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RECENT FINDINGS REGARDING THE

TOXICITY OF PCBS

Implications for the Acushnet Estuary

Risk Assessment

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1.0 INTRODUCTION

Since the passage of the TSCA legislation, polychlorinated biphenyls have been accorded preeminent status as hazardous substances by the government regulatory agencies. The legislation and subsequent regulations were driven by the perceived need to regulate PCBs stringently because of the available information. Three primary lines of research regarding potential health effects weighed heavily at that time: the Yusho episode, the animal carcinogenicity studies by Kimbrough (1975), and reports of the persistence of PCBs in the environment.

"Congress was aware of the toxic effects of PCBs when TSCA was enacted in 1976. PCBs were known to cause birth defects, miscarriages, and stillbirths, as well as skin eruptions, pigmentation of skin and nails, and eye malfunctions....Well documented tests on laboratory animals show that PCBs can cause reproductive failures, gastric disorders, skin lesions and tumors. PCBs are known to be persistent in the environment and to bioaccumulate, posing long-term risks to health and the environment....The overwhelming evidence with respect to the toxicity of PCBs prompted the enactment of Section 6(e) of TSCA," (EPA, 1980).

Given the research findings of the past 15 years, this report will show that the initial information on PCBs has been qualified substantially. The Yusho incident has been shown to be caused by polychlorinated dibenzofurans, rather than PCBs. Studies of the mechanism of carcinogenesis in animals, and the lack of excess cancer in exposed humans, indicate that the cancer potency of PCBs is overstated.

Although this report does not exhaustively review the state of knowledge regarding PCBs, it reviews the scientific understanding of cancer and human health effects studied in relation to PCBs. The TSCA legislation and regulations were developed when the chemistry and biology of PCBs were largely unknown. The knowledge accumulated in the past 15 years has resulted in scientific theory, which should now be included in any risk assessment.

Calculations of risk for dermal absorption and ingestion of sediments are presented. Risk assessment calculations for seafood ingestion have not been included due to uncertainties regarding the contribution of "hot spot" sediments to seafood. However, the results of the GNBHES have been analyzed to determine whether or not PCB exposure has occurred from this pathway.

2.0 TOXICITY INFORMATION PRIOR TO TSCA

At the time that the TSCA legislation was passed and regulations were promulgated, information regarding PCB toxicity suggested that PCBs were carcinogens in animals and possibly in humans, and were capable of causing a wide range of clinical symptoms. These hypotheses were based upon animal carcinogenicity assays, a report of malignant melanoma in humans, and the Yusho poisoning incident in Japan. Additionally, it was evident that PCBs were present in high blood concentrations in a group of Lake Michigan sport fishermen and certain occupationally exposed workers. The biopersistence of PCBs and the fact that all PCBs came from man-made sources made them easily identifiable in the environment. The predictions of health effects caused grave concerns among legislators and regulators. The findings from these studies are presented below.

2.1 The Yusho Incident

In 1968, a disease occurred in northern Japan, characterized by acneiform lesions and pigmentation of the skin with a characteristic distribution over the body, accompanied by a variety of constitutional symptoms. Over the next decade, 1,800 people were found with this condition, which was named "Yusho" disease because of the association with ingestion of a particular brand of rice oil (Kuratsune, 1976). Chemical analysis of chlorinated hydrocarbons was unsophisticated at the time, but eventually, PCBs were found to have contaminated the rice oil. Masuda et al. (1974) discovered that persons exposed to the oil had a different PCB gas chromatographic pattern than did controls, although the concentration of PCBs in the blood was not significantly different from controls.

Clinical symptoms and signs among the Yusho patients which later became well studied included acne, hyperpigmentation of the skin, swelling of the eyes, respiratory symptoms, headaches and numbness and tingling of the extremities (Kuratsune, 1976). Several other findings were reported but, unfortunately, were poorly investigated at the time. Because of the finding of PCB in the rice oil, this clinical condition was initially attributed to PCB toxicity.

2.2 Occupational Exposure Studies

There are clinical reports in the occupational literature, from the 1930's and 1940's, which certain later reviewers have quoted attributing liver toxicity and even death from PCB exposure. However, review of the original articles (Flinn and Jarvick, 1938; Flinn and Jarvick 1936; Greenburg et al., 1930) shows that all of these workers were predominately exposed to polychlorinated naphthalenes. In fact, in most of these early articles, PCBs were not even mentioned.

Chloracne is most consistently described in the early PCB literature. It is an acne-type disorder characterized by pinhead to pea sized, pale, straw-colored cysts. Often there is comedone formation. The lesions have a unique distribution pattern including the face, shoulders, abdomen, scrotum, penis and ears. The nose is typically spared. Individual lesions also tend to last longer than typical acne and can recur. It was thought that chloracne occurs in persons with PCB blood levels greater than 200 ppb (Ouw, 1976) except in those cohorts where exposures occur to other compounds such as chlorinated naphthalenes or dibenzofurans (Good, 1943)

Ouw et al. (1976) studied a group of 34 workers exposed to Aroclor 1242. They reported blood levels averaging approximately 350 ppb. The workers tended to complain of burning of eyes, face, and skin; only one worker was reported to have chloracne. Analysis of standard laboratory tests including liver function tests showed individual abnormalities, but the group means were within normal limits.

Only one report of human cancer was available in 1976. A statistically significant increase in the number of malignant melanoma cases in employees at a chemical plant was reported by Bahn (1976). This "epidemiology" study was described in a letter to the editor but was never published as a complete study. After a letter by Lawrence (1977) critical of the study, Bahn et al. (1977) in another letter defended the original assertions, but agreed that the data were not conclusive. The major source of criticism of Bahn's report was the concurrent exposure of the workers to many other chemicals, some of which were known carcinogens.

2.3 Cancer Studies in Rodents

The major report of animal carcinogenicity was published by Kimbrough et al. (1975). In this study Sherman rats were fed 100 ppm of Aroclor 1260 for 21 months, and hepatocellular carcinoma was reported in 14% (26/184) of the surviving rats. Control rats had less than 1% (1/173) cancer. In addition, precancerous lesions (neoplastic nodules) were found in 78% (144/184) in the experimental group and none of the controls. The health of the animals was not adversely effected by the tumors, and cancer did not metastasize to other organs.

