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# Toxicological Profile for



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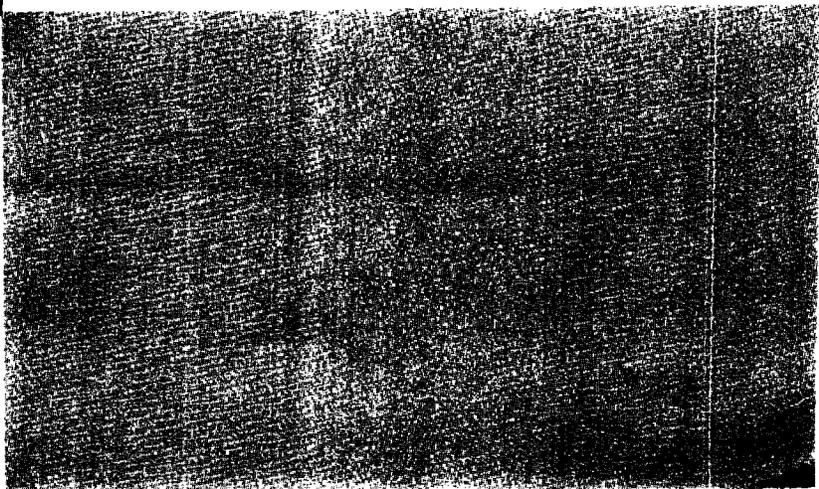
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## SELECTED PCBs (AROCOLOR -1260, -1254, - 1248, -1242, -1232, -1221, and -1016)

Agency for Toxic Substances and Disease Registry  
U.S. Public Health Service

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**TOXICOLOGICAL PROFILE FOR  
SELECTED PCBs  
(Aroclor-1260, -1254, -1248, -1242,  
-1232, -1221, and -1016)**

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Prepared by:

Syracuse Research Corporation  
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Agency for Toxic Substances and Disease Registry (ATSDR)  
U.S. Public Health Service

in collaboration with

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Mention of company name or product does not constitute endorsement by the Agency for Toxic Substances and Disease Registry.

## FOREWORD

The Superfund Amendments and Reauthorization Act of 1986 (Public Law 99-499) extended and amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law (also known as SARA) directed the Agency for Toxic Substances and Disease Registry (ATSDR) to prepare toxicological profiles for hazardous substances which are most commonly found at facilities on the CERCLA National Priorities List and which pose the most significant potential threat to human health, as determined by ATSDR and the Environmental Protection Agency (EPA). The list of the 100 most significant hazardous substances was published in the *Federal Register* on April 17, 1987.

Section 110 (3) of SARA directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list. Each profile must include the following content:

"(A) An examination, summary, and interpretation of available toxicological information and epidemiologic evaluations on a hazardous substance in order to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects.

(B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure which present a significant risk to human health of acute, subacute, and chronic health effects.

(C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans."

This toxicological profile is prepared in accordance with guidelines developed by ATSDR and EPA. The guidelines were published in the *Federal Register* on April 17, 1987. Each profile will be revised and republished as necessary, but no less often than every three years, as required by SARA.

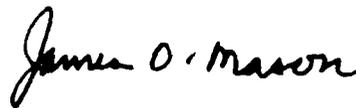
The ATSDR toxicological profile is intended to characterize succinctly the toxicological and health effects information for the hazardous substance being described. Each profile identifies and reviews the key literature that describes a hazardous substance's toxicological properties. Other literature is presented but described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.

*Foreword*

Each toxicological profile begins with a public health statement, which describes in nontechnical language a substance's relevant toxicological properties. Following the statement is material that presents levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Research gaps in toxicologic and health effects information are described in the profile. Research gaps that are of significance to protection of public health will be identified by ATSDR, the National Toxicology Program of the Public Health Service, and EPA. The focus of the profiles is on health and toxicological information; therefore, we have included this information in the front of the document.

The principal audiences for the toxicological profiles are health professionals at the federal, state, and local levels, interested private sector organizations and groups, and members of the public. We plan to revise these documents in response to public comments and as additional data become available; therefore, we encourage comment that will make the toxicological profile series of the greatest use.

This profile reflects our assessment of all relevant toxicological testing and information that has been peer reviewed. It has been reviewed by scientists from ATSDR, EPA, the Centers for Disease Control, and the National Toxicology Program. It has also been reviewed by a panel of nongovernment peer reviewers and was made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.



James O. Mason, M.D., Dr. P.H.  
Assistant Surgeon General  
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## 1. PUBLIC HEALTH STATEMENT

### 1.1 WHAT ARE PCBs?

The abbreviation PCB refers to polychlorinated biphenyls. PCBs are a family of man-made chemicals that contain 209 individual compounds with varying toxicity. Commercial formulations of PCBs enter the environment as mixtures consisting of a variety of PCBs and impurities. Because of the complex nature associated with evaluating the health effects of PCBs, this document will address only seven selected classes of PCBs, which include 35% of all of the different PCBs and 98% of PCBs sold in the United States since 1970. Some commercial PCB mixtures are known in the United States by their industrial trade name, Aroclor. Because of their insulating and nonflammable properties, PCBs have been used widely as coolants and lubricants in transformers, capacitors, and other electrical equipment. The manufacture of PCBs stopped in the United States in October 1977 because of evidence that PCBs accumulate in the environment and may cause health hazards for humans.

### 1.2 HOW MIGHT I BE EXPOSED TO PCBs?

Although PCBs are no longer manufactured, human exposure still occurs. Many older transformers and capacitors still contain fluids that contain PCBs. The useful lifetime of many of these transformers can be 30 years or more.

The two main sources of human exposure to PCBs are environmental and occupational. PCBs are very persistent chemicals that are widely distributed throughout the entire environment. PCBs have been found in at least 216 of 1,177 hazardous waste sites on the National Priorities List (NPL). Background levels of PCBs can be found in the outdoor air, on soil surfaces, and in water. Eating contaminated fish can be a major source of PCB exposure to humans. These PCBs originate in contaminated water, sediment, PCB-laden particulates, and in fish that have eaten PCB-contaminated prey. Although PCBs found in fish are generally concentrated in nonedible portions, the amounts in edible portions are high enough to make consumption a major source of exposure for humans. Compared with the intake of PCBs through eating contaminated fish, exposure through breathing outdoor air containing PCBs is small. Most of the PCBs in outdoor air may be present because of an environmental cycling process. PCBs in water, or on soil surfaces, evaporate and are then returned to earth by rainfall or settling of dust particles. Reevaporation repeats the cycle. Once in the air, PCBs can be carried long distances; they have been found in snow and seawater in the Antarctic. In addition, contaminated indoor air may be a major source of human exposure to PCBs, particularly in buildings that contain PCB-containing devices.

## 2 Section 1

PCBs can be released into the environment from:

- poorly maintained toxic waste sites that contain PCBs,
- illegal or improper dumping of PCB wastes, such as transformer fluids,
- leaks or fugitive emissions from electrical transformers containing PCBs, and
- disposal of PCB-containing consumer products into municipal landfills rather than into landfills designed to hold hazardous wastes.

Consumer products that may contain PCBs are:

- old fluorescent lighting fixtures and
- electrical devices or appliances containing PCB capacitors made before PCB use was stopped.

Occupational exposure to PCBs can occur during:

- repair or maintenance of PCB transformers,
- accidents or spills involving PCB transformers,
- disposal of PCB materials, and
- contact at hazardous waste sites.

### 1.3 HOW DO PCBs GET INTO MY BODY?

PCBs enter the body through contaminated food and air and through skin contact. The most common route of exposure is by eating fish and shellfish from PCB-contaminated water. Exposure from drinking water is minimal. It is known that nearly everyone has PCBs in their bodies, including infants who drink breast milk containing PCBs.

### 1.4 HOW DO PCBs AFFECT MY HEALTH?

Although PCBs have not been manufactured in the U.S. since October 1977, their diminishing but continued presence in certain commercial applications and trade have resulted in low-level exposure to the general population. Prior to 1977, certain occupational settings had, and may still have, higher levels of human exposure. Animal experiments have shown that some PCB mixtures produce adverse health effects that include liver damage, skin irritations, reproductive and developmental effects, and cancer. Therefore, it is prudent to consider that there may be health hazards for humans. Human studies to date show that irritations, such as acnelike lesions and rashes, can occur in PCB-exposed workers. Other studies of people with occupational exposure suggest that PCBs might cause liver cancer. Reproductive and developmental effects may also be related to occupational exposure and eating of contaminated fish. While the role of PCBs in producing cancer, reproductive, and developmental effects in humans cannot be clearly delineated, the suggestive evidence provides an additional basis for public health concern about humans who may be exposed to PCBs. The complexity of relating the specific mixtures for which data are available to exposures in the general population has resulted in a

tendency to regard all PCBs as having a similar health hazard potential, although this assumption may not be true.

#### 1.5 IS THERE A MEDICAL TEST TO DETERMINE IF I HAVE BEEN EXPOSED TO PCBs?

There are tests to determine PCBs in the blood, body fat, and breast milk. These tests are not routine clinical tests, but they can detect PCBs in members of the general population as well as in workers with occupational exposure to PCBs. Although these tests indicate if one has been exposed to PCBs, they do not predict potential health effects. Blood tests are the easiest, safest, and, perhaps, the best method for detecting recent large exposures. It should be recognized that nearly everyone has been exposed to PCBs because they are found throughout the environment and that nearly all persons are likely to have detectable levels of PCBs in their blood, fat, and breast milk.

#### 1.6 WHAT LEVELS OF EXPOSURE HAVE RESULTED IN HARMFUL HEALTH EFFECTS?

Figures 1.1, 1.2, and 1.3 on the following pages show the relationship between exposure to PCBs and known health effects for the PCBs that are covered by this profile. Other PCBs may have different toxic properties. In the first set of graphs, labeled "Health effects from breathing PCBs," exposure is measured in milligrams of PCBs per cubic meter of air ( $\text{mg}/\text{m}^3$ ). In the second and third sets of graphs, the same relationship is represented for the known "Health effects from ingesting PCBs" and "Health effects from skin contact with PCBs." Exposures are measured in milligrams of PCBs per kilogram of body weight per day ( $\text{mg}/\text{kg}/\text{day}$ ). It should be noted that health effects observed by one route of exposure may be relevant to other routes of exposure.

In all graphs, effects in animals are shown on the left side, effects in humans on the right. The first column on the graphs, labeled short-term, refers to known health effects from exposure to PCBs for 2 weeks or less. The columns labeled long-term refer to PCB exposures of longer than 2 weeks. The levels marked on the graphs as anticipated to be associated with *minimal risk of developing health effects* are based on information generated from animal studies; therefore, some uncertainty still exists. Based on evidence that PCBs cause cancer in animals, the Environmental Protection Agency (EPA) considers PCBs to be probable cancer-causing chemicals in humans and has estimated that ingestion of 1 microgram of PCB per kilogram per day for a lifetime would result in 77 additional cases of cancer in a population of 10,000 people or equivalently, 77,000 additional cases of cancer in a population of 10,000,000 people. These risk values are plausible upper-limit estimates. Actual risk levels are unlikely to be higher and may be lower.

#### 1.7 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

For exposure via drinking water, EPA advises that the following concentrations of PCB 1016 are levels at which adverse health effects would not be expected: 0.0035 milligrams PCB 1016 per liter of water for adults and 0.001 milligrams PCB 1016 per liter of water for children.

4 Section 1

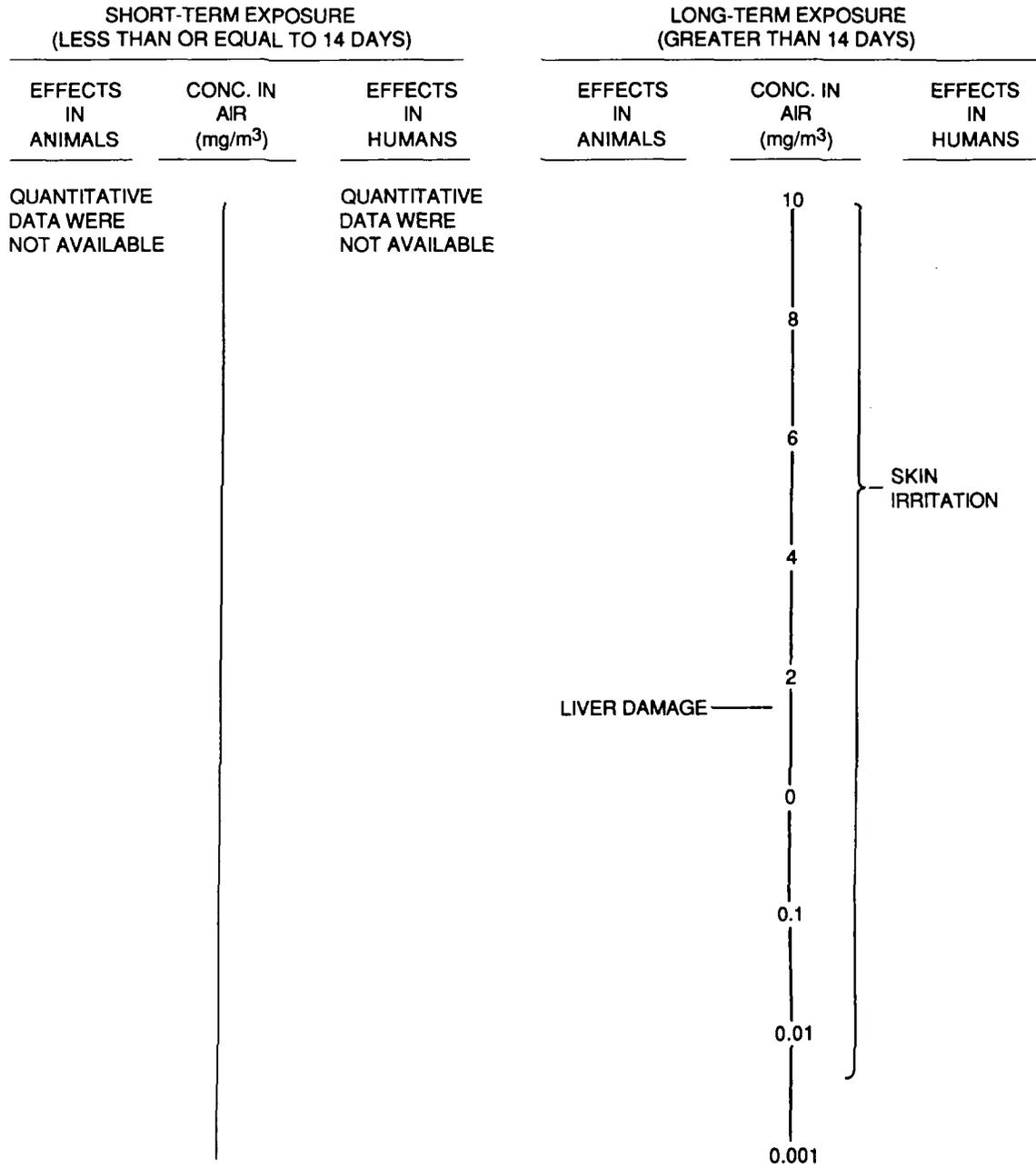


Fig. 1.1. Health effects from breathing PCBs.

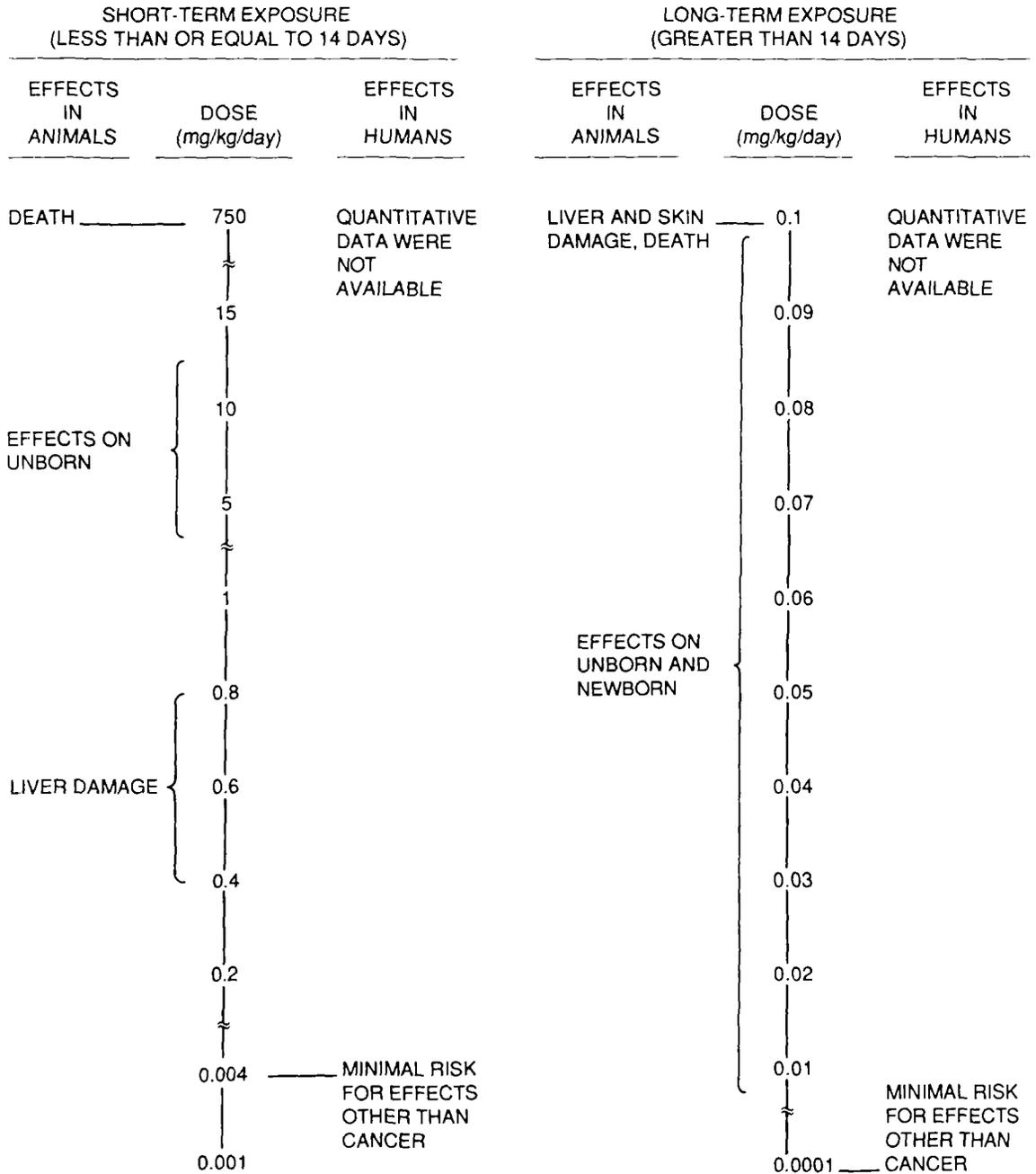


Fig. 1.2. Health effects from ingesting PCBs.

