYS Exhibit 45, subexhibit 6, and the references cited therein with those seen for the higher Aroclors in rats, we conclude that chronic effects produced by Aroclor 1016 at the 100 ppm dosage level are comparable with those produced by Aroclor 1254 or 1260 at the 10 or 20 ppm level. In short,

Aroclor 1016 would appear to be a factor of 5-10 less toxic than the higher Aroclors, implying that the appropriate tolerance limit for its presence in the edible portion of fish should be not 5 ppm, but 25-50 ppm.