Except in one case, earlier studies on the carcinogenicity of PCBs in rodents showed only benign lesions. Studies by Nagasaki et al. (1974) found hepatocellular carcinoma in male mice fed 500 ppm of Kanechlor 500. In all other experimental groups by these authors, either neoplastic nodules or no lesions were reported. These groups included females treated with Kanechlor 500 at 500 ppm, males and females treated with 100 and 250 ppm Kanechlor 500, and Kanechlors 300 and 400 at all concentrations.

Studies by other authors such as Ito et al. (1974) and Kimbrough and Linder (1974) found either no effects or only preneoplastic lesions. Ito et al. investigated Kanechlors 300, 400, and 500 at doses of 100, 500, and 1000 ppm fed to rats. Kimbrough and Linder gave 300 ppm of Aroclor 1254 to mice. These early studies were flawed by animal losses caused by the very high PCB concentrations, and the short duration of dosage.

2.4 Environmental Exposure Studies

An unpublished report by Humphrey (1976) raised fears about the ingestion of fish contaminated with PCBs. The blood levels in 43 people consuming large quantities of Lake Michigan sport fish for 10 or more years ranged up to 336 ppb with a mean of 82 ppm. Consumption of fish for the group was most frequently in the range of 24-to 35 lbs. The average quantity of PCB consumption was 46 mg per year ranging from 14 to 114 mg per year. Study participants were interviewed for medical signs and symptoms, and none were identified which could be correlated with serum PCB level for fish consumption. This study reported no excess in skin problems or other health effects by physical examination.

3.0 RECENT FINDINGS ON HUMAN PCB EXPOSURES

Early studies on PCBs, as discussed in Section 2, were interpreted to show that PCBs were carcinogenic in animals, and possibly in humans; and had caused significant illness. In contrast, recent findings have either refuted prior information or modified the interpretation of initial findings. These studies are reviewed in the following sections.

3.1 Further Analysis of Yusho Disease

After the original reports of the causes of Yusho disease, analytical methodology evolved so that other components of the oil were discovered. Miyata et al. 1977 were the first of many researchers to report finding polychlorinated dibenzofurans (PCDFs) and other chlorinated aromatic hydrocarbons in Yusho rice oil. Evaluations of the oil consumed by Yusho patients have shown that the weight ratio of PCB to PCDF was about 200 (Miyata et al., 1977). In contrast, the ratio of PCB to PCDFs in commercial Aroclors is usually greater than 500,000 (Bowes et al., 1975; Rappe et al., 1980). PCDF contamination in the Yusho episode was generated while the PCBs were used as a heat exchange fluid and maintained for a prolonged period at high temperatures.

Several lines of evidence based upon animal toxicity and biochemical markers have shown that the toxicity of PCDFs are very potent compared to the commercial Japanese PCB mixture implicated in the Yusho. Investigators in Japan have concluded that PCDF's were the major causative agent in Yusho (Kashimoto and Miyata, 1986, Masuda and Yoshimura, 1984, Kunita et al., 1984). In contrast, the low concentration of PCDFs in commercial Aroclors would not be expected to contribute to any adverse health effects.

Additionally, several studies have compared Yusho disease to workers with high levels of exposure to PCBs as evidenced by high blood PCB levels. Recently, Kashimoto and Miyata (1986) have reviewed this information including articles published only in Japanese. They concluded that PCDFs are the only probable explanation for the clinical manifestations of Yusho disease, and that Yusho disease is symptomatically and etiologically different from PCB effects. These conclusions were based upon the following findings comparing Yusho and Yu-Cheng findings (an episode occurring in Taiwan 10 years after Yusho with contaminated rice oil and a similar PCB/PCDF ratio) with occupational exposures to PCBs in Japan:

1. Yu-Cheng patients and Japanese workers had similar PCB blood levels, but the Yu-Cheng patients had severe clinical disease, whereas, the workers had few if any findings.

2. Five years after the Yusho episode, PCB blood levels were in the normal range, yet there was a persistence of clinical findings. In

Japanese workers with highly elevated levels, there were no such findings, and even the mild dermal lesions disappeared soon after cessation of exposure.

In summary, dose-response studies of animal and biochemical systems show that the concentrations of PCDFs found in Yusho (and Yu-cheng) oil caused the clinical disease. There was a distinctive difference in the clinical manifestations of Yusho disease and workers with similar exposures to PCBs.

3.2 Occupational Cancer Epidemiology Studies

Several epidemiology studies have examined the carcinogenic potential of PCBs in humans. Such studies are especially important in the evaluation of carcinogenic potential of PCBs because of the very large occupational exposures compared with environmental exposures.

The largest study is a retrospective mortality study of 2588 capacitor workers the majority of whom were employed at the Aerovox plant in New Bedford, and whose exposures were to Aroclors 1254, 1242, and 1016 (Brown, 1987). The total number of person years in this study was 55,545. The mortality rate for cancer was less than expected (SMR=78) and the overall death rate was also less than expected (SMR=89). The SMR is the standard mortality rate whereby age-adjusted mortality rates are compared to the experimental group and expressed as a percent of expected values.

Brown (1987) reported an SMR=263 (5 observed versus 1.9 expected) for "liver, gall bladder, and biliary tract" cancers. However, in contrast to the rodent results, none of the cases reported by Brown was identified as primary carcinoma of the liver. One cancer was from the gall bladder, three from the bile ducts, and one metastatic tumor with primary site unknown. The grouping of these cancers together is not consistent with their different International Classification of Disease (ICD) codes or with their different etiologies. Zimmerman, (1978) has summarized the differences between liver cell and biliary tract cancers in humans, including their causative agents, and concluded that they are two completely different forms of cancer.

An examination of the site-specific mortality showed that an association with cancer of the rectum originally reported by Brown and Jones (1981) did not remain when the additional person-years were added in this study. Whereas an SMR of 336 was reported in the original study, in the updated study the SMR was 211 (4 observed versus 1.9 expected). This later finding was not statistically significant.

Bertazzi et al. (1987) reported a study of 2100 workers, representing 41,010 person years, in a capacitor manufacturing facility located in Italy. From 1946 to 1964, workers were exposed to mixtures containing 54%

chlorine (Aroclor 1254 and Pyralene 1476), and after 1965 the predominant exposure was to mixtures containing 42% chlorine (Pyralene 3010, 3011). In this study, in contrast to the findings of Brown (1987), there was a statistically significant increase in total cancer deaths (males, SMR=183; females, SMR=226). Only one person had liver cancer and one person had biliary tract cancer. There were also increased deaths due to cancer of the gastrointestinal tract in males (SMR=274), and hematologic cancer in females (SMR=377). With regard to cancer of the gastrointestinal tract, the authors state that one individual with stomach cancer had been hired at an advanced age and received a very short exposure to PCBs. Furthermore, two of the individuals (one with stomach cancer, one with pancreatic cancer) had been security guards with no history of direct PCB exposure. This means that only three of the observed cases may be in people who had any significant exposure to PCBs, and only one individual (with pancreatic cancer) was exposed for more than one year. Likewise, the one case of liver cell cancer occurred in a person exposed for only 0.3 years.