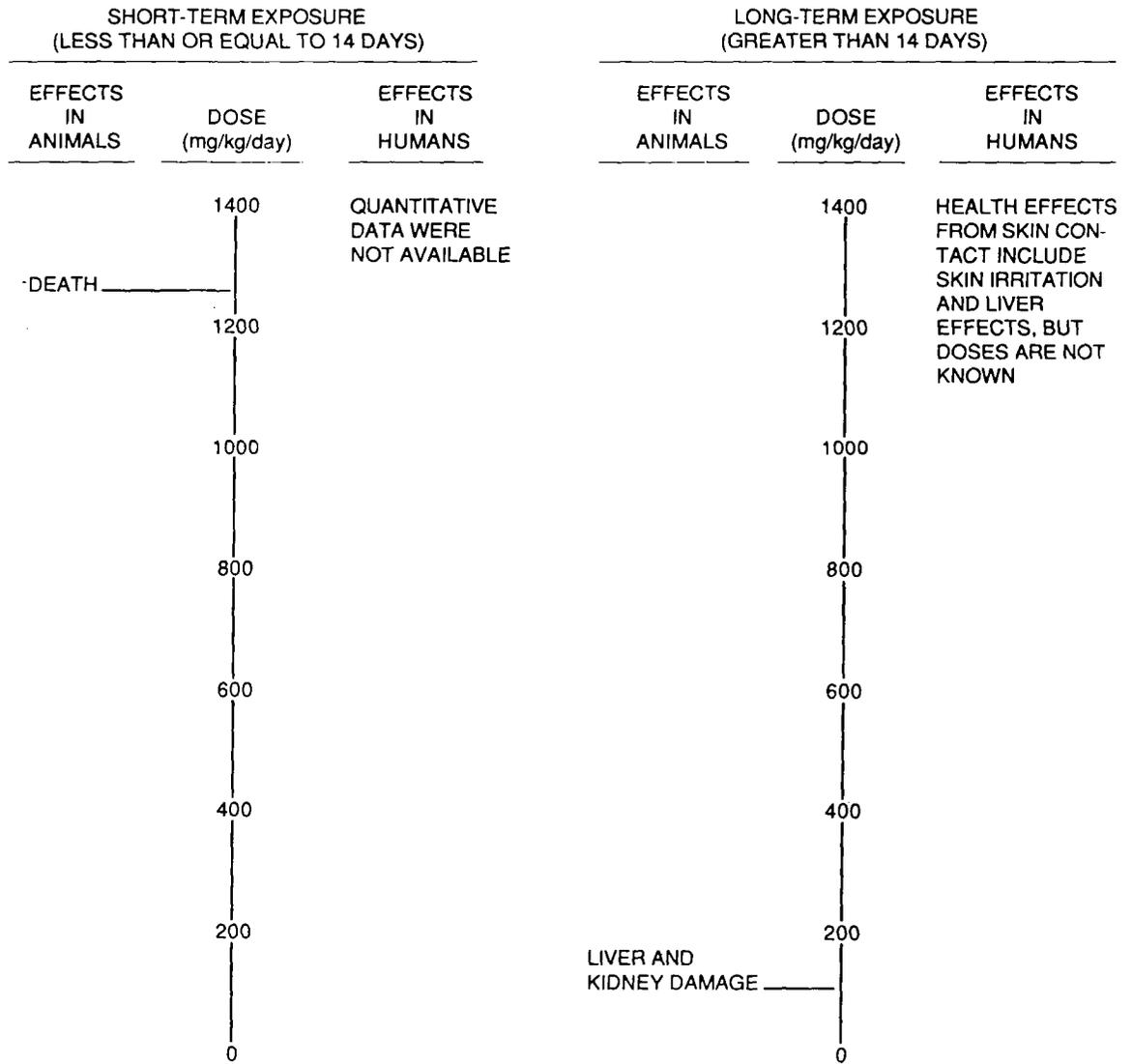


Fig. 1.3. Health effects from skin contact with PCBs.

The EPA has also developed guidelines for the concentrations of PCBs in ambient water (e.g., lakes and rivers) and in drinking water that are associated with a risk of developing cancer. The guideline for ambient water is a range, 0.0079 to 0.79 nanograms of PCBs per liter of water, which reflects the increased risk of one person developing cancer in populations of 10,000,000 to 100,000 people. The guideline for drinking water is a range, 0.005 to 0.5 micrograms of PCBs per liter of water, which also reflects the risk of one person developing cancer in populations of 10,000,000 to 100,000 people.

The Food and Drug Administration (FDA) specifies PCB concentration limits of 0.2 to 3 parts per million (milligrams PCB per kilogram of food) in infant foods, eggs, milk (in milk fat), and poultry (fat).

The National Institute for Occupational Safety and Health (NIOSH) recommends an occupational exposure limit for all PCBs of 0.001 milligram of PCBs per cubic meter of air ( $\text{mg}/\text{m}^3$ ) for a 10-hour workday, 40-hour workweek. The Occupational Safety and Health Administration (OSHA) permissible occupational exposure limits are 0.5 and 1.0  $\text{mg}/\text{m}^3$  for specific PCBs for an 8-hour workday.

## 2. HEALTH EFFECTS SUMMARY

### 2.1 INTRODUCTION

This section summarizes and graphs data on the health effects concerning exposure to PCBs. The purpose of this section is to present levels of significant exposure for PCBs based on key toxicological studies, epidemiological investigations, and environmental exposure data. The information presented in this section is critically evaluated and discussed in Sect. 4, Toxicological Data, and Sect. 7, Potential for Human Exposure.

This Health Effects Summary section comprises two major parts. Levels of Significant Exposure (Sect. 2.2) presents brief narratives and graphics for key studies in a manner that provides public health officials, physicians, and other interested individuals and groups with (1) an overall perspective of the toxicology of PCBs and (2) a summarized depiction of significant exposure levels associated with various adverse health effects. This section also includes information on the levels of PCBs that have been monitored in human fluids and tissues and information about levels of PCBs found in environmental media and their association with human exposures.

The significance of the exposure levels shown on the graphs may differ depending on the user's perspective. For example, physicians concerned with the interpretation of overt clinical findings in exposed persons or with the identification of persons with the potential to develop such disease may be interested in levels of exposure associated with frank effects (Frank Effect Level, FEL). Public health officials and project managers concerned with response actions at Superfund sites may want information on levels of exposure associated with more subtle effects in humans or animals (Lowest-Observed-Adverse-Effect Level, LOAEL) or exposure levels below which no adverse effects (No-Observed-Adverse-Effect Level, NOAEL) have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels, MRL) are of interest to health professionals and citizens alike.

Adequacy of Database (Sect. 2.3) highlights the availability of key studies on exposure to PCBs in the scientific literature and displays these data in three-dimensional graphs consistent with the format in Sect. 2.2. The purpose of this section is to suggest where there might be insufficient information to establish levels of significant human exposure. These areas will be considered by the Agency for Toxic Substances and Disease Registry (ATSDR), EPA, and the National Toxicology Program (NTP) of the U.S. Public Health Service in order to develop a research agenda for PCBs.

## 2.2 LEVELS OF SIGNIFICANT EXPOSURE

To help public health professionals address the needs of persons living or working near hazardous waste sites, the toxicology data summarized in this section are organized first by route of exposure--inhalation, ingestion, and dermal--and then by toxicological end points that are categorized into six general areas--lethality, systemic/target organ toxicity, developmental toxicity, reproductive toxicity, genetic toxicity, and carcinogenicity. The data are discussed in terms of three exposure periods--acute, intermediate, and chronic.

Two kinds of graphs are used to depict the data. The first type is a "thermometer" graph. It provides a graphical summary of the human and animal toxicological end points (and levels of exposure) for each exposure route for which data are available. The ordering of effects does not reflect the exposure duration or species of animal tested. The second kind of graph shows Levels of Significant Exposure (LSE) for each route and exposure duration. The points on the graph showing NOAELs and LOAELs reflect the actual doses (levels of exposure) used in the key studies. No adjustments for exposure duration or intermittent exposure protocol were made.

Adjustments reflecting the uncertainty of extrapolating animal data to man, intraspecies variations, and differences between experimental vs actual human exposure conditions were considered when estimates of levels posing minimal risk to human health were made for noncancer end points. These minimal risk levels were derived for the most sensitive noncancer end point for each exposure duration by applying uncertainty factors. These levels are shown on the graphs as a broken line starting from the actual dose (level of exposure) and ending with a concave-curved line at its terminus. Although methods have been established to derive these minimal risk levels (Barnes et al. 1987), shortcomings exist in the techniques that reduce the confidence in the projected estimates. Also shown on the graphs under the cancer end point are low-level risks ( $10^{-4}$  to  $10^{-7}$ ) reported by EPA. In addition, the actual dose (level of exposure) associated with the tumor incidence is plotted.

Evaluation of the toxicity of Aroclors and other commercial PCB mixtures is complicated by numerous considerations. Because of these considerations, it is assumed, for the purpose of health effects evaluation, that effects resulting from exposure to a specific Aroclor are representative of effects that may be produced by the other Aroclors (see discussion in preface to Sect. 4.3).

### 2.2.1 Key Studies and Graphical Presentations

Dose-response-duration data for the toxicity and carcinogenicity of the PCBs discussed in this profile are displayed in two types of graphs. These data are derived from the key studies described in the following sections. The "thermometer" graphs in Figs. 2.1, 2.2, and 2.3 plot exposure levels vs NOAELs and LOAELs for various effects and durations of inhalation, oral, and dermal exposures, respectively. The graphs of levels of significant exposure in Figs. 2.4, 2.5, and 2.6 plot end-point-specific NOAELs, LOAELs, and/or minimal levels of risk for acute ( $\leq 14$  days), intermediate (15-364 days), and chronic ( $\geq 365$  days) durations for inhalation, oral, and dermal exposures, respectively.

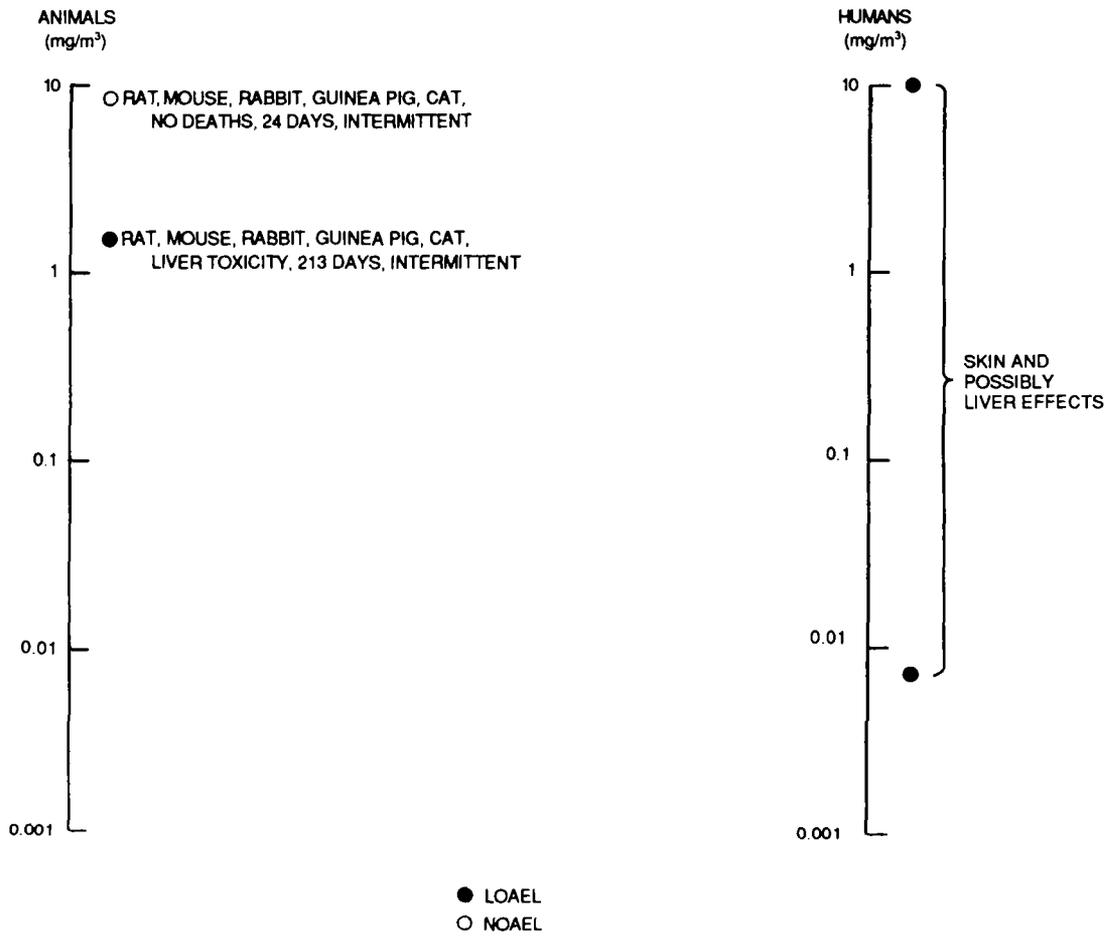
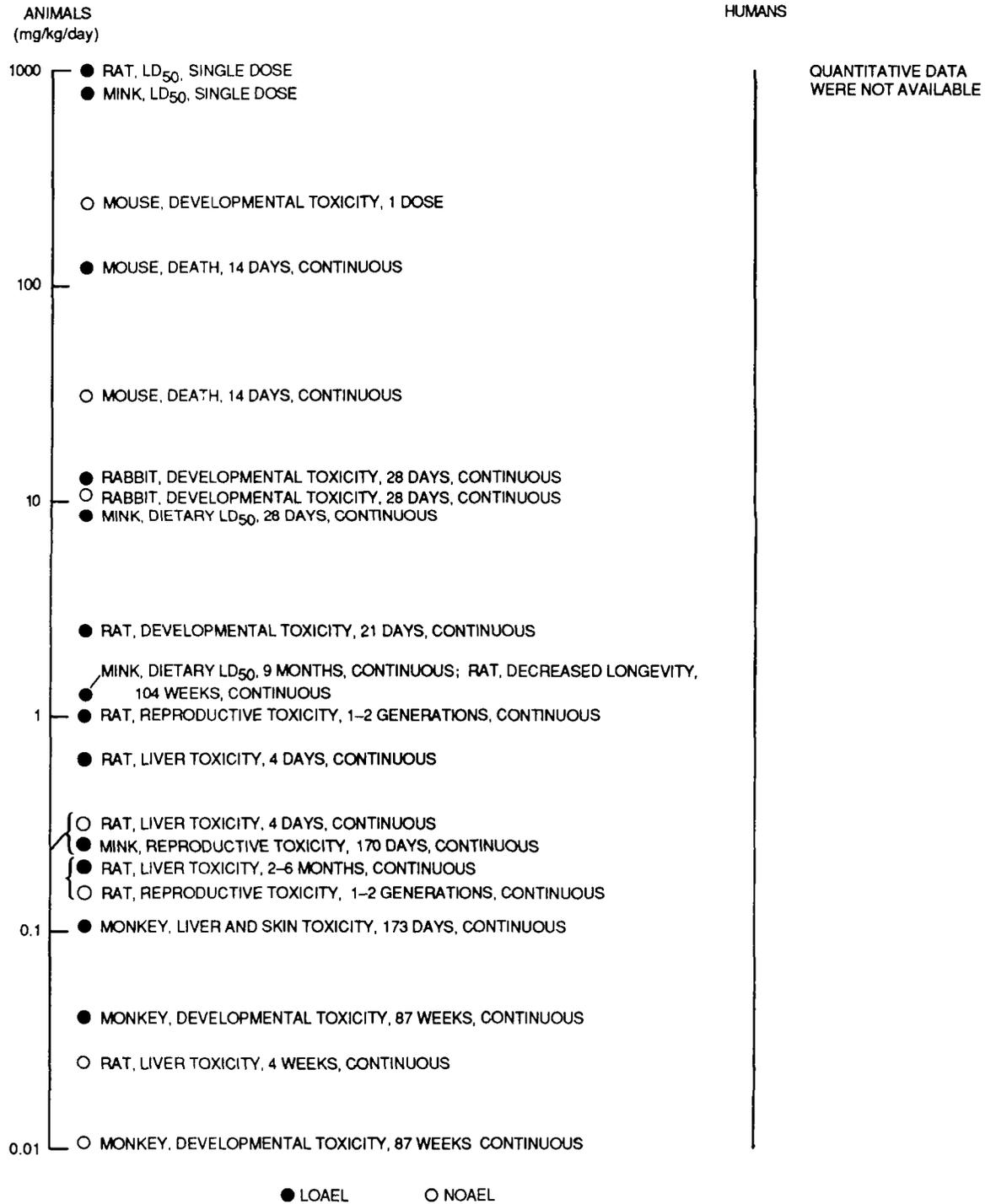


Fig. 2.1. Effects of PCBs—inhalaion exposure.



**Fig. 2.2. Effects of PCBs—oral exposure.**

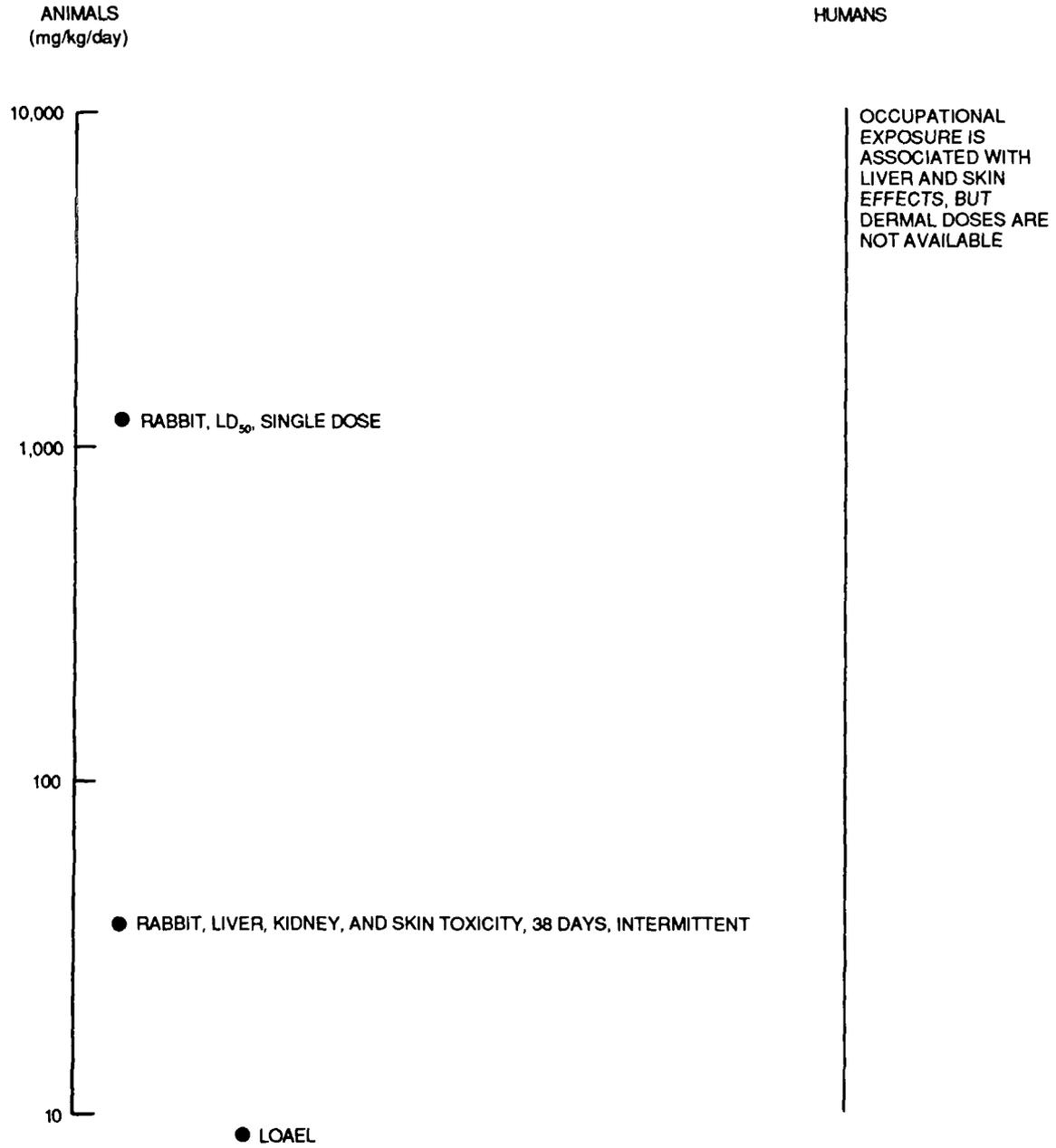


Fig. 2.3. Effects of PCBs—dermal exposure.

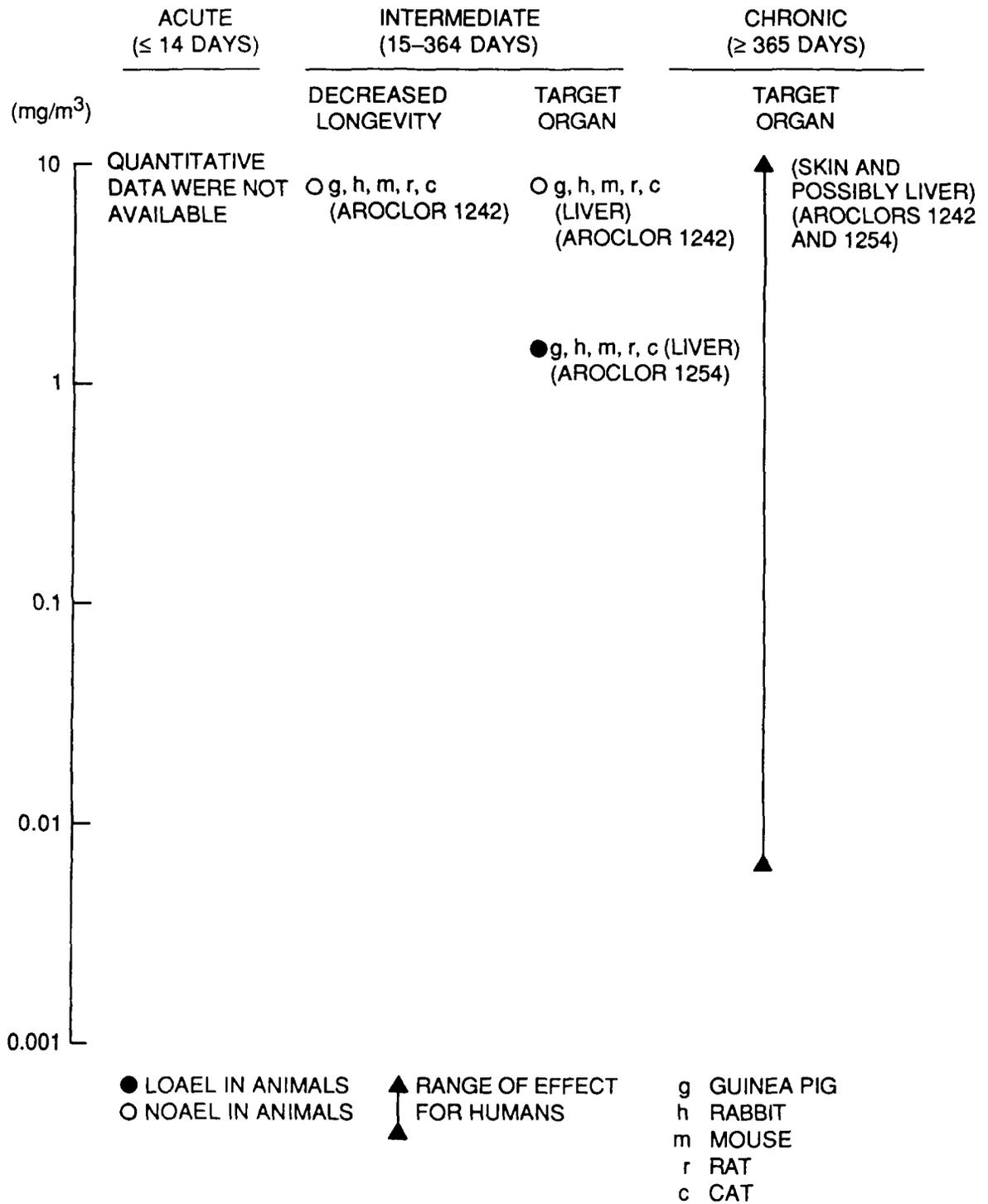


Fig. 2.4. Levels of significant exposure for PCBs—inhalation.

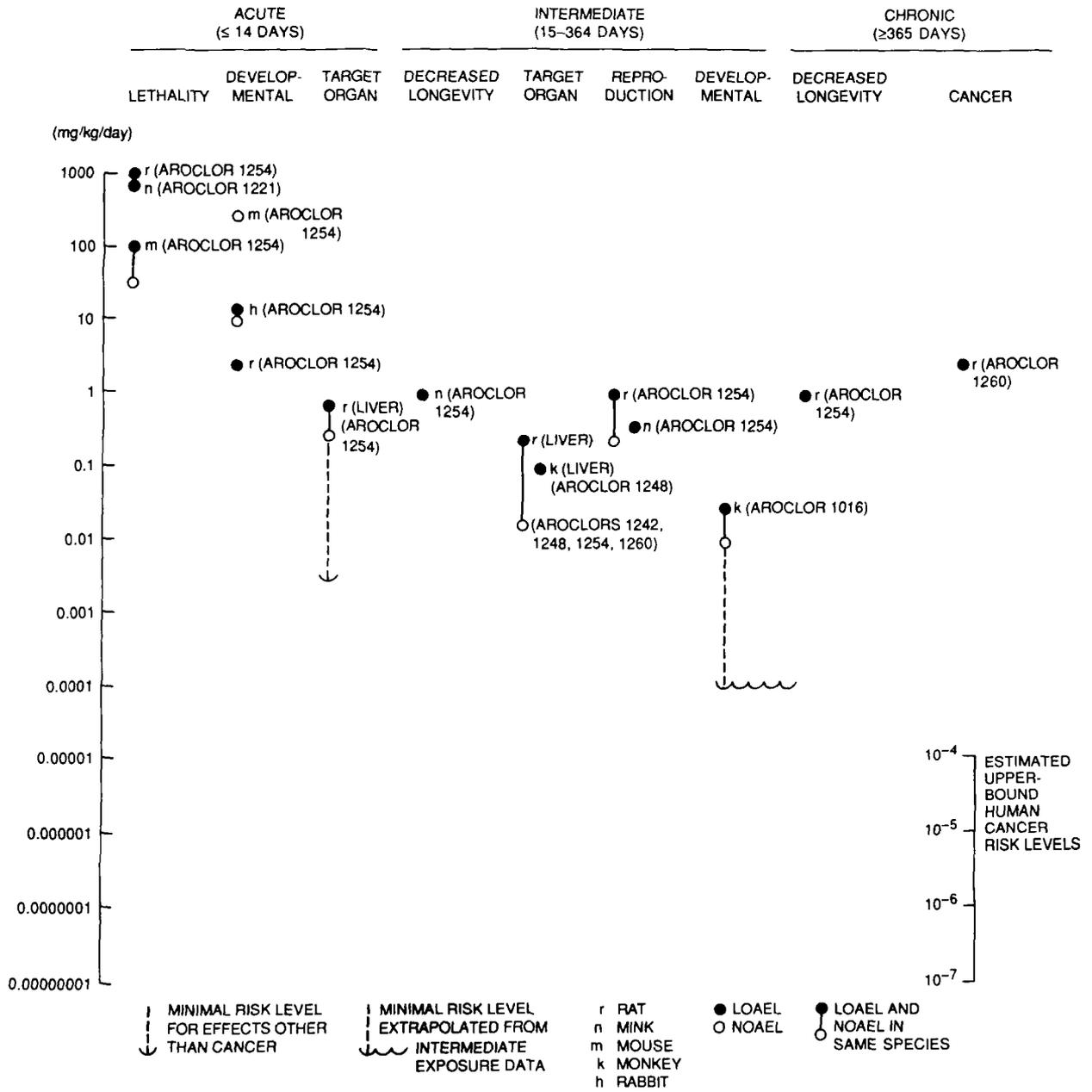


Fig. 2.5. Levels of significant exposure for PCBs—oral.

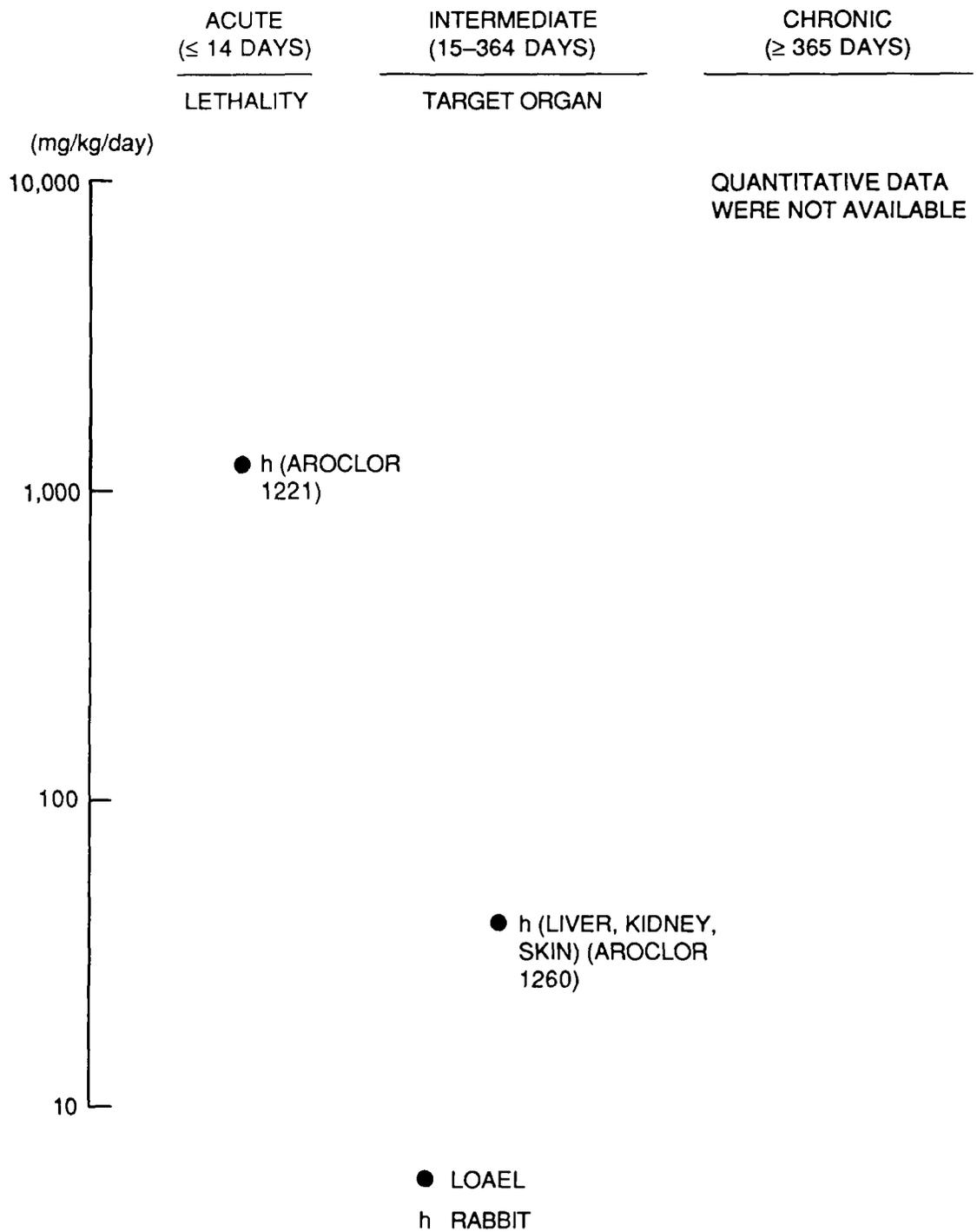


Fig. 2.6. Levels of significant exposure for PCBs—dermal.

Dermal exposure contributes significantly to occupational exposure, but the relative contributions of dermal and inhalation exposure in occupational settings has not been discerned (Wolff 1985). Furthermore, occupational exposure levels are expressed as concentrations of PCBs in air, making it difficult to quantitate dermal exposure doses. For this reason, effects of occupational exposure are discussed under inhalation exposure and plotted in Figs. 2.1 and 2.4 (graphs for inhalation exposure).

#### 2.2.1.1 Inhalation

**Lethality and decreased longevity.** Data regarding inhalation exposure levels that produce death in humans were not available. Exposure to near saturation vapor concentrations of heated Aroclor 1242 ( $8.6 \text{ mg/m}^3$ ) 7 h/day, 5 days/week for 24 days was not lethal for cats, rats, mice, rabbits, or guinea pigs (Treon et al. 1956). This concentration represents a NOAEL for lethality for intermediate inhalation exposures (see Figs. 2.1 and 2.4). No data were available regarding lethality/decreased longevity of animals due to acute or chronic inhalation exposure to PCBs.

**Systemic/target organ toxicity.** Oral toxicity studies in animals have established that the liver and cutaneous tissues are primary target organs of PCBs. Human health surveys have associated occupational exposure to PCBs with increased serum levels of liver-associated enzymes and dermatologic effects such as chloracne and skin rashes (Sects. 4.3.2.1 and 4.3.2.2). The results of some of these studies are equivocal, and exposure levels were not reported or inadequately characterized. Furthermore, although inhalation is considered a major route of exposure, the contribution of dermal exposure to total occupational exposure is also significant.

Fischbein et al. (1979, 1982, 1985) reported data suggestive of associations between serum levels of PCBs and SGOT levels and dermatologic effects in workers who had been exposed to 8-h time-weighted average concentrations of Aroclors, primarily 1242 and 1254, ranging from  $0.007\text{-}11.0 \text{ mg/m}^3$ . Because of limitations of this study (Sects. 4.3.2.1 and 4.3.2.2), these effects could be regarded as inconclusive and cannot be associated with specific exposure concentrations. It is, however, appropriate to plot the range of Aroclor concentrations from this study in Figs. 2.1 and 2.4 because similar effects have been observed in other health surveys of PCB-exposed workers, information regarding human liver histopathology is lacking, and the liver and skin are unequivocal targets of PCB toxicity in animals. This concentration range is intended to approximate typical concentrations in occupational environments that may be associated with hepatic and dermatologic alterations.