In a small study by Gustavsson et al. (1986), mortality and cancer incidence was studied among 142 capacitor workers in Sweden. Exposures were to oil of 42% chlorine content, and all workers had been employed at least six months. Although this study was too small to determine site specific cancer incidence, total cancer deaths were not significantly different from the expected rate (SMR=130).

An unpublished report by Zack and Musch (1979) gave the results of study of Monsanto chemical workers exposed to PCBs for at least three months. In this study there were 88 workers in the total and 30 deaths. The only result to reach statistical significance was deaths due to diseases of the circulatory system exclusive of arteriosclerotic heart disease.

3.3 Studies of Other Human Health Effects

Several publications report various health effects related to PCBs although few have clinical relevance. The primary manifestation is the development of dermatological disorders such as chloracne and irritant dermatitis. Specific laboratory biochemical alterations in groups of persons have been observed. A few studies have associated PCB exposure with hypertensive, neurological, and pulmonary effects that are not consistent with many other studies.

Early findings regarding chloracne were described in Section 2.2. Fischbein et al., (1982) reported that a group of workers suffered hyperpigmentation, hyperkeratosis, comedones and chloracne; PCB blood levels correlated with the dermatologic findings. Other authors who have also reported chloracne include Maroni et al. (1981) and Chase et al. (1982). In both of these cases, the PCB exposures were high and for many years duration. In contrast, chloracne has not been reported in environmental

exposures (Humphrey, 1983; Baker, 1980).

Alterations in group mean blood liver-associated enzymes have been reported in several studies but not in parameters of liver function such as bilirubin, albumin and prothrombin times (Chase et al., 1982; Kreiss, 1981; Smith, 1982; Lawton, 1985). The ability to metabolize antipyrine as measured by its half-life was faster in five workers in one study (Alvares, 1977) but normal in 47 workers of another (Emmett, 1988). It should be noted that while the mean levels of serum alanine aminotransferase, aspartate aminotransferase and gamma-glutamyl transpeptidase were statistically different between exposed and unexposed workers, the groups' means and individual levels of most persons were within laboratory reference ranges (Kreiss, 1981; Smith, 1982; Chase, 1982; Lawton, 1985). The clinical significance of these findings also remains uncertain since workers do not develop clinical manifestations of hepatitis. An Italian study of workers exposed to Pyralene, a PCB mixture similar to Aroclor 1242, reported an unexpected incidence of hepatomegaly (Maroni, 1981). This finding has not been reported by any other investigators.

Several studies correlated serum lipid levels with blood PCB levels. Chase et al. (1982) found a statistically significant, age-adjusted, positive correlation of plasma PCB levels with triglycerides but not with cholesterol. Smith et al., (1982) investigated 228 workers and found a significant correlation with HDL cholesterol. Kreiss et al. (1981) and Baker et al. (1980) investigated groups of people who were environmentally exposed to both PCBs and DDT and reported positive correlations of serum PCB values with serum cholesterol or triglycerides. The cause and significance of these lipid findings are unknown. While it has been postulated that PCBs are related to abnormal lipid metabolism, more recent evidence suggests that the correlation reflects PCB solubility in serum lipids, thereby changing partitioning (Emmett, 1988; Lawton, 1985; Emmett, 1985; Guo, 1987). Furthermore, cardiovascular disease, the major health effect that would be predicted from increased lipid levels, has not been shown to be increased in PCB exposed cohorts (Brown, 1987; Gustavsson et al., 1986; Bertazzi et al., 1987).

Other PCB-related health effects have been suggested in the scientific literature. An association between PCB exposure and symptoms such as headache, fatigue and nervousness has been reported in one study (Fischbein, 1979) but not corroborated in six other studies (Takamatsu, 1984; Smith, 1982; Maroni, 1981; Chase, 1982; Stehr-Green, 1986; Emmett, 1988). Neurological testing was reported to be altered in one study (Smith, 1982), but not identified in four others (Chase, 1982; Fischbein, 1979; Smith, 1982; Acquavella, 1986).

Blood pressure was positively correlated with serum PCB levels in one study (Kreiss, 1981); however, the author later characterized the finding as uncertain (Kreiss, 1985). Elevated blood pressures were not reported in 10 other published studies (Emmett, 1988; Akagi, 1985; Takamatsu, 1984;

Stehr-Green, 1986; Fischbein, 1979; Baker, 1980; Chase, 1982; Acquavella, 1986; Smith, 1982; Maroni, 1981). Alterations in pulmonary function tests of workers exposed to PCB's have been reported in one study (Warshaw, 1979), but could not be duplicated in another investigating the same group of workers (Lawton, 1985). Emmett (1988) did not find any association between PCBs and pulmonary function tests.

Reproductive effects of PCB exposure have also been studied. Fein (1984) surveyed infants born to mothers who consumed moderate quantities of contaminated lake fish. Both fish consumption and PCB levels in cord serum were associated with lower birth weight and smaller head circumference. Taylor et al. (1989) studied women capacitor manufacturers and reported lower birth weights due to shortened gestational ages. Gladden et al. (1988) studied neurological development in relationship to trans-placental exposures and reported that lower psychomotor development at six and twelve months of age correlated with PCB blood level. In all the above studies, the mean differences between groups were small and the authors concluded that the effects of PCBs would be either minimal compared with other factors which affect growth, or not clinically important. In another study, no PCB-related clinical effects could be identified in children with environmental exposures at one year of age (Rogan, 1987).

3.4 Environmental Exposure Studies

Many studies of persons exposed environmentally to PCB sources have now been described in the literature. As will be discussed, except for consumption of sport fish and persons who had occupational exposures in addition to environmental exposures, there have been no positive findings.