In the only animal inhalation study of PCBs, degenerative liver lesions, a frank effect, occurred in cats, rats, mice, rabbits, and guinea pigs that were exposed to  $1.5 \text{ mg/m}^3$  Aroclor 1254 vapor for 7 h/day, 5 days/week for 213 days (Treon et al. 1956). This FEL is plotted on Figs. 2.1 and 2.4. Histologic effects were not produced in those species exposed to Aroclor 1242 ( $1.9 \text{ mg/m}^3$ , 7 h/day, 5 days/week for 214 days;  $8.6 \text{ mg/m}^3$ , 7 h/day, 5 days/week for 24 days). The higher

NOAEL of  $8.6 \text{ mg/m}^3$  for intermediate-duration inhalation exposure is plotted on Fig. 2.4. Since the FEL for Aroclor 1254 is lower than the NOAEL for Aroclor 1242, a minimal risk level cannot be derived for Aroclors as a class.

**Developmental toxicity.** Pertinent data regarding developmental effects of PCBs via inhalation exposure in animals were not located in the available literature. A report of slightly reduced birth weight and gestational age in infants born to mothers with occupational exposure to Aroclors (Taylor et al. 1984) is inconclusive and lacks monitoring data.

**Reproductive toxicity.** Pertinent data regarding reproductive effects of PCBs via inhalation exposure in humans or animals are not available.

**Genotoxicity.** The PCBs have produced generally negative results in *in vivo* and *in vitro* genotoxicity assays (Sect. 4.3.5 on genotoxicity in toxicological data section).

**Carcinogenicity.** Occupational studies (Brown 1986, Bertazzi et al. 1987) provide inadequate but suggestive evidence for carcinogenicity of PCBs by the inhalation route (see Sect. 4.3.6.1). Data regarding the carcinogenicity of inhaled PCBs in animals are not available.

#### 2.2.1.2 Oral

**Lethality and decreased longevity.** Data regarding oral exposure levels that produce death in humans were not available. Single-dose oral LD50s for PCBs have been reported for rats and mink. The lowest values are 750 mg/kg for Aroclor 1221 in mink (Aulerich and Ringer 1977) and 1,010 mg/kg for Aroclor 1254 in rats (Garthoff et al. 1981). These FELs are plotted on Figs. 2.2 and 2.5 for lethality due to acute oral exposure.

In mice fed diets containing 1,000 ppm Aroclor 1254 for 14 days, 3 of 5 died by day 15 (Sanders et al. 1974). No mice fed diets containing 250 ppm Aroclor 1254 for 14 days died. Thus, 250 ppm is a NOAEL, and 1,000 ppm is a FEL for lethality in mice for short-term oral exposure. Assuming that a mouse consumes a daily amount of food equal to 13% of its body weight (EPA 1986a), the NOAEL is equivalent to 32.5 mg/kg/day, and the FEL is equivalent to 130 mg/kg/day. These levels are plotted on Figs. 2.2 and 2.5 for lethality for acute oral exposure. Hornshaw et al. (1986) determined LC50s of Aroclor 1254 for dietary exposure in mink to be 79-84 ppm for 28 days and 47-49 ppm for 28 days followed by a 7-day withdrawal period. In mink fed Aroclor 1254 for 9 months, the LC50 was 6.65 ppm (Ringer et al. 1981). Assuming that mink consume 150 g of feed per day and weigh 800 g (Bleavins et al. 1980), 47 ppm is equivalent to an LD50 of 8.8 mg/kg/day (see Fig. 2.2), and 6.65 ppm is equivalent to an LD50 of 1.25 mg/kg/day. This FEL is plotted on Figs. 2.2 and 2.5 for intermediate exposure.

Reduced survival occurred in rats fed diets containing  $\geq 25$  ppm Aroclor 1254 for 104 weeks (NCI 1978). Assuming that rats consume the equivalent of 5% of their body weight per day in food (EPA 1986a), then 1.25 mg/kg/day represents a FEL for chronic oral exposure in rats (see Figs. 2.2 and 2.5). NOAELs for increased mortality were not identified in these studies.

**Systemic/target organ toxicity.** The liver and cutaneous tissues are primary targets of PCB toxicity in orally exposed animals.

Rats were fed diets containing 0, 4, 8 or 16 ppm Aroclor 1254 for 4 days (Carter 1985); relative liver weights were significantly increased at >8 ppm and serum levels of HDL cholesterol were significantly increased at 16 ppm. The 8-ppm and 16-ppm concentrations, which correspond to 0.4 and 0.8 mg/kg/day, respectively, if rat food consumption is assumed to be 5% of body weight per day, represent a NOAEL and LOAEL for acute oral exposure (see Figs. 2.2 and 2.5). The NOAEL is the basis for the minimal risk level for acute oral exposure (Fig. 2.5).

In intermediate-duration studies, hepatic microsomal enzyme activities were increased in rats treated with diet concentrations of 0.5, 5, or 50 ppm Aroclors 1242, 1248, 1254, or 1260 for 4 weeks (Litterst et al. 1972). Dietary exposure to 5 ppm Aroclor 1242 for 2 to 6 months produced increased liver lipid content in rats (Bruckner et al. 1974) and >20 ppm Aroclor 1254, or 1260 for 28 days (Chu et al. 1977) or 8 months (Kimbrough et al. 1972) produced frank degenerative liver alterations in rats. Dietary concentrations of 0.5 ppm Aroclors 1242, 1248, 1254, and 1260 and 5 ppm Aroclor 1242, therefore, represent the highest NOAEL and lowest LOAEL, respectively, for intermediate-duration hepatic effects in rats. Assuming that rats consume 5% of their body weight in food per day, the NOAEL and LOAEL provided 0.025 and 0.25 mg/kg/day, respectively (see Figs. 2.2 and 2.5).

Two monkeys that died from dietary exposure to 2.5 or 5.0 ppm Aroclor 1248 for 173 or 310 days, respectively, had frank liver lesions (Barsotti et al. 1976). Although this study is limited by the number of animals, other studies with monkeys corroborate these FELs, as chloracne and gastric lesions were also associated with intermediate-duration exposure to 2.5 or 5.0 ppm Aroclor 1248 (Barsotti and Allen 1975, Barsotti et al. 1976, Thomas and Hinsdill 1978). The lowest monkey FEL (2.5 ppm) is equivalent to 0.105 mg/kg/day (see Figs. 2.2 and 2.5) if it is assumed that monkey food consumption is 4.2% of body weight per day (EPA 1986a).

Chronic feeding studies with rats (NCI 1978, Morgan et al. 1981, Ward 1985, Norback and Weltman 1985, Kimbrough et al. 1975), conducted at concentrations (>20 ppm) that were higher than the lowest FELs in the intermediate-duration monkey studies, did not produce degenerative liver lesions but did produce preneoplastic and proliferative liver lesions. Chronic (12 to 16 month) feeding studies were conducted with 2.5 and 5.0 ppm Aroclor 1248 in monkeys (Barsotti and Allen 1975, Barsotti et al. 1976), but skin lesions and other effects (as indicated above and in subsequent sections) occurred after several months of exposure. Therefore, it is inappropriate to identify effect levels for systemic effects resulting from chronic oral exposure because of the types of liver lesions (preneoplastic) in rats and the short latency for cutaneous and other effects in monkeys.

**Developmental toxicity.** Slight effects on birth weight, head circumference, gestational age and/or neonatal behavior have been reported in infants of mothers who were consumers of PCB-contaminated fish (Fein 1984; Fein et al. 1984; Jacobson et al. 1984a, 1984b, 1985)

and infants of mothers who had no known specific source of PCB exposure (Rogan et al. 1986, 1987). Although these studies suggest an association with PCB exposure, these effects cannot conclusively be attributed to PCBs because of potential and documented exposure to other chemicals, inconsistency between studies, and other limitations discussed in Sect. 4.3.3.2.

Collins and Capen (1980a) fed diets containing Aroclor 1254 at 0, 50, or 500 ppm to female rats during gestation and lactation. Significantly ( $P < 0.001$ ) reduced litter size occurred at 500 ppm. At both 50 and 500 ppm, the neonates and weanlings had ultrastructural lesions in the thyroid follicular cells and reduced serum levels of thyroid hormone. Thus, 50 ppm is the LOAEL for fetotoxicity due to oral exposure in rats. Assuming that a rat consumes a daily amount of food equal to 5% of its body weight (EPA 1986a), 50 ppm is equivalent to 2.5 mg/kg/day. The LOAEL is indicated on Figs. 2.2 and 2.5 for developmental toxicity in rats.

Gestational exposure to Aroclor 1254 by gavage produced fetotoxic effects in rabbits exposed on days 1-28 at doses  $>12.5$  mg/kg/day but not  $<10$  mg/kg/day (Villeneuve et al. 1971). The dose of 10 mg/kg/day, therefore, represents a NOAEL for developmental effects in rabbits (see Figs. 2.2 and 2.5, acute exposure). The dose of 12.5 mg/kg/day represents a FEL for developmental effects in rabbits because it produced fetal deaths.

Haake et al. (1987) reported that treatment of pregnant C57BL/6 mice with Aroclor 1254 by gavage at 244 mg/kg on day 9 of gestation did not result in any fetuses with cleft palate. This dose is plotted on Figs. 2.2 and 2.5 as a NOAEL for developmental toxicity in mice.

Monkeys that were fed diets containing 1.0 ppm of Aroclor 1016 for approximately 7 months prior to mating and during pregnancy (total duration  $87 \pm 9$  weeks) delivered infants with reduced birth weights, but this effect did not occur at 0.25 ppm (Barsotti and Van Miller 1984). Assuming that a monkey consumes a daily amount of food equal to 4.2% of its body weight, the daily dosages in the 1.0 ppm (LOAEL) and 0.25 ppm (NOAEL) groups were 0.04 and 0.0105 mg/kg/day, respectively. The NOAEL serves as the basis for the minimal risk level for intermediate and chronic oral exposure as derived by EPA (1988a). Fetal mortality, a frank effect, occurred at  $>2.5$ -ppm (0.1-mg/kg/day) dietary concentrations of Aroclor 1248 in other studies with monkeys (Allen and Barsotti 1976; Allen et al. 1979, 1980).

**Reproductive toxicity.** There are no studies regarding reproductive effects of PCBs in humans. Diets that provided  $>2$  ppm of Aroclor 1254 for 4 months prior to mating and during gestation were lethal to fetuses and caused reproductive failure in mink (Aulerich and Ringer 1977, Bleavins et al. 1980). Assuming that mink consume 150 g of feed per day and weigh 800 g (Bleavins et al. 1980), then the 2-ppm FEL provided 0.38 mg/kg/day (see Figs. 2.2 and 2.5).

Reduced litter sizes occurred at Aroclor 1254 dietary concentrations of  $>20$  ppm but not  $<5$  ppm in one- and two-generation reproduction studies with rats (Linder et al. 1974). The dietary concentrations of 5 ppm (NOAEL) and 20 ppm (FEL) provided 0.25 and

1 mg/kg/day, respectively, if rat food consumption is assumed to be 5% of body weight per day (EPA 1986a). These levels are plotted on Figs. 2.2 and 2.5 for reproductive effects of intermediate oral exposure in rats.

**Genotoxicity.** The PCBs have produced generally negative results in *in vivo* and *in vitro* genotoxicity tests (Sect. 4.3.5 on genotoxicity in toxicological data section).

**Carcinogenicity.** EPA (1988a) used the Norback and Weltman (1985) study as the basis for a quantitative carcinogenicity risk assessment for PCBs. The dietary level of 100 ppm Aroclor 1260 was converted to an intake of 5 mg/kg/day by assuming that a rat consumes food equal to 5% of its body weight per day. This dosage was converted to a TWA dosage of 3.45 mg/kg/day (see Fig. 2.5) to reflect the fact that rats received 100 ppm for 16 months, 50 ppm for 8 months, and 0 ppm for the last 5 months. The rat dosage was converted to an equivalent human dose of 0.59 mg/kg/day on the basis of relative body surface areas. Incidences of trabecular carcinomas, adenocarcinomas, and neoplastic nodules in the liver were combined to produce total incidences of 45/47 in treated females and 1/49 in controls. Using these data, EPA (1988a) calculated a human  $q_1^*$  of  $7.7 \text{ (mg/kg/day)}^{-1}$ . Dosages corresponding to risk levels of  $10^{-4}$ ,  $10^{-5}$ ,  $10^{-6}$ , and  $10^{-7}$  are  $1.3 \times 10^{-5}$ ,  $1.3 \times 10^{-6}$ ,  $1.3 \times 10^{-7}$ , and  $1.3 \times 10^{-8}$  mg/kg/day, respectively. The  $10^{-4}$  to  $10^{-6}$  risk levels are indicated on Fig. 2.5. Aroclor 1260 is assumed to be representative of all PCB mixtures because there is no information regarding which constituents of any PCB mixture might be carcinogenic; therefore, the potency estimate for Aroclor 1260 applies to all PCB mixtures (EPA 1988b).

#### 2.2.1.3 Dermal

Occupational exposure to PCBs is considered to be by the inhalation route in this profile, since air levels are commonly monitored in the workplace. It is clear, however, that under occupational conditions dermal exposure would also occur. This was recognized by ACGIH (1986) when a skin notation was placed with the TLV. Dermal adsorption and exposure can occur from contact of the skin with the vapors of PCB as well as actual dermal contact with the compound or from contact with dust or surfaces to which the PCBs are absorbed. Although it is realized that dermal exposure may be a major route of exposure in the occupational setting, quantitation of the relative contribution to body burden of absorbed PCBs from the inhalation and dermal routes is not possible for most studies. The study of Maroni et al. (1981a,b) permits some quantitation of dermal exposure, as discussed under systemic/target organ toxicity below.

**Lethality and decreased longevity.** Human data are not available. Median lethal doses for single dermal applications of PCBs to rabbits ranged from  $>1,269 \text{ mg/kg}$  for Aroclors 1242 and 1248 to  $<3,169 \text{ mg/kg}$  for Aroclor 1221 (Fishbein 1974). As only ranges of median lethal doses were reported, the lowest dose (1,269 mg/kg) is indicated on Figs. 2.3 and 2.6.

**Systemic/target organ toxicity.** Occupational exposure to PCBs involves dermal contact, but, for reasons discussed previously, occupational exposure data were discussed primarily under inhalation exposure.

The study of capacitor workers by Maroni et al. (1981a,b) indicated that dermal exposure to PCBs at 2-28  $\mu\text{g}/\text{cm}^2$  of skin (on the hands) was not associated with clear evidence of liver disease, but may have been associated with liver enzyme induction in some of the workers. Assuming a total surface area for the hands of 910  $\text{cm}^2$  (Hawley 1985) and body weight of 70 kg, the dermal exposure would have been 0.026-0.364 mg/kg/day. Because the workers were also exposed to PCBs by inhalation (48-275  $\mu\text{g}/\text{m}^3$ ), and because interpretation of the study is confounded by the lack of a control group, the dermal exposure range is not plotted on Figs. 2.3 and 2.6.

Dermal application of Aroclor 1260 to rabbits on 5 days/week at a dose of 118 mg/day for 38 days (27 total applications) produced degenerative lesions of the liver and kidneys, increased fecal porphyrin elimination, and hyperplasia and hyperkeratosis of the follicular and epidermal epithelium (Vos and Beems 1971). As body weight appeared to be approximately 2.7 kg (Vos and Beems 1971), the FEL of 118 mg/day is equal to a dose of 43.7 mg/kg/day (see Figs. 2.3 and 2.6).

**Developmental and reproductive toxicity.** Pertinent data regarding developmental and reproductive effects of dermal exposure to PCBs were not located in the available literature.

**Genotoxicity.** The PCBs have produced generally negative results in in vivo and in vitro genotoxicity tests (Sect. 4.3.5 on genotoxicity in toxicological data section).

**Carcinogenicity.** Occupational exposure to PCBs, which involves inhalation as well as dermal exposure, provides inadequate evidence of carcinogenicity in humans (Sect. 4.3.6 on carcinogenicity in toxicological data section). In two-stage carcinogenesis studies with mouse skin, Aroclor 1254 did not produce evidence of promoter or complete carcinogen activity and was not tested adequately for initiator activity (Sect. 4.3.6.3 on carcinogenicity of dermal exposure in toxicological data section).

## 2.2.2 Biological Monitoring as a Measure of Exposure and Effects

### 2.2.2.1 Exposure

PCBs are pervasive environmental contaminants that are found in body tissues and fluids of the general population. Because they are lipophilic, PCBs are preferentially stored in adipose tissue and are present in serum and human milk. Serum and adipose PCB levels are indicators of exposure, but may not provide accurate estimations of exposure or body burden because the concentration of PCBs in serum varies with the concentration of lipids in serum and variations in procedure and methods of data reporting may preclude interlaboratory comparison (Kimbrough 1987a).

Concentrations of PCBs in human adipose tissue and milk fat are 100 to 200 times higher than in serum (Kimbrough 1987a). Average PCB levels below 2 ppm in milk fat and 100 ppb in whole milk have normally been found, and the fat concentration in human milk averages 2.5-4.5% (Jensen 1983, Jensen et al. 1980, Rogan et al. 1987).

In the National Human Adipose Tissue Survey (NHATS), 46 composite adipose tissue samples collected during surgical procedures or during autopsies during fiscal year 1982 were analyzed for organochlorine compounds (EPA 1986b). Of the 46 samples, 83% contained PCBs as follows: 22% contained trichlorobiphenyl, 53% contained tetrachlorobiphenyl, 73% contained pentachlorobiphenyl, 73% contained hexachlorobiphenyl, 53% contained heptachlorobiphenyl, 40% contained octachlorobiphenyl, 13% contained nonachlorobiphenyl, and 7% contained decachlorobiphenyl. Statistical analyses for baseline estimates and time trends for PCBs in human adipose tissue in the NHATS for 1970-1983 have been performed (Lucas 1982, EPA 1985e). These analyses indicate that the estimated percentage of individuals with PCB levels >3 ppm increased to a peak of approximately 10% in 1977 and decreased steadily to near zero by 1983. The percentage of individuals having PCB levels >1 ppm decreased steadily from a high value near 50% in 1972 to a low value near 9% in 1983. Although these data indicate that PCB amounts are decreasing, the percentage of individuals with detectable levels (approximately 1 ppm) increased from approximately 85% in 1972 to nearly 100% in 1983. The percentage of people who had PCB levels >1 ppm increased with age and was greater in males than in females, but there was no significant difference between races. The Northeast Census Region historically (i.e., in the middle 1970s) had the greatest percentage of people with PCB levels >1 ppm, but, in recent years, the difference between the northeast and other regions no longer exists.

Anderson (1985) discussed the use of adipose tissue biopsy in assessing human exposure to PCBs. Because adipose tissue is the primary storage site of PCBs, adipose tissue samples have been the preferred biological specimen. Analysis of PCBs in adipose tissue provides a direct measure of body burden, but has disadvantages over analysis of serum levels because collection of samples is invasive and time-consuming. Based on data that adipose tissue levels of PBBs (polybrominated biphenyls) and DDT are directly correlated with serum levels of PBB and DDT, it can be predicted that PCB adipose levels will also correlate with serum levels. Anderson (1985) recommended that whenever an adipose tissue sample is obtained at biopsy, a paired serum sample should be collected and the two tissues be analyzed for PCBs. Once the correlation is characterized, blood samples may become the preferred choice for monitoring, unless identification of low exposures is required.

Wolff (1985) reported data on blood levels of PCBs in workers in relation to exposure levels (Table 2.1) and blood and adipose tissue levels of PCBs in workers in relation to duration of employment (Table 2.2). Generally, higher exposure levels result in higher blood and adipose tissue levels of PCBs, but because PCBs accumulate in the body, exposure duration is at least as important as exposure level.

**Table 2.1. PCB levels in blood of exposed workers (Aroclors 1016, 1242, 1248)**

Air levels (mg/m <sup>3</sup> )	Blood levels (ng/mL)		
	Mean	High	<i>N</i>
0.3–2	1,060	3,500	19 “Inside” <sup>a</sup>
	440	1,400	14 “Outside” <sup>a</sup>
0.05–0.275	130	407	60
0–0.26	355	3,330	26 High exposed
	149	1,500	55 Low exposed
	89	370	140 Never exposed
0.1–1	118	2,530	110 High exposed
	48	604	180 Other

<sup>a</sup>Workers who were exposed inside or outside the impregnation room.

Source: Wolff 1985.

**Table 2.2. PCB blood levels (Aroclor 1254) and duration of exposure**

Mean duration of employment (years)	Mean blood concentration (ng/mL)	<i>N</i>	Mean adipose concentration (μg/g)	<i>N</i>
16 ± 8	24 <sup>a</sup>	258	17	53
	6 <sup>b</sup>	32	4	8
17	33 <sup>c</sup>	86	5.6	36
3.8	14 <sup>d</sup>	15	1.4	5
4.3	12 <sup>e</sup>	19	1.3	9

<sup>a</sup>Persons with more than 5 years employment; geometric means; geometric mean of 53 plasma samples which matched the adipose samples was 54 ng/mL.

<sup>b</sup>Persons with less than 5 years employment; geometric means.

<sup>c</sup>Persons exposed.

<sup>d</sup>Persons nominally exposed.

<sup>e</sup>Nonexposed.

Source: Wolff 1985.

Kreiss (1985) reviewed available data, including unpublished Centers for Disease Control (CDC) data, for serum PCB concentrations in U.S. populations without occupational exposures for 1968-1983. These data and more recent data of Sahl et al. (1985a,b) and the Massachusetts Department of Public Health (1987) (i.e., the New Bedford Study) are summarized in Table 2.3. Mean serum levels were usually between 4 and 8 ng/mL, with 95% of the individuals having concentrations <20 ng/mL (Kreiss 1985). Cross-sectional data concerning PCB levels in a representative sample of the U.S. population are not available because the various groups were monitored during investigations of pesticide residues, food chain contamination, hazardous waste sites, and occupational exposure in which a nonexposed control group was necessary. Mean serum PCB levels in some populations that consumed contaminated fish are several times higher than mean levels in populations that did not consume contaminated fish (Table 2.3). The mean PCB levels in these studies approach those associated with occupational exposure (Table 2.4), but are within the range of the general population groups. Interpretation of the data in Tables 2.3 and 2.4 is complicated by differences in analytical methodology and methods of population selection and data reporting (Kreiss 1985).

PCB levels in adipose tissue and in human milk fat are 100 to 200 times higher than serum levels (Kimbrough 1987a). PCB concentrations averaged 1.5 ppm in the breast milk of 1,057 women in Michigan (Wickizer et al. 1981).

#### 2.2.2.2 Effects

Several studies of general population subjects attempted to correlate serum PCB levels with health indices. Baker et al. (1980) found that plasma triglyceride levels increased significantly with serum PCB concentrations in residents of Bloomington, Indiana, including workers occupationally exposed to PCBs. Chloracne or systemic symptoms of PCB toxicity were not noted, and there were no significant correlations between PCB levels and hematologic, hepatic, or renal function indices. Kreiss et al. (1981) reported that serum PCB levels were positively associated with serum cholesterol levels, gamma-glutamyl transpeptidase (GGTP) levels, and measured blood pressure in residents of Triana, Alabama, that were exposed via consumption of contaminated fish. Rates of borderline and definite hypertension were 30% higher than those expected on the basis of national rates. The associations in the above studies were independent of predictors of PCB levels such as age, sex, and/or consumption of alcohol and fish. The hypertension and other effects in the Kreiss et al. (1980) study cannot be attributed solely to PCBs because the strongest correlation was between log PCB and log DDT serum levels. Low and moderate serum levels of PCBs did not appear to be associated with increased blood pressure in residents of New Bedford, Mass., who were exposed via consumption of contaminated seafood.

Steinberg et al. (1986) determined that five serum analytes ( $\beta$ -glucuronidase, 5'-nucleotidase, triglycerides, cholesterol, and total bilirubin) correlated positively and significantly with log concentrations of serum total PCBs in residents who lived or worked in the vicinity of an electrical manufacturing plant. Aroclor 1260 was

**Table 2.3. Serum PCB concentrations in U.S. populations without occupational exposure to PCBs and in subpopulations consuming fish from PCB-contaminated waters**

Area and sampling method	Number of subjects	Year	PCB level, ng/mL				Range	References
			Arithmetic mean	Geometric mean, median <sup>a</sup>	Arithmetic standard deviation	95% Confidence interval		
<b>Populations without occupational exposures, 1968–1983</b>								
Charleston County, S.C., volunteers	616	1968	4.9	–	–	–	0–29	Finklea et al. 1972
Lake Michigan random non-fish-eaters	29	1973	17.3	15 <sup>a</sup>	–	–	<5–41	Humphrey 1983a
Bloomington, Ind., volunteers and controls	110	1977	18.8	–	10.8	17–21	6–79	Baker et al. 1980
Michigan PBB cohort	1,631	1978–79	7.7	6.4	–	–	<1–57	Kreiss et al. 1982
Billings, Mont., random packinghouse workers	17	1979	7.5	5.8	6.8	4–11	2–30	Drotman et al. 1981
Franklin, Idaho, volunteers	105	1979	–	–	–	–	<5	Drotman et al. 1981
Random unexposed workers	19	1979	12	–	–	–	10–27	Chase et al. 1982
Newton, Kans., volunteers	7	1979	4.9	4.2	3.1	2–8	2–11	Vernon et al. 1981
Lake Michigan random non-fish-eaters	418	1980	–	6.6 <sup>a</sup>	–	–	<3–60	Humphrey 1983a
Canton, Mass., volunteers	10	1980	7.1	5.2	5.2	3–11	1–18	Condon 1983
Old Forge, Pa., volunteers	138	1981	3.6	–	–	–	<3–43	Reid and Fox 1982

Table 2.3 (continued)

Area and sampling method	Number of subjects	Year	PCB level, ng/mL				Range	References
			Arithmetic mean	Geometric mean, median <sup>a</sup>	Arithmetic standard deviation	95% Confidence interval		
Jefferson, Ohio, volunteers	59	1983	5.8	4.4	6.5	4-8	1-45	Welty 1983
Fairmont, W. Va., volunteers	40	1983	6.7	5.0	5.3	5-8	1-23	Welty 1983
Norwood, Mass., volunteers	990	1983	4.9	4.2	3.5	4-6	2-30	Condon 1983
Los Angeles-Long Beach, Calif., work force <sup>b</sup>	738	1982-84	5	4 <sup>a</sup>	4.37	-	<1-37	Sahl et al. 1985a,b
<b>Populations without occupational exposures consuming PCB-contaminated fish</b>								
Lake Michigan volunteer sportfishers	90	1973	72.7	56 <sup>a</sup>	-	-	25-366	Humphrey 1983b
Triana, Ala., volunteers	458	1979	22.2	17.2	22.3	20-24	3-158	Kriess et al. 1981
Lake Michigan volunteer sportfishers	572	1980	-	21.4 <sup>a</sup>	-	-	<3-203	Humphrey 1983b
New Bedford, Mass., random sample	840	1981-82	5.84	3.88 <sup>a</sup>	7.78	-	0.38-154.20	Massachusetts Department of Public Health 1987
New Bedford, Mass., known exposure to contaminated seafood	110	1981-82	13.34	9.48 <sup>a</sup>	14.02	-	1.40-87.97	Massachusetts Department of Public Health 1987

<sup>a</sup>Median.<sup>b</sup>Pre-employment survey of utility company workers.

Source: Kriess 1985; Sahl et al. 1985a,b; Massachusetts Department of Public Health 1987.

Table 2.4. Serum PCB concentrations in populations with occupational exposure

Facility	Number of subjects	PCB levels, ng/mL				Range	References
		Arithmetic mean	Geometric mean	95% Confidence interval			
Railway car maintenance	86	33.4	-	-	-	10-312	Chase et al. 1982
Capacitor plant	34	394 <sup>a</sup>	-	234-554	-	trace-1,700	Ouw et al. 1976
Capacitor plant	290	124 <sup>b</sup> 48 <sup>c</sup>	67 <sup>b</sup> 21 <sup>c</sup>	98-150 <sup>c</sup> 38-58 <sup>c</sup>	-	6-2,530 <sup>b</sup> 1-546 <sup>b</sup>	Fischbein et al. 1979 Wolff et al. 1982a
Capacitor plant	80	342 <sup>a</sup>	-	-	-	41-1,319	Maroni et al. 1981a
Capacitor plant	221	-	119 <sup>b</sup> 25.3 <sup>c</sup>	-	-	1-3,330 <sup>b</sup> 1-250 <sup>c</sup>	Smith et al. 1982
Public utility	14	-	24 <sup>b</sup> 24 <sup>c</sup>	15-39 <sup>b</sup> 16-35 <sup>c</sup>	-	5-52 <sup>b</sup> 7-24 <sup>c</sup>	Smith et al. 1982
Private utility	25	-	22 <sup>b</sup> 29 <sup>c</sup>	17-25 <sup>b</sup> 20-43 <sup>c</sup>	-	9-48 <sup>b</sup> 7-250 <sup>c</sup>	Smith et al. 1982
Utility	1,058	4	3 <sup>d</sup>	3.65 <sup>e</sup>	-	<1-26	Sahl et al. 1985b

<sup>a</sup>Blood level.<sup>b</sup>Lower chlorinated PCBs.<sup>c</sup>Higher chlorinated PCBs.<sup>d</sup>Median.<sup>e</sup>Standard deviation.

Source: Kreiss 1985.

significantly and positively correlated with several of the analytes, but Aroclor 1242 was correlated significantly and negatively only with HDL-cholesterol.

Umbilical cord serum levels of PCBs have been correlated with reduced birth weight and size, shorter gestation, and neonatal behavioral effects in a few reports (Fein 1984; Fein et al. 1984; Jacobson et al. 1984a, 1985; Rogan et al. 1986). Although increased levels of PCBs in cord blood may be predictors of these kinds of effects, the effects are not well validated and not attributable solely to PCBs. Cord serum levels associated with these effects are reported in Sect. 4.3.3 (developmental toxicity in toxicological data section).

Positive correlations between PCBs in blood and levels of triglycerides and liver-associated enzymes have been reported in workers with occupational exposure to PCBs (Baker et al. 1980, Ouw et al. 1976, Fischbein et al. 1979, Maroni et al. 1981b, Chase et al. 1982, Smith et al. 1982, Fischbein 1985, Lawton et al. 1985, Emmett 1985, Drill et al. 1981, Kreiss 1985). The associations between blood PCBs and triglycerides should be regarded as equivocal because of partitioning phenomena, as levels of PCBs in serum appear to be determined by serum lipid content. Evaluation of associations between serum PCBs and liver-associated enzymes is complicated by inconsistent and inconclusive data and lack of correction for confounding variables such as alcohol consumption. Indicators of possible liver enzyme induction (e.g., GGPT) are most commonly associated with PCB levels, and associations with indicators of possible hepatocellular damage (e.g., SGOT, SGPT) have been demonstrated only in occupationally exposed groups with higher ranges of PCB levels (Kreiss 1985). The clinical significance of the alterations in liver-associated enzymes is uncertain, as the increases may be nonspecific, and indices of obstructive liver disorders have not been demonstrated even in occupationally exposed groups.

Maroni et al. (1981b) examined the health condition and PCB blood levels of 80 capacitor manufacturing and testing plant workers who were exposed to PCBs (42% mean chlorine content) for many years. Sixteen of the workers had asymptomatic hepatic involvement as determined by hepatomegaly (12 workers) and serum enzyme elevations (AST, ALT, GGTP, SGOT and/or SPCH). A significant positive association was found between the prevalence of hepatic involvement and blood PCB concentrations, particularly trichlorobiphenyl blood concentrations ( $X^2$  trend,  $P < 0.001$ , 0.001 and 0.05 for total chlorobiphenyls, trichlorobiphenyls, and pentachlorobiphenyls, respectively). Mean blood concentrations of chlorobiphenyls, trichlorobiphenyls, and pentachlorobiphenyls were significantly higher in the workers with hepatic involvement compared to the workers without abnormal findings (Student's t-test,  $P < 0.001$ , 0.001 and 0.01, respectively, for the three classes of chlorinated biphenyls); mean trichlorobiphenyl concentrations were 215  $\mu\text{g}/\text{kg}$  (range 77-407  $\mu\text{g}/\text{kg}$ ) in the workers with abnormal liver findings and 92  $\mu\text{g}/\text{kg}$  (range 13-345  $\mu\text{g}/\text{kg}$ ) in those without abnormal liver findings. The authors suggested that trichlorobiphenyls may reflect current PCB exposure levels more closely than pentachlorobiphenyls. There were no significant differences in age or duration of exposure between the workers with and without abnormal liver findings. Evaluation of the hepatic findings in this study is complicated by the small number of

cases, but the enzyme alterations were mild and the prevalence and severity of the hepatic effects do not appear to be associated with duration of exposure. Unrelated health problems that may have contributed to the hepatic effects were described in three of the workers.

### 2.2.3 Environmental Levels as Indicators of Exposure and Effects

#### 2.2.3.1 Levels found in the environment

The purpose of this subsection is to summarize available data that suggest that levels of PCBs found in environmental media (primarily soil, drinking water, and food) (see Sect. 7.2) are associated with significant human exposure and/or effects. Schwartz et al. (1983) found a significant positive correlation ( $P < 0.001$ ) between fish consumption measures and PCB levels in maternal serum and milk. The specific PCBs present were not correlated with the various Aroclor mixtures. From their data, Schwartz et al. (1983) determined that serum PCB levels increase by 0.15 ng/mL and milk levels increase by 0.12 ng/g for every 0.45 kg of PCB-contaminated fish consumed, but the rate of fish consumption by the subjects in the study was not stated. Humphrey (1976) reported mean blood PCB levels of 0.073 ppm in 105 people whose annual consumption of Lake Michigan fish equaled or exceeded 24 lb. The estimated intake of PCBs by 82% of these people ranged from 0.49 to 3.94  $\mu\text{g}$  PCB/kg/day and averaged 1.7  $\mu\text{g}$ /kg/day. Drotman et al. (1983) found a positive correlation between the PCB concentration in human breast milk and the number of contaminated eggs consumed by lactating women. The same farm was the source of the eggs in this study, but representative concentrations of PCBs were not reported. As indicated in Sect. 7.2.4.1, however, the average concentration of Aroclor residues in contaminated eggs in 1970-1976 was 0.072 ppm.

#### 2.2.3.2 Human exposure potential

The purpose of this subsection is to discuss the chemical-specific issues involved in human exposure of PCBs from water, soil, and food. Experimental monitoring data have shown that PCB concentrations are higher in sediment and suspended matter than in the associated water column, and this is in agreement with the high soil adsorption constants for PCBs. The partitioning between suspended matter and water will be isomer specific and should correlate with the octanol/water partition coefficient of individual isomers. Thus, lower chlorinated PCBs should have a greater tendency to partition to the water than higher chlorinated PCBs (see Sect. 6.3.1 on transport and partitioning in environmental media). This implies that human exposure to the higher chlorinated isomers from whole water (water + sediment) will be greater than from settled water. Therefore, all other factors being equal, the human exposure potential to higher chlorinated PCBs from contaminated waters may tend to increase as exposure to sediment and suspended matter increases.

In general, PCBs are strongly adsorbed in most soils; therefore, leaching will not generally occur. This implies that the exposure will be greatest at the point of initial adsorption. In many instances, this may be at or near the soil surface. The principal route of human

exposure to PCBs from a spill in soil at a restricted-access outdoor site is through inhalation of air (EPA 1987a). Soil ingestion and dermal contact with soil would not be expected to be significant routes of exposure at a limited-access site. EPA (1987a) calculated that PCB levels of 25 ppm in soil would present less than a  $1 \times 10^{-7}$  risk to people on site who work more than 0.1 km from the actual spill area (assuming that the spill area is <0.5 acre). Nonetheless, ingestion is considered the primary route of exposure from spills at a nonrestricted residential site, although it is anticipated that some exposure would occur through inhalation also. Although dermal exposure can occur at soil sites where access is possible, it is expected that the PCBs will adsorb to the soil particles, reducing the rate of dermal absorption. The bioavailability of PCBs through inhalation may be higher for the lower chlorinated congeners since their tendency to volatilize from soil is greater than the tendency of the higher chlorinated congeners to volatilize.