Stehr-Green et al. (1988) summarized the results of PCB blood testing from ten studies of persons with the highest presumed environmental exposures from the presence of a nearby site containing large amounts of PCBs. These people were hypothesized to have numerous routes of exposure, and the likelihood of exposure via inhalation, ingestion and dermal absorption (direct contact with transformer fluid or contaminated soils) was high at all the twelve sites. One of the sites studied in this report was New Bedford. The authors concluded that the only pathways which caused a possible increase in blood levels were seafood consumption or occupational exposures.

Details of some of the investigations are unavailable for review; however, examples of these ATSDR site-studies will illustrate the conclusions of Stehr-Green et al. Studies of a capacitor manufacturing plant in Bloomington, Indiana (Stehr-Green et al., 1986) showed that on-site soil samples ranged up to 330,000 ppm and off-site soil samples at residences ranged up to 3500 ppm. Surface water showed PCB levels ranging up to 18 ppb. Persons were selected for analysis because they occupied residences nearby, swam in or ate fish from contaminated waters, or were involved in

playing or digging in the contaminated soils. No significant differences were found between exposed individuals and controls.

A study of residents nearby the Paoli railyard was conducted by ATSDR (1987). Soil samples in yards and streets ranged up to 6,400 ppm and local creeks and trout were also reported to have elevated levels. A study of 66 randomly selected persons were selected for study. The Blood levels in this group ranged from 1-24 ppb with a mean of 4.4 ppb. A substudy of 22 persons (excluding one individual with occupational exposure), who lived in residences at which at least one soil sample was above 150 ppm, found a range of 1-31 ppb with an average of 5.3 ppb in the blood. ATSDR concluded that these blood levels were not different from background. The only statistical finding was that PCB blood levels were highly correlated with age.

In 1987, the "Final Report of Greater New Bedford PCB Health Effects Study 1984-1987" (GNBHES) was completed. The purpose of this study was to determine whether persons in New Bedford have increased levels of PCBs in blood and whether these increases could be correlated with consumption of local seafood.

The results of this study show that among 840 people representing the general New Bedford population, no increase in the levels of blood PCBs was found. Because of this result, the authors concluded that "contact with ambient soils may not be a significant route to PCBs." The authors also suggested that the lack of elevated PCB levels is due to the success of the enforcement of the fishing ban. However, another conclusion is that residents did not receive significant exposure from PCBs in New Bedford seafood. Two quotes from the report which support this conclusion are the following:

1. "...recreational fishing still occurs in banned areas."
2. "...Even before the general discovery of the massive contamination problems, the general public was not directly or knowingly catching and eating fish from these areas." (p. 56)

A second part of the New Bedford study (the prevalence study) looked at persons who might be at greater risk for elevated blood levels because of consumption of seafood and occupational exposure. In this group, the authors reported a greater percentage of people with higher PCB blood levels. However, correlations with exposures, even for the consumption of lobster and tomalley, were not found in the detailed analysis. It is quite possible that the reported higher levels were related to occupational exposure or other confounding variables such as age. The average age of the "prevalence" group was 40 years, whereas the average age of the "enrichment" group was 53 years. Blood PCB levels have been correlated with age in other studies of many populations (Kreiss et al., 1981; Baker et al., 1980; ATSDR, 1987). The results of this study will be discussed

further in Section 6.1. This study will be analyzed in greater detail in Section 6.1.

4.0 CANCER MECHANISM AND PCB RISK ASSESSMENT

Toxicologic tests on animals are conducted with high doses of substances in order to produce significant levels of effects. However, such results cannot be directly applied to human exposures without some method of predicting the relevance of these effects at low doses. Traditional dose-response curves are plotted as dose or log(dose) versus effect or log(effect). When dose-response information is examined for non-carcinogenic, toxic effects, a threshold dose (dose below which no effect is observable) can usually be found. Protective mechanisms such as limited absorption, metabolic degradation and excretion act as barriers to the target organ.

Early dosimetry studies of cancer caused by radiation led to the development of hypothetical dose-extrapolation models without threshold doses. This hypothetical method was extended to include all chemical carcinogens even though such models ignore absorption, transport, and metabolic barriers, as well as DNA repair mechanisms. The argument against a threshold dose is even more specious for promoting agents, which act through metabolic rather than genetic mechanisms. Promoters would be expected to have dose-response curves and thresholds consistent with other non-genetic toxic effects. The importance of this distinction is the large impact that such modeling has upon the issue of acceptable exposures for humans.

4.1 Model Systems for Liver Cancer

Experimental results on the development of cancer from chemical exposures have led to the development of models containing many sequential stages required for the expression of cancer. This multistage model has several processes involved, some of which may be reversible. Although such models have been developed for many tissues, one of the most thoroughly studied is the liver: the main target organ of concern for PCBs.

In the various models for hepatocellular carcinoma as reviewed by Farber and Cameron (1980), metabolically activated chemicals react to produce altered nucleotide defects or altered DNA control which then may cause cells to become transformed into initiated cells. In some cases this process can be repaired or reversed. Certain chemicals and radiation are known to act at this level resulting in initiated cells.

These initiated cells may be promoted through a process which favors the proliferation of the initiated cells over normal cells resulting in neoplastic nodules. Promotion is usually a slow process, requiring months or years. This process is caused by many chemicals including phenobarbital; endogenous substances such as steroid hormones and other growth factors; and many halogenated hydrocarbons including PCBs. Following promotion, several subsequent steps appear to be necessary for progression

to hepatocellular carcinoma. The result of progression is development of a neoplasm having the characteristics ascribed to cancer.

Thus, in the evaluation of a chemical carcinogen, it is important to distinguish between genetic and epigenetic mechanisms. For agents acting at those steps which require genetic change, an argument can be made for using the traditional EPA approach of a linear extrapolation without a threshold. However, for those steps involved in growth promotion, a threshold dose below which no effect would be expected is supported by the experimental evidence.

Therefore, it is important to know whether PCBs are genotoxic or act at growth promotion stages in the development of cancer. Also, it is necessary to understand that substances such as PCBs may show positive results in two year rat bioassays through promotional effects alone.

4.2 Carcinogenesis Assays of PCBs

Since the study of Kimbrough (1975), additional studies have associated some PCB mixtures with liver cancer in rodents treated for a lifetime at a high dose (Schaeffer et al. 1984; Norback and Weltman, 1984). These studies have shown positive findings only at 100 ppm in the food for Aroclor 1260 and Clophen A60 (a German product similar to Aroclor 1260). The studies of Aroclor 1260 have been used by EPA to determine a carcinogenic potency in humans.

These results have been interpreted to show that PCBs act as a complete carcinogen. However, it is clear that initiated cells can result from other causes during the course of rodent experiments. Several studies have shown that rodents spontaneously generate preneoplastic foci, nodules, and cancer (Schulte-Hermann et al., 1983; Ward, 1983). Hepatocellular carcinoma and neoplastic nodules also have occurred in the control groups of two of the PCB cancer bioassay studies (Schaeffer et al. 1984; Kimbrough, 1975). Therefore, untreated rats have both initiated and promoted liver cells during their lifetime. Schulte-Hermann et al. (1983) have commented that the standard dietary chow contains fish meal, which could be a major dietary source of nitrosamines.

4.3 Promotion and Inhibition of Hepatic Tumors by PCBs

Many studies have shown that PCBs act as promoters of cancer when given after initiating (mutagenic) agents. Preston et al., (1981) showed convincingly that Aroclor 1254 was also capable of increasing the incidence of hepatocellular carcinoma initiated by prior treatment with diethylnitrosamine (DEN). Animals were given 100 ppm PCB in the diet for 18 weeks after treatment with DEN for 5 weeks. The cancer rate for DEN treatment alone was 16% compared with 64% and 84% in two different Aroclor

1254 treated groups.

Nishizumi (1976, 1980) reported that Kanechlor 500 accelerated the development of liver tumors in rats exposed previously to DEN. These promoting effects also could be produced with DDT and phenobarbital. Kimura et al. (1976) showed that Kanechlor 400 was capable of increasing the incidence of hepatocellular carcinoma when given after 3'-methyl-4-dimethyl-aminoazobenzene (Me-DAB). When Me-DAB was give alone, 47% of the rats had neoplastic nodules and 13% had cancer; whereas, 100% had neoplastic nodules and 64% had cancer when PCBs were given after the initiating agent.

PCBs are also known to inhibit the development of cancer when given prior to initiation by DEN. Makiura et al. (1974) found that simultaneous administration of PCBs with DEN and other carcinogens resulted in a large decrease in their cancer potency. This inhibition was also found by Nishizumi (1980) when rats were exposed to PCBs in utero and through nursing before the administration of DEN. Similarly, Kimura et al. (1976) found that administering PCBs before rather than after Me-DAB resulted in no cancer versus a 64% cancer rate in rats not treated with PCBs.

4.4 Mutagenicity Assays of PCBs

In vitro and in vivo systems have been used to assess the mutagenic potential of PCBs. The Ames test for frame shift mutations in Salmonella typhimurium is the most widely used test for mutagenesis (Ames et al., 1975). Shoeny et al. (1979) tested Aroclor 1254 in the strains recommended by Ames et al.. In all cases, Aroclor 1254 was not mutagenic with or without metabolic activation. Tests of 4-monochlorinated biphenyl, two different tetrachlorinated biphenyls, and one hexachlorinated biphenyl also gave negative results (Sheony, 1982). Hsai et al. (1978) tested 2,5,2',5'-tetrachlorobiphenyl and its 4-hydroxy and 3,4-oxide derivatives in four strains of Salmonella typhimurium. None of the compounds showed mutagenic effects when tested with or without metabolic activation. Mutagenicity of Aroclor 1242 and Clophen A60 was also tested by Hattula (1985) in a mammalian cell assay using V79 Chinese hamster cells for selection of ouabain resistant mutants. Neither mixture of PCBs showed mutagenicity.

The only researchers to report mutagenicity in the Ames test have since reported that they were subsequently unable to repeat the results. Wyndham et al. (1976) reported a positive response to 4-monochlorinated biphenyl, a lesser response to Aroclor 1221, and little or no response to 2,2',5,5'-tetrachlorobiphenyl or Aroclor 1268. One of the authors has reported that repeat experiments were unable to confirm these positive findings (Safe, 1989).

The only positive results for in vivo testing of PCBs have been

reported by Peakall et al. (1972) for chromosome aberrations in embryos of ring doves fed 10 ppm Aroclor 1254. However, the differences between the six controls (0.8%) and the thirteen embryos in the PCB treated group (1.8%) was not tested for statistical significance; therefore, no conclusions can be drawn from the results of this study. In addition, the length of the treatment regime and the nature of the chromosomal abnormalities were not adequately described in this study.

All other in vivo tests proved to have negative results. Nilsson and Ramel (1974) tested Clophen 30 and 50 on Drosophila melanogaster for loss of sex chromosomes as a measure of a chromosome breaking action and nondisjunction of the sex chromosomes. The tests showed negative results. Dikshith et al. (1975) found no chromosomal damage or arrested rate of spermatogenesis when rats were fed Aroclor 1254 at 50 mg/kg for seven days. Green et al. (1975) found no effect in a test for dominant lethality in rats treated with Aroclors 1242 and 1254. In another investigation, Green et al. (1975) found no chromosomal abnormalities in bone marrow cells in animals fed Aroclors 1242 or 1254. Also, these authors found no effect upon cytogenetic appearance in spermatogonial cells after administration of Aroclor 1242.

4.5 Threshold Dose Determination for PCBs

Oesterle and Deml (1984) and Deml and Oesterle (1987) demonstrated a threshold dose for PCB promotion of DEN initiated rat liver. They used a method having two experimental groups, weanling and adult rats; and they measured the number and size of enzyme altered foci (EAF), which are a stage of liver cancer occurring before neoplastic nodules. The biochemical changes in the EAF measured were the loss of ATPase, emergence of GGTase, and glycogen storage. These results indicate that a threshold dose existed for Clophen A50 at 1 mg/kg-3 times per week in all parameters.

Additionally, Oesterle and Deml measured EAF in rats treated only with Clophen A50. The incidence of these preneoplastic lesions was much lower than in the groups pretreated with DEN. The results show that for weanling rats a threshold dose for EAF exists between 10 and 25 mg/kg/week (1.4-3.6 mg/kg/day). This is true for all parameters of measurement. In the adult rats, a similar threshold was found for the area but not the numbers of EAFs. However, there was evidence that the lowest dose (1.4 mg/kg/day) was close to a threshold for ATPase and glycogen storage.

4.6 Relative Carcinogenicity of Different PCB Mixtures

The EPA has used comparative carcinogenic and biochemical studies in order to determine the relative carcinogenic risk of different mixtures of polychlorinated dibenzodioxins and furans (EPA, 1987). Similar principles

should apply to the relative carcinogenic potencies of PCBs, thereby adjusting risk factors according to Aroclor type.