## 2.3 ADEQUACY OF DATABASE

### 2.3.1 Introduction

Section 110 (3) of SARA directs the Administrator of ATSDR to prepare a toxicological profile for each of the 100 most significant hazardous substances found at facilities on the CERCLA National Priorities List. Each profile must include the following content:

- "(A) An examination, summary, and interpretation of available toxicological information and epidemiologic evaluations on a hazardous substance in order to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects.
- (B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure which present a significant risk to human health of acute, subacute, and chronic health effects.
- (C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans."

This section identifies gaps in current knowledge relevant to developing levels of significant exposure for PCBs. Such gaps are identified for certain health effects end points (lethality, systemic/target organ toxicity, developmental toxicity, reproductive toxicity, and carcinogenicity) reviewed in Sect. 2.2 of this profile in developing levels of significant exposure for PCBs, and for other areas such as human biological monitoring and mechanisms of toxicity. The present section briefly summarizes the availability of existing human and animal data, identifies data gaps, and summarizes research in progress that may fill such gaps.

Specific research programs for obtaining data needed to develop levels of significant exposure for PCBs will be developed by ATSDR, NTP, and EPA in the future.

### 2.3.2 Health Effect End Points

#### 2.3.2.1 Introduction and graphic summary

The availability of data for health effects in humans and animals is depicted on bar graphs in Figs. 2.7 and 2.8, respectively.

The bars of full height indicate that there are data to meet at least one of the following criteria:

1. For noncancer health end points, one or more studies are available that meet current scientific standards and are sufficient to define a range of toxicity from no effect levels (NOAELs) to levels that cause effects (LOAELs or FELs).
2. For human carcinogenicity, a substance is classified as either a "known human carcinogen" or "probable human carcinogen" by both EPA and the International Agency for Research on Cancer (IARC) (qualitative), and the data are sufficient to derive a cancer potency factor (quantitative).
3. For animal carcinogenicity, a substance causes a statistically significant number of tumors in at least one species, and the data are sufficient to derive a cancer potency factor.
4. There are studies which show that the chemical does not cause this health effect via this exposure route.

Bars of half height indicate that "some" information for the end point exists, but does not meet any of these criteria.

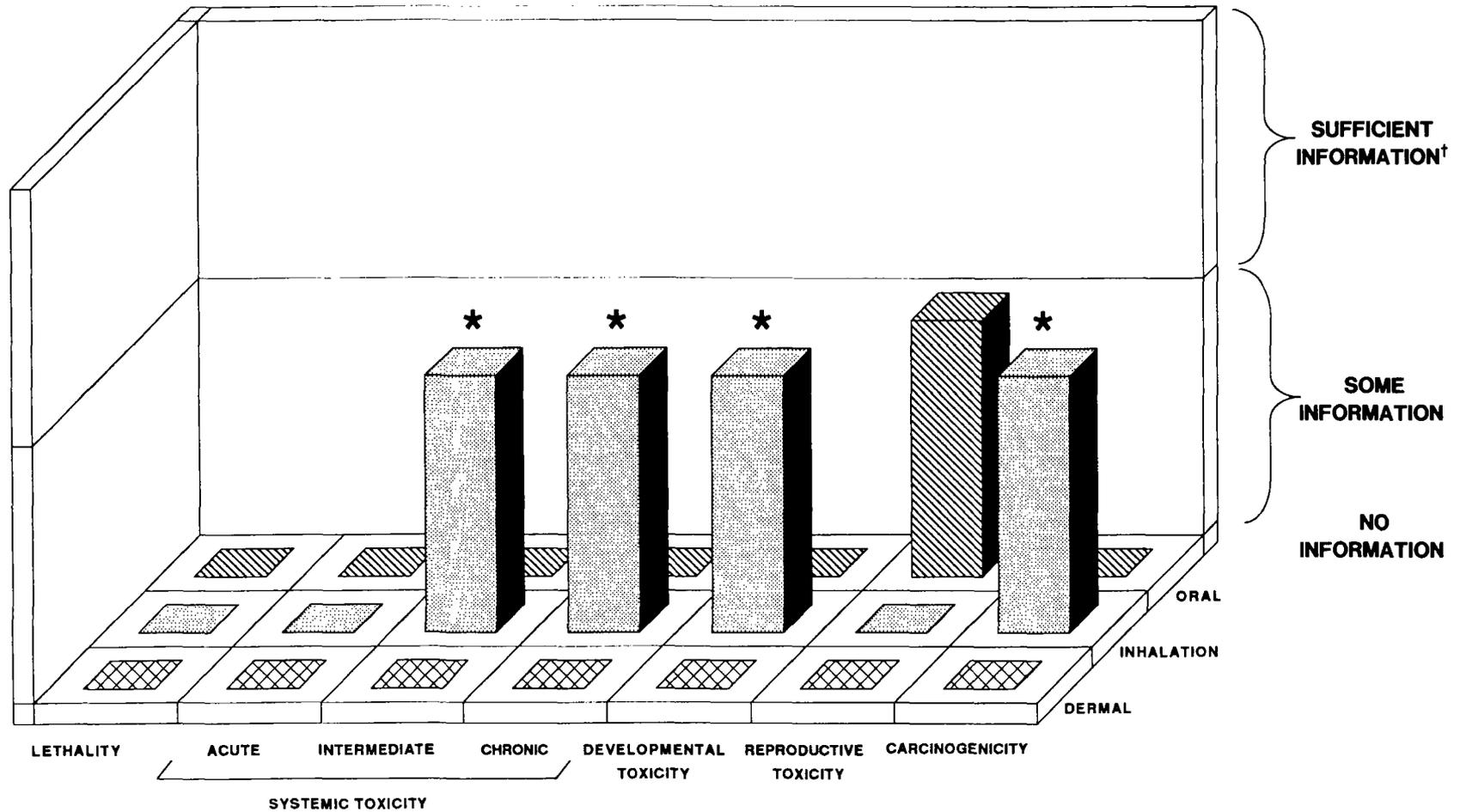
The absence of a column indicates that no information exists for that end point and route.

#### 2.3.2.2 Descriptions of highlights of graphs

Data concerning effects of PCBs in humans that are useful for quantitative risk assessment are not available. The available data pertain primarily to intermediate- or chronic-duration occupational exposures in which the exposures are inadequately monitored and do not correlate with duration and intensity of exposure. Occupational exposures to PCBs involve significant dermal exposure, but, as discussed previously, occupational concentrations are expressed in milligrams per cubic meter of air ( $\text{mg}/\text{m}^3$ ), which makes it difficult to determine dermal doses. For this reason, occupational exposure data were discussed under inhalation exposure. Children born to mothers who consumed PCB-contaminated fish had some developmental effects, but the effects cannot be directly attributed to PCBs; therefore, the bar for developmental effects due to oral exposure indicates that there are some data.

The toxicity and carcinogenicity of the PCBs in animals by the oral route are reasonably well characterized. Determination of toxicity effect levels for chronic oral exposure is precluded by occurrence of proliferative/neoplastic alterations. Effects of acute oral, inhalation, and dermal exposures to the PCBs in animals have not been extensively investigated because concern for effects in humans is centered on intermediate/chronic-duration oral exposures.

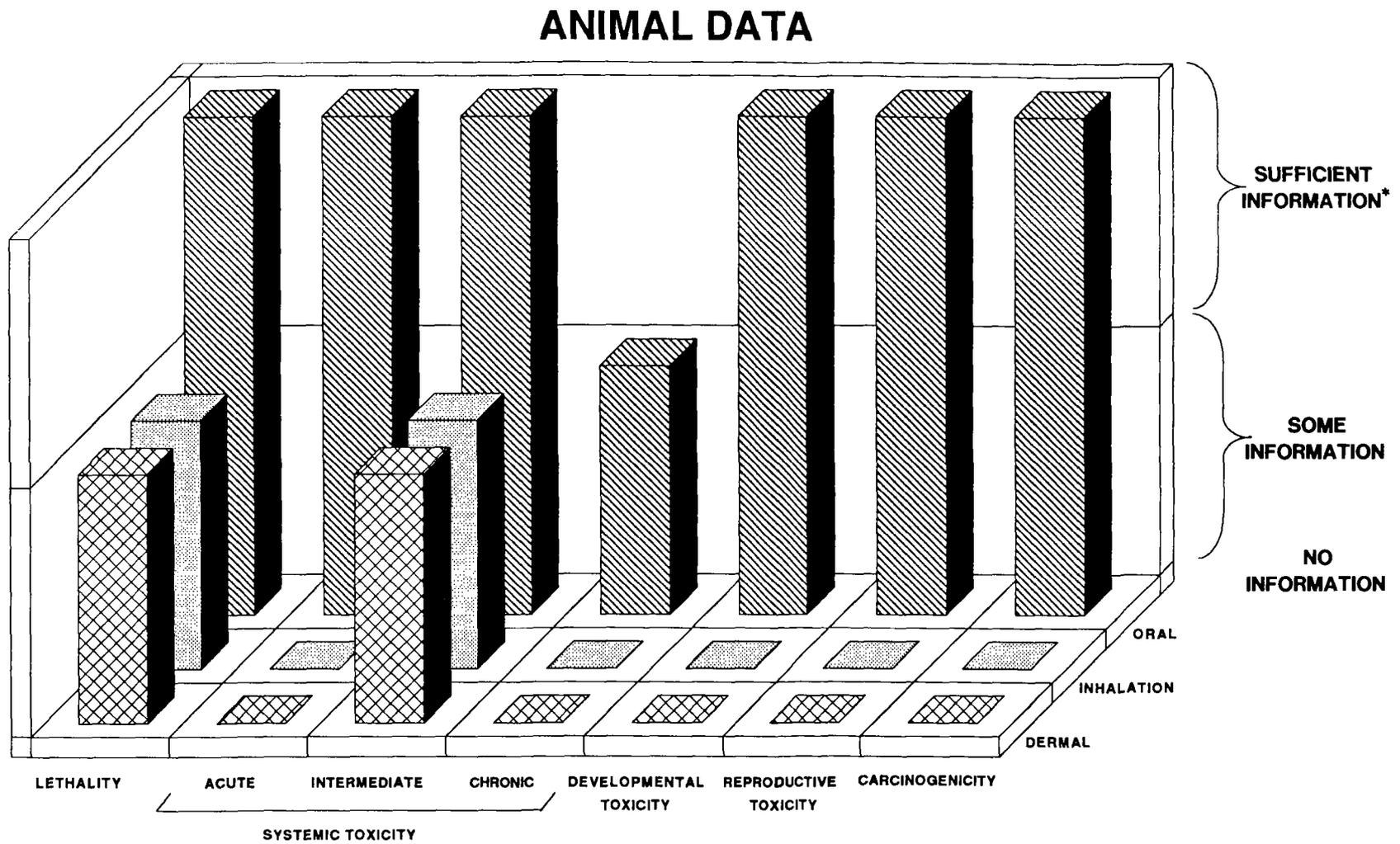
# HUMAN DATA



\*Data exist for occupational exposure, which is primarily via inhalation, but dermal exposure is likely to occur.

†Sufficient information exists to meet at least one of the criteria for cancer or noncancer end points.

Fig. 2.7. Availability of information on health effects of PCBs (human data).



**Fig. 2.8. Availability of information on health effects of PCBs (animal data).**

### 2.3.2.3 Summary of relevant ongoing research

J.L. Jacobson of Wayne State University is conducting a study sponsored by the National Institute of Environmental Health Sciences to evaluate the impact of PCBs on physical, cognitive, and neurological development in early childhood. The children, examined at age 4, were exposed to moderate levels of PCBs, or maternal serum PCB levels were high near the time of birth (NTIS 1987).

W.J. Rogan of the National Institute of Environmental Health Sciences is conducting a follow-up study of children exposed to PCBs through breast milk. The children under study are a cohort of 856 North Carolina children exposed to relatively low levels of PCBs and a cohort of 108 children from Taiwan exposed to relatively high levels of PCBs (NTIS 1987).

### 2.3.3 Other Information Needed for Human Health Assessment

#### 2.3.3.1 Pharmacokinetics and mechanisms of action

Quantitative data concerning the pharmacokinetics of PCBs following inhalation and dermal exposure are lacking. Such data could greatly assist efforts to evaluate health effects resulting from inhalation and dermal exposure to PCBs. Further studies should be conducted concerning the distribution of PCBs, especially regarding the distribution of PCBs in the plasma compared to adipose tissue.

Ongoing studies concerning pharmacokinetics and mechanisms of action were not located.

#### 2.3.3.2 Monitoring of human biological samples

PCBs can be measured in serum, adipose tissue, and milk. These measurements can indicate elevated exposure but do not provide information concerning the route of exposure. Although biological monitoring is useful for documenting exposures, it has limited applicability at this time.

Biological monitoring methods indicate body burden of PCBs that have accumulated over a lifetime. Adequate methods are not available to distinguish exposure routes, short or intermittent exposures, or low-level exposures due to the bioaccumulation and slow excretion of PCBs.

The Indiana State Department of Health (population survey in Monroe County, Indiana) is conducting a study that will provide information on PCB body burden levels in conjunction with selected health outcomes. Several smaller studies concerning monitoring of biological samples are being conducted by the CDC.

#### 2.3.3.3 Environmental considerations

Methodology of sufficient sensitivity and specificity to measure PCBs in the environment exists; however, various laboratories may not have access to state-of-the-art equipment.

There are no data on the effect of the environmental matrix or vehicle on the bioavailability of specific PCBs and PCB mixtures.

Studies with 2,3,7,8-TCDD indicate that the vehicle may play a significant role in the relative bioavailability of 2,3,7,8-TCDD and related compounds (e.g., PCBs) (EPA 1985b).

There appears to be a fairly good understanding of the general environmental fate and transport of PCBs; however, the environmental fate and transport at specific sites may vary markedly from one site to another. Therefore, the environmental fate of PCBs at a specific site may not be understood very well without considerable additional information. In terms of the general understanding of environmental fate and transport, more experimental data are required to understand the potential importance of photolysis in degrading the more highly chlorinated PCBs, which are more persistent in the environment. In addition, a better understanding of the environmental cycling of PCBs is needed to assess future exposure from current environmental sinks such as PCBs adsorbed to sediments.

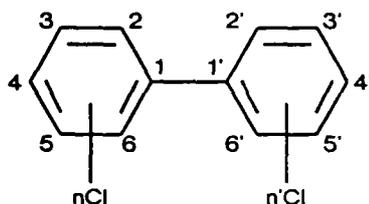
No studies were found that involve the environmental interaction of PCBs with other pollutants.

The U.S. EPA is currently funding studies regarding the environmental fate and transport of PCBs in the New Bedford Harbor and the Great Lakes in order to develop data related to this issue.

### 3. CHEMICAL AND PHYSICAL INFORMATION

#### 3.1 CHEMICAL IDENTITY

Data pertaining to the chemical identity of the Aroclors are listed in Table 3.1. Aroclors are mixtures of chlorinated biphenyls. The general chemical structure of chlorinated biphenyls is as follows:



(where  $n$  and  $n'$  may vary from 0 to 5).

The numbering system for the biphenyl structure is also shown above.

Aroclor products are identified by a four-digit numbering code in which the first two digits (12) indicate that the parent molecule is biphenyl and the last two digits indicate the chlorine content by weight. Thus, Aroclor 1242 is a chlorinated biphenyl mixture with an average chlorine content of 42%. The exception to this designation method is Aroclor 1016, which retained the 1016 designation by which it was known during development (Mieure et al. 1976). Aroclor 1016 is a mixture that contains primarily mono-, di-, and trichloro isomers and has an average chlorine percentage (41.5%) that is very similar to Aroclor 1242.

#### 3.2 PHYSICAL AND CHEMICAL PROPERTIES

Selected physical and chemical properties of the Aroclors are presented in Table 3.2. Table 3.3 identifies the approximate molecular composition of the Aroclors.

Data pertaining to the pyrolysis of PCBs, which results in the formation of polychlorinated dibenzofurans (PCDFs), have been reviewed (EPA 1988a). Several studies involving pyrolysis of specific PCB isomers have found that the pyrolysis products include PCDFs, chlorinated benzenes, naphthalenes, phenyl ethynes, biphenylenes, and hydroxy PCBs. There appear to be four major paths for production of PCDFs from PCBs: (1) loss of two ortho chlorines, (2) loss of ortho hydrogen as well as chlorine, (3) loss of an ortho hydrogen as well as chlorine but involving a shift of chlorine from the 2 to the 3 position, and (4) loss of two ortho hydrogens (EPA 1988a). The formation of PCDFs from the

pyrolysis of PCBs occurred when an electrical transformer in an office building in Binghamton, New York, accidentally caught fire on February 5, 1981 (Schecter and Tiernan 1985, Tiernan et al. 1985).