As previously discussed, several studies have reported hepatocellular carcinoma in rodents which received 100 ppm of Aroclor 1260 or Clophen A60 (Kimbrough, 1975; Schaeffer et al. 1984; Norback and Weltman, 1984). Other studies have been done on Aroclor 1254 (NCI, 1978; Kimbrough and Linder, 1974), and although neoplastic nodules (benign tumors) were found, there were no significant increase in hepatocellular carcinomas.

Only one study has been performed comparing the relative potency of different commercial mixtures of PCBs. The study by Schaeffer et al. (1984) compared the relative ability of 100 ppm in the diet of Clophens A60 and A30 to produce hepatocellular carcinoma in rats. These two PCB mixtures are similar to Aroclors 1260 and 1242, respectively. In this study male weanling rats were fed either Clophen A60 or A30 for approximately 800 days. The PCB treated rats lived significantly longer than the control group. After 800 days hepatocellular carcinoma rates were 61% for Clophen A60, 3% for Clophen A30, and 2% for the controls. Differences in neoplastic nodule formation likewise showed a difference in cancer potency. However, these are difficult to quantitate from the study since only the highest stage in the development of cancer was reported per animal.

The lifetime study of Aroclor 1254 in F344 rats by the NCI (1978) is also supportive of the lower cancer potency of lower chlorinated PCB mixtures. By comparing the findings of the NTP study with that of 100 ppm in the diet of Aroclor 1260 by Kimbrough, a difference in cancer potential is observed. Although the NTP study found neoplastic nodules, no significant hepatocellular carcinoma at 100 ppm in the diet was found. Therefore, Aroclor 1254 either is not carcinogenic or has less potency than Aroclor 1260.

5.0 DISCUSSION OF PCB HEALTH EFFECTS

The results of the occupational epidemiology studies, which were summarized in Section 3.2, show a complete lack of consistent results. The Bertazzi study found increased total cancer, but the other studies did not. Associations found in one study with site specific cancer (or other disease) were contradicted by other studies: Bahn, malignant melanoma; Brown, liver and biliary cancer; Bertazzi, hematologic and gastrointestinal cancer; and Zack and Munsch, circulatory disease. (The gastrointestinal cancer increase of Bertazzi was not indicative of a liver or biliary cancer increase since there was only one case of each.)

In order to determine causation from associations Bradford-Hill (1965) has identified nine criteria. The most important criterion is strength of association; but the second most important is consistency of clinical findings between studies. As previously discussed, the epidemiology studies were not consistent and appear to refute each other's findings. Therefore, an association between occupational exposure to PCBs and cancer has yet to be shown.

Studies of the mechanism of cancer in animals may explain the lack of positive findings in the human occupational epidemiology studies. The existence of a postulated threshold dose for cancer promotion, far greater than any "Virtually Safe Dose" (VSD), would explain the lack of findings in humans. The consequences of treating PCBs as a promoter with a threshold dose versus a complete carcinogen are enormous. The difference in acceptable risk for the two methods of extrapolation is several orders of magnitude.

Another reason for the lack of findings in humans is that liver cancer in rodents may not predict cancer in humans. There are several animal studies which show that PCBs given before or simultaneously with initiating agents decrease the probability of cancer. Only when initiating agents are given first do PCBs increase cancer incidence in rodents. Additionally, in the all three major assays of cancer in rodents, the animals in the treated groups survived either longer or the same as the controls. The type of cancer in rodents does not appear to be debilitating as cancer is in humans, and there was a lack of metastatic activity.

Consequently, it is highly unlikely that PCBs at the levels found in environmental settings are responsible for the development of liver cancer. Our inability to demonstrate such effects in studies of over 100,000 person-years in highly exposed persons from occupational settings argues against the risk from PCBs at current environmental exposures.

The only human health effect that has been found consistently in human studies is confined to the skin. Chloracne occurs in a small percentage of persons who have sufficient exposures resulting in greater than 200 ppb blood levels. This chloracne is not the persistent type

found in Yusho disease. An association between serum lipids and PCB blood concentrations is best explained as an increased partitioning into the blood by the higher fat content. Studies of small changes in developmental testing and growth in infants from exposed mothers still require further confirmation, and additional studies are needed to determine the persistence of such effects. The clinical findings and epidemiology studies regarding Yusho and Yu-Cheng have not proven to be helpful to determine the toxicity of PCBs in humans. As discussed in Section 3.1, these studies may explain PCDF effects, but not those of PCBs. Kimbrough (1987) has reviewed the PCB literature and concluded that, "So far, no significant chronic health effects have been causally associated with exposure to PCBs or PBBs.

Studies of environmental exposures have not shown any health effects even when elevated blood levels have been found. However, the only definitive studies which find elevated PCB blood levels correlated to fish consumption are those of Humphrey (1976, 1983). Other studies of environmental exposures have shown that, even when populations have multiple pathways of exposure available, only fish consumption or concurrent occupational exposures have been shown to be correlated with elevated blood levels.

6.0 HUMAN EXPOSURES TO SEDIMENTS IN THE UPPER ESTUARY

The possible pathways of human exposure to PCBs in the New Bedford area from the presence of sediments in the upper Acushnet Estuary include the following:

1. Ingestion of aquatic biota.
2. Direct contact with the sediments.
3. Ingestion of the sediments.

A risk assessment for human ingestion of fish or lobster would be very difficult to develop because of the lack of information regarding the future contribution of PCBs from "hot spot" sediments to the edible portions of these biota. There are two important variables which cause the uncertainty: reduction in the "hot spot" concentration via biodegradation, leaching into the water, and volatilization; and transport to the site of biota consumption. The EPA apparently has not studied these important issues. Because of these unknowns a risk assessment calculation of fish and lobster consumption cannot be attempted in this report. However, the GNBHES report will be evaluated to determine the possibility of significant contribution from this pathway due to existing sediment conditions.

6.1 Seafood Ingestion Exposure

The GNBHES report provides information regarding the current body burdens due to the ingestion of seafood from the New Bedford area. The results of the prevalence study show that the general population has a PCB body burden which is the same as that of the general population. Of the 840 subjects studied, 1.3% had levels above 30 ppb and 2.7% above 20 ppb in contrast to expected rates of 1% and 5%, respectively. The mean levels in this population was 4.2%. These findings lead the authors to conclude that "...prevalence to elevated serum PCB levels of Greater New Bedford is low."