Table 3.1. Chemical identity of the Aroclors

	Chemical name <sup>a</sup>							References
	Aroclor 1016	Aroclor 1221	Aroclor 1232	Aroclor 1242	Aroclor 1248	Aroclor 1254	Aroclor 1260	
Synonyms	PCB-1016 Polychlorinated biphenyl with 41.5% Cl	PCB-1221 Polychlorinated biphenyl with 21% Cl	PCB-1232 Polychlorinated biphenyl with 32% Cl	PCB-1242 Polychlorinated biphenyl with 42% Cl	PCB-1248 Polychlorinated biphenyl with 48% Cl	PCB-1254 Polychlorinated biphenyl with 54% Cl	PCB-1260 Polychlorinated biphenyl with 60% Cl Chlorodiphenyl (60% Cl)	SANSS 1987
Trade names	Aroclor <sup>b</sup>	Aroclor	Aroclor	Aroclor	Aroclor	Aroclor	Aroclor	
Chemical formula	See Table 3.3	See Table 3.3	See Table 3.3	See Table 3.3	See Table 3.3	See Table 3.3	See Table 3.3	
Wiswesser line notation <sup>c</sup>	NA	NA	NA	NA	NA	NA	NA	
Chemical structure	See text	See text	See text	See text	See text	See text	See text	
Identification Nos.								
CAS Registry No.	12674-11-2	11104-28-2	11141-16-5	53469-21-9	12672-29-6	11097-69-1	11096-82-5	SANSS 1987
NIOSH RTECS No.	TQ1351000	TQ1352000	TQ1354000	TQ1356000	TQ1358000	TQ1360000	TQ1362000	SANSS 1987
EPA Hazardous Waste No. <sup>d</sup>	3502	3502	3502	3502	3502	3502	3502	EPA 1980a
OHM-TADS No.	8500400	8500401	8500402	8500403	8500404	8500405	8500406	EPA-NIH 1987
DOT/UN/NA/IMCO Shipping No.	UN2315	UN2315	UN2315	UN2315	UN2315	UN2315	UN2315	Chemline 1987
STCC No.	4961666	4961666	4961666	4961666	4961666	4961666	4961666	Stone 1981
Hazardous Substances Data Bank No.	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	1822	HSDB 1987
National Cancer Institute No.	Unknown	Unknown	Unknown	Unknown	Unknown	C02664	Unknown	NCI 1978

<sup>a</sup>These are the current chemical names as indexed by the Chemical Abstracts Service (CAS).

<sup>b</sup>Aroclor is the trade name for chlorinated biphenyls made by Monsanto.

<sup>c</sup>Wiswesser line notations are not applicable for mixtures.

<sup>d</sup>Designation prior to May 19, 1980.

Table 3.2. Physical and chemical properties of PCBs

	Aroclor designation							References
	1016	1221	1232	1242	1248	1254	1260	
Molecular weight <sup>a</sup>	257.9	200.7	232.2	266.5	299.5	328.4	375.7	Hutzinger et al. 1974
Color	Clear	Clear	Clear	Clear	Clear	Light yellow	Light yellow	Monsanto 1974
Physical state	Oil	Oil	Oil	Oil	Oil	Viscous liquid	Sticky resin	Monsanto 1974
Odor	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	
Melting point, °C	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	
Boiling point, °C (distillation range)	325–356	275–320	290–325	325–366	340–375	365–390	385–420	Monsanto 1974
Autoignition temperature	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	
Solubility								
Water, mg/L	0.42	0.59 (24°C)	Unknown	0.24 0.34 0.10 (24°C)	0.054 0.06 (24°C)	0.012 0.057 (24°C)	0.0027	Monsanto 1974, Paris et al. 1978, Hollifield 1979
Organic solvents	Very soluble	Very soluble	Very soluble	Very soluble	Very soluble	Very soluble	Very soluble	EPA 1985a
Density, g/cm <sup>3</sup> at 25°C	1.33	1.15	1.24	1.35	1.41	1.50	1.58	Monsanto 1974
Partition coefficient Log octanol–water <sup>b</sup>	5.6	4.7	5.1	5.6	6.2	6.5	6.8	<i>b</i>
Vapor pressure, mm Hg at 25°C	4 × 10 <sup>-4</sup>	6.7 × 10 <sup>-3</sup>	4.06 × 10 <sup>-3</sup>	4.06 × 10 <sup>-4</sup>	4.94 × 10 <sup>-4</sup>	7.71 × 10 <sup>-5</sup>	4.05 × 10 <sup>-5</sup>	Monsanto 1974, Callahan et al. 1979
Henry's law constant, atm-m <sup>3</sup> /mol at 25°C <sup>c</sup>	2.9 × 10 <sup>-4</sup>	3.5 × 10 <sup>-3</sup>	Unknown	5.2 × 10 <sup>-4</sup>	2.8 × 10 <sup>-3</sup>	2.0 × 10 <sup>-3</sup>	4.6 × 10 <sup>-3</sup>	<i>c</i>
Refractive index	1.6215–1.6235 (25°C)	1.617–1.618 (20°C)	Unknown	1.627–1.629 (20°C)	Unknown	1.6375–1.6415 (25°C)	Unknown	IARC 1978

Table 3.2 (continued)

	Aroclor designation							References
	1016	1221	1232	1242	1248	1254	1260	
Flash point, °C (Cleveland open cup)	Unknown	176	238	None	None	None	None	Hubbard 1964
Flammability limits	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	
Conversion factors Air (25°C) <sup>d</sup>	1 mg/m <sup>3</sup> = 0.095 ppm	1 mg/m <sup>3</sup> = 0.12 ppm	1 mg/m <sup>3</sup> = 0.105 ppm	1 mg/m <sup>3</sup> = 0.092 ppm	1 mg/m <sup>3</sup> = 0.08 ppm	1 mg/m <sup>3</sup> = 0.075 ppm	1 mg/m <sup>3</sup> = 0.065 ppm	

<sup>a</sup>Average mass from Table 3.3.

<sup>b</sup>These log  $K_{ow}$  values represent an average value for the major components of the individual Aroclor. Experimental values for the individual components were obtained from Hansch and Leo 1985.

<sup>c</sup>These Henry's law constants were estimated by dividing the vapor pressure by the water solubility. The first water solubility given in this table was used for the calculation. The resulting estimated Henry's law constant is only an average for the entire mixture; the individual chlorobiphenyl isomers may vary significantly from the average. Burkhard et al. (1985) estimated the following Henry's law constants (atm·m<sup>3</sup>/mol) for various Aroclors at 25°C: 1221 ( $2.28 \times 10^{-4}$ ), 1242 ( $3.43 \times 10^{-4}$ ), 1248 ( $4.4 \times 10^{-4}$ ), 1254 ( $2.83 \times 10^{-4}$ ), 1260 ( $4.15 \times 10^{-4}$ ).

<sup>d</sup>These air conversion factors were calculated by using the average molecular mass as presented under molecular weight.

**Table 3.3. Approximate molecular composition of PCBs  
(percent)**

Empirical formula	Aroclor designation						
	1016	1221	1232	1242	1248	1254	1260
$C_{12}H_{10}$	<0.1	11	<0.1	<0.1	ND <sup>a</sup>	<0.1	ND
$C_{12}H_9Cl$	1	51	31	1	ND	<0.1	ND
$C_{12}H_8Cl_2$	20	32	24	16	2	0.5	ND
$C_{12}H_7Cl_3$	57	4	28	49	18	1	ND
$C_{12}H_6Cl_4$	21	2	12	25	40	21	1
$C_{12}H_5Cl_5$	1	<0.5	4	8	36	48	12
$C_{12}H_4Cl_6$	<0.1	ND	<0.1	1	4	23	38
$C_{12}H_3Cl_7$	ND	ND	ND	<0.1	ND	6	41
$C_{12}H_2Cl_8$	ND	ND	ND	ND	ND	ND	8
$C_{12}H_1Cl_9$	ND	ND	ND	ND	ND	ND	ND
Average molecular mass	257.9	200.7	232.2	266.5	299.5	328.4	375.7

<sup>a</sup>ND = none detected.

Source: Hutzinger et al. 1974.

## 4. TOXICOLOGICAL DATA

### 4.1 OVERVIEW

Evaluation of the toxicokinetics and toxicity of PCBs is complicated by the fact that PCBs are mixtures of a variety of different congeners and impurities, each with its own characteristics. Aroclor PCBs are the subject of this profile, but toxicokinetic studies often examined specific congeners, and many toxicological studies used mixtures of PCBs other than Aroclors, particularly Kanechlors and Clophens. Kanechlors and Clophens are similar to Aroclors but are produced in Japan and Germany, respectively, rather than in the United States, and differ in methods of production, chlorine composition, and polychlorinated dibenzofuran (PCDF) contamination. The reported range of PCDFs is 0-2 ppm in Aroclors and 5-20 ppm for Japanese and European PCBs (Drill et al. 1981). Reference to Kanechlors and Clophens is made occasionally to support statements made about Aroclors because effects produced by Aroclors, Kanechlors, and Clophens are generally assumed to be similar, particularly for mixtures of equivalent chlorine percentages (Kimbrough 1987a). Non-Aroclor toxicity data are not considered in detail because of the aforementioned differences in composition and because reported lowest effect levels are lower for Aroclors than Kanechlors or Clophens.

The general population is exposed to PCBs primarily by the oral route (through food, particularly fish). It is possible that indoor air may be a significant source of PCB exposure. Inhalation and dermal exposure are the primary routes of occupational exposures, but the relative contribution of these routes is unknown.

Studies of the absorption of PCBs following oral exposure indicate that gastrointestinal absorption of most isomers is >90%. The limited data concerning the absorption of PCBs following inhalation and dermal exposure indicate that PCBs can be absorbed via these exposure routes, but the data are not sufficient for quantitative estimates.

Distribution of ingested or injected Aroclors follows a biphasic pattern. During the first day following dosing, the PCBs distribute to the liver and muscle tissue. Because of their lipophilicity, the PCBs are then redistributed to the fat, skin, and other fat-containing organs. Heavily chlorinated congeners redistribute to adipose tissue to a greater extent than the less chlorinated congeners, although the type of chlorine substitution is also a factor.

A number of studies indicate that PCBs can cross the placenta and locate in the fetus. PCBs also concentrate in milk. Higher PCB levels may reach the offspring through nursing than through placental transfer.

The metabolism of PCBs is dependent on the number and position of chlorine atoms, with lesser chlorinated isomers metabolized more readily than more chlorinated isomers. PCB metabolites tend to be 3- or 4-hydroxy compounds. Evidence suggests that metabolism proceeds through an arene oxide intermediate except for the 3-hydroxy metabolites, which are formed by a different pathway involving, at least in part, direct hydroxylation. The position and degree of chlorination substantially influence the rate and extent of metabolism. Metabolism is facilitated by the presence of at least two adjacent unsubstituted ring carbons, particularly in the 3,4,5 or 3',4',5' positions.

PCBs that are metabolized with more difficulty tend to be excreted almost exclusively through the biliary route, while the metabolites of mono-, di-, and trichlorinated isomers are also eliminated through the urine. Urinary metabolites are in the form of conjugates, including glucuronides and sulfates. Glutathione conjugates have also been identified.

Higher chlorinated PCBs tend to persist in the body longer than lower chlorinated PCBs. For example, biological half-lives in the rat range from approximately 1 day for 2,2'-dichlorobiphenyl to 460 days for 2,2',4,4',5,5'-hexachlorobiphenyl.

Aroclors appear to have a low order of acute lethality. Data for non-Aroclor PCB mixtures and specific PCB isomers suggest that mice and guinea pigs are more sensitive than rats. Aroclors are lethal at much lower total doses when administered subchronically or chronically than acutely, indicating that PCBs bioaccumulate to concentrations that are toxic.

Animal studies have shown that the liver and cutaneous tissues are the major target organs for Aroclors. Aroclors have also been shown to produce stomach and thyroid alterations, immunosuppressive effects, and porphyria in animals. Animals are sensitive to repeated exposures to Aroclors as a result of rapid bioaccumulation to toxic levels. Monkeys are particularly sensitive to the toxic effects of Aroclors. Toxic effects have not been documented in humans who were exposed to Aroclors via the environment. Occupational exposure to Aroclors has been associated with reversible skin lesions and subclinical alterations in serum enzymes that are suggestive of liver enzyme induction and possible hepatocellular damage.

More serious health effects were observed in humans who consumed rice oil that had been contaminated with Kaneclors in Japan ("Yusho" incident) and Taiwan ("Yu Cheng" incident). Although there is an historical linkage between Yusho and PCBs and some regulatory documents ascribe health effects from these incidents to PCBs, effects from the incidents are not reviewed in this report because exposure was to Kaneclors and because the effects cannot be attributed specifically to the Kaneclors. The Kaneclors were heated in thermal heat exchangers before the rice oil contamination and during cooking and contained relatively high concentrations of PCDFs and polychlorinated quaterphenyl contaminants. There appears to be general agreement that the PCDF contaminants, particularly the more potent isomers, contributed significantly to the health effects observed in the Yusho and Yu Cheng

patients. Please refer to Kuratsune and Shapiro (1984) and Kimbrough (1987a) for a more complete discussion of this topic.

Aroclors appear to be fetotoxic but not teratogenic in various species of animals, including rats, mice, rabbits, and monkeys, but the possibility that contaminants (e.g., PCDFs) may be responsible for the effects should be recognized. Slight decreases in birth weight, gestational age, and/or neonatal behavioral performance have been reported in infants born to mothers who had environmental or occupational exposure to PCBs. These effects are inconclusive and not definitely attributable to PCBs.

Oral exposure to Aroclors produced deleterious effects on reproduction in monkeys, mink, and, at higher doses, rodents.

PCBs have produced generally negative results in *in vitro* and *in vivo* mutagenicity assays.

Feeding studies in laboratory animals demonstrated the carcinogenicity of several PCB mixtures, but it is not clear which components of the mixture or metabolites are actually carcinogenic. The liver is the primary target of PCB carcinogenicity.

## 4.2 TOXICOKINETICS

### 4.2.1 Absorption

#### 4.2.1.1 Inhalation

**Human.** Inhalation exposure and dermal exposure are the primary routes of occupational exposure to PCBs, but the relative contribution of each route has not been discerned (Wolff 1985).

**Animal.** Six rats were exposed to an aerosol of a PCB mixture (Pydraul A200, 42% chlorine) at a concentration of  $30 \text{ g/m}^3$  (0.5 to  $3 \text{ }\mu\text{m}$  particles) (Benthe et al. 1972). PCB concentrations in the liver after exposure for 15 min were >50% of the maximum concentration attained after exposure for 2 h ( $70 \text{ }\mu\text{g/g}$  tissue). These data indicate that the PCBs were readily absorbed, but the data were not sufficient for more quantitative estimates of amount or rate of absorption.

#### 4.2.1.2 Oral

**Human.** The general population is exposed to PCBs primarily by the oral route (primarily by consumption of contaminated fish). Schwartz et al. (1983) found elevated levels of PCBs in the serum and breast milk of women who ate PCB-contaminated fish from Lake Michigan. Humphrey (1976) reported blood levels of PCBs in people who consumed contaminated sport fish from Lake Michigan in 1973. Annual consumption of  $\geq 24$  lb resulted in a mean blood level of 0.073 ppm ( $n = 105$ , s.d. not reported), while annual consumption of  $\leq 6$  lb resulted in a mean blood level of 0.020 ppm ( $n = 37$ , s.d. not reported). Blood levels of PCBs in persons who ate no fish averaged 0.017 ppm ( $n = 16$ , s.d. not reported). The estimated intake of PCBs by 82% of the people who consumed  $\geq 24$  lb ranged from 0.49 to  $3.94 \text{ }\mu\text{g PCB/kg/day}$  and averaged  $1.7 \text{ }\mu\text{g/kg/day}$ . These studies indicate that PCBs are absorbed by the gastrointestinal tract, but do not provide information regarding the extent of absorption.

**Animal.** Drill et al. (1981) and EPA (1985a) reviewed a number of animal studies indicating that PCBs, including Aroclors, are absorbed readily from the gastrointestinal tract following oral administration. Albro and Fishbein (1972) examined the absorption of 19 PCB congeners and unchlorinated biphenyl in rats treated by gavage at doses of 5, 50, or 100 mg/kg. Determination of PCBs in feces collected for 4 days indicated that absorption of all congeners was >90%. Using rhesus monkeys, Allen et al. (1974a,b) determined over 2-week periods that >90% of a single oral dose of 1.5 or 3.0 g/kg Aroclor 1248 was absorbed. Bleavins et al. (1984) determined over a period of 5 weeks that European ferrets absorbed 85.4% of a single dose of [<sup>14</sup>C]-labeled Aroclor 1254 (0.05 mg) given in food.

In contrast to the above studies, Norback et al. (1978) claimed that 59.3 to 87% of a single oral dose of 2,4,5,2',4',6'-hexachlorobiphenyl passed unabsorbed through the intestine of monkeys during the first week after dosing. It was unclear why relatively little of this isomer was absorbed. There are no data on the effect of the environmental matrix or vehicle on the bioavailability of specific PCBs and PCB mixtures. Studies with 2,3,7,8-TCDD indicate that the vehicle may play a significant role in the relative bioavailability of 2,3,7,8-TCDD and related compounds (e.g., PCBs) (EPA 1985b).

#### 4.2.1.3 Dermal

**Human.** In a study of occupational exposure of electrical workers to PCBs (Pyralen 3010 and Apirolino, 42% chlorine content), Maroni et al. (1981b) concluded that absorption of PCBs occurred mainly through the skin. Quantitative data were not available.

**Animal.** Single doses of <sup>14</sup>C-labeled PCBs (42% and 54% chlorine content) were applied to the skin of rhesus monkeys (4.1 and 19.3 μg/cm<sup>2</sup> 42% chlorine) and guinea pigs (4.6 μg/cm<sup>2</sup> 42% chlorine and 5.2 μg/cm<sup>2</sup> 54% chlorine) that were lightly clipped of hair (Wester et al. 1983). The application sites were washed with water and acetone after 24 h, and radioactivity in the urine was determined during the 28 days (monkeys) and 16 days (guinea pigs) following dosing. Absorption ranged from approximately 15-34% of the applied radioactivity in the monkeys and averaged approximately 33% (42% chlorine) and 56% (54% chlorine) of the applied radioactivity in the guinea pigs. When <sup>14</sup>C-labeled PCB (42% chlorine) was applied to guinea pig skin and immediately washed with water and acetone, approximately 59% of the dose was recovered. When both mixtures were applied to guinea pig skin, left for 24 h and then washed, approximately 1% of the 42% chlorine content PCB and 20% of the 54% chlorine content PCB doses were recovered.

Using tritium-labeled PCBs (40% chlorine), Nishizumi (1976) found evidence for dermal absorption of PCBs in rats via follicular diffusion. Quantitative data were not provided.