The results of the enrichment study have been utilized to indicate a higher body burden among New Bedford residents who have increased seafood consumption. However, a review of the criteria for admittance to the study indicates that past or present employment at either of the two capacitor manufacturing facilities was also used to include people in the study. Importantly, the enrichment study was not designed to investigate people who ate locally caught seafood, but the study was supposed to investigate the possible health problems of people who had increased body burdens of PCBs. This study was never done, however, because the blood PCB levels were not high enough.

The results of the enrichment study reported PCB blood levels greater than that of the prevalence study. The median PCB blood level was 9.48 ppb and the mean was 13.34 ppb. The analysis of seafood consumption by PCB blood level did not show any association for any of the types of biota (Table 22, GNBHES). However, an analysis of industry by employment showed that 10 persons who worked in the "electrical machinery, equipment, supplies" category were above the median and only one was below the median (Table 23, GNBHES). Likewise, exposure to certain materials such as putty, sealants, varnishes and wood preservatives were also associated with higher PCB blood levels (Table 24, GNBHES). Therefore, the criteria were successful in finding people whose occupational exposures resulted in higher PCB blood levels, but did not show an association with seafood consumption. Additionally, the age of the enrichment group was significantly higher than the prevalence group which has been reported to be correlated with blood PCB level.

The importance of these findings is enhanced by the observations in the study regarding the continuance of local seafood consumption at the time that the GNBHES was done.

"An even more important observation regarding trends among persons who report local seafood consumption might be that despite widespread public education regarding the local PCB contamination problems, 61.4% of the enrichment sample and 36.3% of prevalence sample indicated that their level of local consumption had either increased or been maintained." (GNBHES, p.86)

This finding would indicate that at the time of the GNBHES study, the level of local seafood consumption was sufficient so that the study should have found a relationship of seafood consumption with PCB blood level, if this were a significant pathway.

The only trends in the data linking local seafood consumption were reported in Figures 10 and 11 of the GNBHES report. In Figure 10 there is reportedly a greater consumption of local versus general seafood consumption related to PCB blood level, and in Figure 11 a relationship of frequency of seafood consumption with blood level. The authors of this study did not report statistical tests of these results, nor did they test for confounding variables such as age or occupation. Age was found to also be related to blood PCB level in the prevalence group. Occupational exposures were related to blood PCB levels in the enrichment group.

6.2 Direct Contact with Sediments

It is considered unlikely that human exposure would occur from either direct contact with or ingestion of sediments in higher concentrations of the "hot spot." The sequestered location of the PCB-containing sediments, their mud-like consistency, and the unlikely possibility of human activity

at that part of the estuary would prevent human contact. The "hot spot" sediment is not accessible on a regular basis since it is not adjacent to any residences, and access is hindered by fencing. Calculations are developed in this section to determine the risk associated with inadvertent exposure to a sediment concentration of 300 ppm. Such a concentration would be the upper limit found in most of the accessible upper estuary (Serapas, 1989).

The risk assessment calculations for ingestion and dermal contact are presented in Tables 2-5. The calculations have been based upon one "episode" of contact per lifetime in order to determine the number of such episodes which would be acceptable for a given risk level. This is done because it is not possible to estimate a frequency for inadvertent exposure. Such an episode is envisioned as an adult or child exposing themselves to the contaminated location for a four hour period. Dermal contact would cease after the sediment was washed off the skin. Although it seems very unlikely that a child ages 1-5 could have access to this mud-like sediment, a calculation for dermal contact and ingestion of a portion of this sediment is included for discussion purposes.

The results of these calculations give risks of 2.39, 1.77, and 1.40×10^{-8} for each episode of dermal contact depending upon whether it occurs during 1-5, 6-16 years of age, or in an adult, respectively. Therefore, any one episode would fall far outside of a level of concern for carcinogenic risk. For a risk of 10^{-5} , 400-700 such episodes during a lifetime depending upon whether one uses the young child or adult values.

For the improbable event of oral ingestion by a young child the risk per episode is calculated to be 1.81×10^{-7} . Therefore, approximately fifty-five such episodes would be acceptable for a risk level of 10^{-5} .

For dermal contact, a skin surface concentration of one mg/sq cm is assumed based upon the studies of Lepow et al. (1975) and Roels et al. (1980). In the latter study soil amounts in contact with the skin were measured for children actively playing in the dirt. The soil surface concentration ranged from 0.8 to 1.7 mg/sq cm. In the study by Lepow et al., soil surface concentrations were not directly measured, but calculations can be derived from their data resulting in less than one mg/sq cm.

Calculations for total skin surface area calculated in Table 1 based upon the formula of Gehan and George (1970) using standard height and weight measures for the age represented. An average total skin surface area is then calculated for three age groups: 1-5 years, 6-16 years, and adults. The percentage of the skin in contact with the sediment would be 12%, which includes the total surfaces of the hands and feet (Way, L.W., 1983).

The carcinogenicity potency factor assumes a lifetime of exposure at

the given daily dose. Because the exposure duration in this example is for one day in a lifetime, an exposure duration factor is included as follows:

$$\frac{\text{one lifetime}}{70 \text{ years}} \times \frac{\text{one year}}{365 \text{ days}} = 3.91 \times 10^{-5}$$

Absorption efficiency by the dermal route for PCBs has not been studied for PCBs bound to soil. However, Wester et al. (1983) have studied the adsorption of PCBs in solvent by the skin of monkeys and guinea pigs. The 24 hour adsorption ranged from 15 to 56% in these studies. Because of the physical chemical similarity between PCBs and TCDD, studies of absorption of soil bound TCDD can be used to approximate PCB absorption. Shu et al. (1988) reported a 50-fold reduction of TCDD absorption in rats when bound to soil. Due to lower absorption rates in humans versus rats, Shu et al. concluded that TCDD dermal absorption in rats would be less than one percent for a twenty-four hour exposure and less than 0.5% for a four-hour exposure.

In the case of oral absorption calculated in Table 5, the assumption is made that a child would ingest 100 mg of soil per episode. Two studies have investigated the amount of soil ingested by children (Binder, et al., 1986; Clausing, et al., 1987). LaGoy (1987) summarized these studies and concluded that the average soil ingestion rate for a child is 100 mg/day.

The assumption will be made that the oral absorption efficiency is 30% for PCBs. The only study of PCB absorption following oral absorption in animals is an unpublished report by Charles et al. (1978) who found that activated charcoal reduced the absorption to about 15% as measured in the liver and adipose tissue. Studies of TCDD bound to soil by Poigner and Schlatter (1980) found 65% and 44% absorption for TCDD bound to soil after 10-15 hours and eight days, respectively. Presumably, absorption would be less for more tightly bound TCDD. Umbreit et al. (1986) reported 0.5% and 26% absorption for soils from two different TCDD contamination sites. Shu et al. (1988) reported a mean bioavailability rate of 43% for TCDD in the soil.

In all the calculations presented in Tables 2-5 a carcinogenicity potency factor of 7.7 risk/mg/kg-day is used for the purposes of illustration. This is the most conservative value recommended by EPA at this time. However, as presented in this report, the scientific evidence would argue for a potency factor which is much less. The evidence presented in Section 4 shows that PCBs act to promote carcinogenesis, and this cancer mechanism would argue for a threshold dose. The dose-response studies of Oesterle and Deml (1984) summarized in Section 4.5 give a threshold dose of 1.4 mg/kg-day. All the dosage rate corresponding to the risk presented in Tables 2-5 would be several orders of magnitude below this threshold dose, thereby resulting in no cancer risk with a considerable margin of safety. Furthermore, the studies on the relative carcinogenic potential

of different PCB mixtures summarized in Section 6.1 shows that the carcinogenic potential of the PCB types in the Ascushnet Estuary would be less potent than Aroclor 1260, which is the PCB mixture used to determine the carcinogenicity potency factor. Therefore, the calculated risks are much less than those calculated, and based upon the threshold dose are zero.

7.0 SUMMARY AND CONCLUSIONS

This report has examined the PCB literature on cancer and human health effects. The original literature which caused grave concerns regarding PCB toxicity at the time of TSCA legislation have been modified by several lines of scientific investigation. The original studies of human toxicity from the Yusho incident have been shown to have PCDFs rather than PCBs as the causative agents. Furthermore, numerous occupational studies of persons exposed to large amounts of PCBs over many years have shown chloracne to be the only toxic effect.

Studies reporting PCB-related liver cancer in rodents have been confirmed; however, the PCBs do not produce a mutagenic effect. The production of rodent cancer by PCBs appears to act through a promotional mechanism, resulting in the proliferation of initiated cells. Such a mechanism would argue for a threshold dose below which no cancer is produced. Several occupational epidemiologic studies have been completed, and the analysis of these studies do not show a causal link between PCB exposure and cancer or other illnesses.

Human exposures to environmental contamination have not shown an increase PCB body burden except through the consumption of seafood. However, studies of persons with environmental exposure through seafood have not demonstrated any deleterious health effects. Studies of the New Bedford population have not shown elevated body burdens for PCBs. In a substudy of persons with occupational PCB exposures and consumption of local seafood, occupational exposures were clearly correlated with PCB levels.

Risk assessment calculations for dermal exposure to and ingestion of Ascushnet sediment containing 300 ppm PCB have not shown risk levels of concern from cancer. Because of the unlikely occurrence of exposure, risks were calculated for each "episode" of exposure. It was determined that approximately 400-700 such episodes during a lifetime of dermal exposure would lead to a risk of between zero and 10^{-5} . Similarly, a child between the ages of one and five could have fifty-five episodes of oral ingestion for a risk of between zero and 10^{-5} . These hypothetical risks are upper limits, and at these PCB levels, the risks are most likely zero. This is due to the extremely conservative model used for calculating a carcinogenicity potency factor. The threshold dose model, which may be more appropriate for PCBs would conclude that all of these risks are zero.

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TABLE 1
SURFACE AREA AND WEIGHT CALCULATIONS

AGE	X	PARAMETER Y	Z	HEIGHT cm	WEIGHT kg	SURFACE sq meters
1	0.02667	0.38217	0.53937	82	11	0.52
2	0.02667	0.38217	0.53937	90	13	0.59
3	0.02667	0.38217	0.53937	98	15	0.66
4	0.02667	0.38217	0.53937	106	17	0.73
5	0.0305	0.35129	0.54375	112	19	0.79
Average for 1-5 years				97.60	15.00	0.66
6	0.0305	0.35129	0.54375	118	21	0.85
7	0.0305	0.35129	0.54375	124	24	0.93
8	0.0305	0.35129	0.54375	129	26	0.99
9	0.0305	0.35129	0.54375	135	30	1.09
10	0.0305	0.35129	0.54375	141	34	1.18
11	0.0305	0.35129	0.54375	147	38	1.27
12	0.0305	0.35129	0.54375	154	43	1.38
13	0.0305	0.35129	0.54375	159	48	1.49
14	0.0305	0.35129	0.54375	163	53	1.58
15	0.0305	0.35129	0.54375	167	57	1.66
16	0.0305	0.35129	0.54375	169	60	1.71
Average for 6-16 years				146.00	39.45	1.29
ADULT	0.01545	0.54468	0.46336	170	70	1.81

TABLE 4
RISK FOR ONE EPISODE OF DERMAL CONTACT
SEDIMENT LEVEL 300 PPM
ADULT

FACTOR	VALUE	REFERENCE
Sediment Concentration	0.0003 mg PCB/mg soil	300 ppm
Soil Deposition	1 mg/sq cm	Section 7.2
Total Skin Surface Area	18100 sq cm	Table 1
Fraction of Surface	0.12	Section 7.2
Exposure Duration	3.91E-05	Section 7.2
Absorption Efficiency	0.005	Section 7.2
Average Weight Reciprocal	0.014 /kg	Table 1
Carcinogenicity Potency	7.7 risk/mg/kg-day	Section 7.2

RISK	Zero to 1.4E-08
NUMBER OF EPISODES FOR ACCEPTABLE RISK	Greater than 713

TABLE 5
RISK FOR ONE EPISODE OF SEDIMENT INGESTION
SEDIMENT LEVEL 300 PPM
CHILD 1-5 YEARS OLD

FACTOR	VALUE	REFERENCE
Sediment Concentration	0.0003 mg PCB/mg soil	300 ppm
Soil Ingestion	100 mg	Section 7.2
Exposure Duration	3.91E-05	Section 7.2
Average Weight Reciprocal	0.067	Table 1
Absorption Efficiency	0.3	Section 7.2
RISK	Zero to 1.81E-07	
NUMBER OF EPISODES FOR ACCEPTABLE RISK	Greater than 55	