#### 4.2.2 Distribution

##### 4.2.2.1 Inhalation

**Human.** Wolff et al. (1982b) examined the relative concentrations of PCB congeners in plasma and adipose tissue of 26 persons

occupationally exposed to PCBs (20 to 54% chlorine). Exposure was not discussed, but it probably included both inhalation and dermal exposure. The results indicated that PCB congeners with chlorines in both 4 positions were the major components in plasma and adipose tissue. PCBs with unsubstituted 3,4 positions on at least one ring were observed at lower concentrations in plasma and adipose. The adipose-plasma partition ratio calculated for Aroclor 1248 residues was 185, while the partition ratio for Aroclor 1254 residues was 190. In a more recent study of 173 workers from the same population, adipose-plasma partition ratios of 210, 190, and 200 were determined for Aroclors 1242, 1254, and 1260, respectively (Brown and Lawton 1984).

**Animal.** Maximum PCB concentrations in the liver and brain of rats occurred 2 and 24 h, respectively, after a single 30-min exposure to 30 g/m<sup>3</sup> of Pydraul A200 aerosol (42% chlorine) (Benthe et al. 1972). Concentrations in these tissues subsequently declined, while adipose concentrations reached a maximum after 48 h.

#### 4.2.2.2 Oral

**Human.** A number of studies reviewed by EPA (1988a) indicate that PCBs concentrate in human breast milk. Exposures in these studies were most likely oral, but may have included both inhalation and dermal exposure. Wolff (1983) reported the half-life for the decline in concentration of PCBs (percentage chlorine in compounds not stated) in breast milk to be 5 to 8 months and found that the concentration of PCBs in breast milk was 4 to 10 times that in maternal blood. Similar results were reported by Jacobson et al. (1984b).

Ando et al. (1985) examined the PCB concentration in maternal blood and milk and the placenta of six Japanese women. They found that the congeners present were more typical of Kanechlor 500 than Kanechlors 300, 400, or 600. The results indicated that as the chlorine content of the PCB congeners increased, the correlation between the placental content of congeners and maternal blood and milk also increased.

PCBs were detected in the umbilical tissues, umbilical blood, amniotic fluid, and baby's blood from a woman who was occupationally exposed to Kanechlors 300 and 500 in a capacitor factory (Yakushiji et al. 1978). PCB levels in these tissues and fluids were considerably less than in the mother's blood. Maternal serum concentrations of PCBs were also higher than cord serum concentrations in women who resided in western Michigan (Jacobson et al. 1984b) and upstate New York (Bush et al. 1984) (i.e., in regions with easy access to fish from the Great Lakes).

Kraul and Karlog (1976) determined PCB levels in abdominal fat, brain, and liver from necropsies completed in 1972 and 1973 in Copenhagen, Denmark. The ratios of PCB levels were reported as 1:3.5:81 for brain:liver:fat, indicating that adipose was the site of greatest bioaccumulation of the tissues studied.

**Animal.** Following absorption, PCBs, including Aroclors, are distributed in a biphasic manner. The compounds rapidly (minutes to hours) clear from the blood and accumulate in the liver and muscles (Drill et al. 1981). PCBs may be translocated from the liver to adipose tissue for storage or be metabolized in the liver, with metabolites

excreted in the urine or bile. The accumulation of PCBs in lipophilic tissues is dependent on the structure-dependent metabolic rates of the individual congeners.

Muehleback and Bickel (1981) treated rats by gavage with a single dose of 0.6 or 3.6 mg/kg [<sup>14</sup>C]-2,4,5,2',4',5'-hexachlorobiphenyl. The rats were examined 1 h, 24 h, 6 weeks, 20 weeks, or 40 weeks after dosing. The results showed the highest levels of PCBs in muscle, liver, fat, and skin early in the study. By the end of the study, the highest PCB levels were found in adipose tissue followed by skin, muscle, and liver. During the 40-week study period, only 16% of the total dose was excreted.

Gage and Holm (1976) determined concentrations in abdominal fat of mice 7 and 21 days after the mice were dosed by gavage with a single dose (13-165 µg/mouse) of 1 of 14 PCB congeners. Relatively low levels (<10 ng/g/µg dose) were found at 7 days for 4,4'-, 3,2',4',6'-, and 2,3,4,2',4',6'-isomers, with relatively high levels (≥100 ng/g/µg dose) for 2,4,5,2',4',5-, 4,2',4',6'-, and 2,4,2',4'-PCBs.

Kurachi and Mio (1983a) exposed mice to Kanechlor 400 at 100 mg/kg in the diet for 5 to 20 days. Analysis of tissues at the end of the feeding period indicated high levels of PCBs in the gonads. High levels of PCBs were also found in skin, adipose tissue, adrenals, and kidneys. A second group of mice were kept on the PCB diet for 20 days in a rotation cage to cause fatigue. Mobilization of fat deposits was observed with liver PCB levels in fatigued mice 10 times greater than in mice fed the same diets but allowed to rest.

A number of animal studies have demonstrated that PCB mixtures and specific congeners and isomers can cross the placental barrier and enter the fetuses (EPA 1988a). High levels of PCBs accumulate in the mammary gland where they are secreted in the fat portion of the milk. Masuda et al. (1979) fed PCBs to pregnant mice through the first 18 days of gestation and found the highest levels of serum PCBs in offspring 1 to 2 weeks old as compared with 18-day fetuses or with older offspring. In studies in which monkeys were exposed prior to and during gestation, signs of PCB-induced intoxication in nursing but not newborn offspring were observed (Allen and Barsotti 1976, Iatopoulos et al. 1978). Results such as these have led some investigators to conclude that transfer through nursing may account for higher exposure of young than does placental transfer.

Groups of 24 rhesus monkeys were maintained on diets that provided Aroclor 1016 at doses of 0, 4.5, or 18.1 mg/kg/day throughout gestation and a 4-month gestation period (Barsotti and Van Miller 1984). At birth, the concentrations of the PCBs in the skin of infants were similar to concentrations in the subcutaneous fat of the mothers. At weaning, the PCB content in the mesenteric fat of the infants was 4 to 7 times greater than in the subcutaneous fat of the mothers. Gas chromatographic patterns showed that the adult adipose tissue did not include the total spectrum of peaks observed in the Aroclor 1016 standard, that all of the peaks observed in the standard occurred in the neonate skin, and that the peaks in the mesenteric fat at weaning and 4 months after weaning were qualitatively similar to those in the adult adipose tissue. These data suggested an inability of the fetus to metabolize and excrete

certain congeners that are more readily metabolized and eliminated by adults and older infants.

Bleavins et al. (1984) fed female European ferrets a single dose of [<sup>14</sup>C]-labeled Aroclor 1254 in the diet (0.05 mg) early (day 14) or late (day 35) in gestation and determined the placental transfer of PCBs. They found that placental transfer to the kits was 0.01% (per kit) of the maternal dose when dams were exposed early in gestation and 0.04% (per kit) when dams were exposed late in gestation. Placental transfer of PCBs was considerably less than mammary transfer, with the ratio of placental to mammary transfer at 1 week of lactation 1:15 and 1:7 for offspring of dams dosed early and late in gestation, respectively.

#### 4.2.2.3 Dermal

Data concerning the distribution of Aroclors following dermal exposure of humans or animals were not located. Because PCBs are lipophilic, the compounds should concentrate in adipose tissue regardless of the route of exposure.

### 4.2.3 Metabolism

#### 4.2.3.1 Human

2,2',4,4',5,5'-Hexa-CB was the PCB congener found in the highest concentration in human adipose tissue, while 2,2',4,4',6,6'-hexa-CB was not detected (Jensen and Sundstrom 1974). As both of these compounds are found in commercial PCB mixtures and in the environment, the presence of the 2,2',4,4',5,5'-hexa-CB congener in adipose tissue appears to be related to resistance to metabolism (EPA 1988a). That this congener is not metabolized or is minimally metabolized is also indicated by the finding that the blood concentration of this congener in 17 PCB-poisoned patients decreased only 10% over 300 to 500 days (Chen et al. 1982). The measurements began 7 months to a year after the outbreak of poisoning. The results of in vitro metabolism studies with human liver microsomes also demonstrate minimal metabolism of this congener (Schnellman et al. 1983, 1984).

There were lower concentrations of PCBs with unsubstituted 3,4 positions on at least one of the phenyl rings than PCBs with substitutions in the 2,4 or 3,4 positions on both rings in the blood and adipose tissue from capacitor-manufacturing facility workers (Wolff et al. 1982a).

#### 4.2.3.2 Animal

The metabolism of PCBs has been investigated in numerous studies with animals and reviewed by EPA (1988a) and Drill et al. (1981). A variety of substrates have been tested, and the PCBs were usually administered by the oral or parenteral routes. General findings of these studies reported by EPA (1988a) are presented below.

Phenolic products are the major PCB metabolites although sulfur-containing metabolites (e.g., methylsulfones), *trans*-dihydrodiols, polyhydroxylated PCBs, and methyl ether derivatives have also been identified. Although the effects of chlorine substitution patterns on sites of oxidation have not been studied systematically, EPA (1988a) suggests the following:

1. Hydroxylation is favored at the para position in the least chlorinated phenyl ring unless this site is sterically hindered (i.e., 3,5-dichloro substitution).
2. In the lower chlorinated biphenyls, the para position of both biphenyl rings and carbon atoms that are para to the chloro substituent are all readily hydroxylated (Sparling et al. 1980).
3. The availability of two vicinal unsubstituted carbon atoms (particularly C5 and C4 in the biphenyl nucleus) also facilitates oxidative metabolism of the PCB substrate but is not a necessary requirement for metabolism.
4. As the rate of chlorination increases on both phenyl rings, the rate of metabolism decreases.
5. The metabolism of specific PCB isomers by different species can result in considerable variations in metabolite distribution.

PCB metabolites tend to be 3- or 4-hydroxy compounds. The occurrence of *trans*-dihydrodiol metabolites suggests that metabolism of PCBs proceeds through formation of arene oxide intermediates (EPA 1988a). 3-Hydroxybiphenyl appears to be formed by a different mechanism, at least in part via direct hydroxylation (Billings and McMahon 1978). Arene oxides are potential electrophiles that have been implicated in cellular necrosis, mutagenicity, and carcinogenicity. The toxicological significance of PCB metabolism is unknown, but most studies suggest that the parent hydrocarbon initiates most of the common toxic responses by initial binding to the cytosolic receptor protein (EPA 1988a). The role of metabolism in the genotoxicity of PCBs has not been delineated.

PCB metabolites are usually more polar than the parent compounds and conjugated with glucuronides or sulfates prior to elimination. Rats and mice that were exposed to di-, tetra-, or penta-CBs by intraperitoneal injection or diet eliminated metabolites of glutathione conjugates and other sulfur-containing compounds (Kurachi 1983, Kurachi and Mio 1983b).

#### 4.2.4 Excretion

##### 4.2.4.1 Inhalation

Data concerning the excretion of PCBs in humans and animals following inhalation exposure were not available.

##### 4.2.4.2 Oral

The excretion of PCBs is to a large extent dependent on the metabolism of PCBs to more polar compounds (EPA 1988a). At equilibrium, the elimination of PCBs from all tissues will be dependent on the structure-dependent metabolism rates of the individual PCB congeners. For example, biological half-lives in the rat range from 1.15 days for 2,2'-dichlorobiphenyl to approximately 460 days for 2,2',4,4',5,5'-hexachlorobiphenyl (Tanabe et al. 1981, Wyss et al. 1986). Metabolites of the more highly chlorinated congeners are eliminated primarily via the feces (Goto et al. 1974).

**Human.** Chen et al. (1982) report on the determination of PCBs in the blood of humans in Taiwan after they consumed rice-bran oil contaminated with Kanechlor 500 and PCDFs. Blood samples from 17 patients were examined, with 2 to 3 samples taken from each patient 2 to 17 months apart. The results indicated that the tetra- and some penta-isomers tend to be eliminated more rapidly than other penta-, hexa-, and hepta-isomers. Half-lives for the 2,4,5,2',4'- and 2,3,4,3',4'-penta-isomers in blood were determined to be 9.8 and 8.7 months, respectively. The data also indicated that two adjacent unsubstituted carbon atoms at the meta-para positions facilitated metabolism and subsequent elimination from the blood.

**Animal.** Hashimoto et al. (1976) examined the excretion of [ $^{14}\text{C}$ ] PCB compounds given once a week to rats by gavage at a total dose of 6.35 to 7.85 mg/kg over a period of 5 to 50 weeks. The PCBs studied were predominantly tetra- and hexa-chlorinated isomers. The results indicated that 1.9 to 4.9% of the dose of tetra-PCBs was excreted in the urine collected for 7 days after the last dose, with the higher amounts excreted in rats treated for longer periods. In rats treated with hexa-PCBs, only 0.6% of the dose was excreted in the urine collected for 7 days after the last dose (treatment was for 5 weeks only). About 47 to 68% of the dose of both tetra- and hexa-isomers was excreted in the feces, most of which was excreted in 2 days after the last dose.

Mizutani et al. (1977) studied the elimination of tetra-CB isomers in mice fed diets containing a single isomer at 10 ppm for 20 days. Biological half-lives for the individual isomers were 0.9, 9.2, 3.4, 0.9, and 2.1 days for 2,3,2',3'-; 2,4,2',4'-; 2,5,2',5'-; 3,4,3',4'-; and 3,5,3',5'-, respectively. The authors were not able to relate the difference in rates of elimination to chlorine substitution patterns.

In a study of the influence of molecular structure on the excretion of 14 PCB congeners in mice, Gage and Holm (1976) found that the 4,4'-; 3,3',4',6'-; 2,3,2',4',6'-; and 2,3,4,2',4',5'-isomers were eliminated most rapidly. These compounds had at least one pair of ortho-meta vicinal carbon atoms unsubstituted, a configuration thought to be important for rapid metabolism and excretion. The most slowly eliminated compounds were 2,4,5,2',4',5'- and 2,3,4,2',4',5'-hexa-isomers.

Felt et al. (1977) examined the elimination of [ $^{14}\text{C}$ ]-2,5,4'-tri-CB in rhesus monkeys. The monkeys were fed 550 mg of the compound in fruit daily for 84 days. On the basis of total excreted and recovered radioactivity, the half-life of 2,5,4'-tri-CB was found to be 4.5 to 4.8 days.

Bleavins et al. (1984) examined the excretion of PCBs in female European ferrets given a single dose of 0.05 mg [ $^{14}\text{C}$ ]-labeled Aroclor 1254 in food. The results showed that urinary excretion accounted for  $\leq 1/10$  of the quantity of PCB that was eliminated in the feces. Excretion of PCBs was highest during the first week following dosing, when 22.1 and 1.8% of the absorbed dose was excreted in the feces and urine, respectively.

#### 4.2.4.3 Dermal

Data concerning the excretion of PCBs by humans or animals following dermal exposure were not located.

#### 4.2.4.4 Parenteral routes

**Human.** No data were located in the available literature.

**Animal.** Injection studies indicate that PCBs can be excreted unmetabolized into the gastrointestinal tract. Yoshimura and Yamamoto (1975) recovered unmodified tetra-CB from the duodenal contents of rats injected intravenously with tetra-CB. Daily excretion for 4 days ranged from 0.5 to 0.8% of the total dose per day. Goto et al. (1974) found that 4.7 to 23.2% of injected PCBs were excreted unchanged into the gastrointestinal tract by 10 days postdosing, with the excretion of a penta-isomer greater than the excretion of di-, tri-, or tetra-isomers.

### 4.3 TOXICITY

Evaluation of the toxicity of Aroclors and other commercial PCB mixtures is complicated by numerous factors, including differences in isomer/congener/mixture composition and toxicity, differences in species susceptibility, quantitatively inconsistent data, and varying degree of contamination with toxic chemicals such as chlorinated dibenzofurans. In addition, there is a lack or paucity of toxicological data for some of the Aroclors (most of the studies were conducted with the higher chlorinated Aroclors), and a paucity of data for the most sensitive species (monkey and mink). Also, it should be recognized that PCBs to which people may be exposed may be very different from the original PCB mixture because of changes in congener and impurity composition resulting from environmental and/or biological transformation. Because of the aforementioned concerns, current data are considered inadequate to differentiate between the toxicity and carcinogenicity of PCB mixtures with any reasonable degree of confidence. Therefore, it is assumed, for the purpose of health effects evaluation, that effects resulting from exposure to a specific Aroclor are representative of effects that may be produced by the other Aroclors. In the following sections, data delineating the threshold region of the most toxic Aroclor for specific end points are presented. Although the relative contribution of the inhalation and dermal routes in occupational exposures is unknown, health effects data for exposed workers are discussed in the inhalation subsections.

#### 4.3.1 Lethality and Decreased Longevity

##### 4.3.1.1 Inhalation

**Human.** Pertinent data were not located in the available literature.

**Animal.** Inhalation LC50s of Aroclor were not located in the available literature. Rozanova (1943) reported that all four rats exposed to Solvol (a European PCB mixture) at concentrations of 10 g/m<sup>3</sup> for 3 h became comatose and died, while 11 similar exposures at 0.5 g/m<sup>3</sup> resulted in only one death. Liver and renal damage was noted along with

congestion in the heart and spleen. Insufficient detail was available to determine how the atmosphere was generated or what methods were used to verify the concentration. Treatment-related mortality was not observed in groups of 9 to 10 rats, 6 to 10 mice, 3 to 4 rabbits, 4 to 6 guinea pigs or 1 cat that were exposed 7 h/day, 5 days/week to vapor concentrations of 8.6 mg/m<sup>3</sup> (0.83 ppm) Aroclor 1242 for 24 days, 5.4 mg/m<sup>3</sup> (0.41 ppm) Aroclor 1254 for 121 days, 6.83 mg/m<sup>3</sup> (0.66 ppm) Aroclor 1242 for 120 days, 1.5 mg/m<sup>3</sup> (0.11 ppm) Aroclor 1254 for 213 days, or 1.9 mg/m<sup>3</sup> (0.18 ppm) Aroclor 1242 for 214 days (Treon et al. 1956). It was necessary to heat the Aroclors to 55 to 138°C to attain the above concentrations, and 8.6 mg/m<sup>3</sup> Aroclor 1242 was "approaching saturation" concentration. These concentrations may be low as the technique used to estimate them was invalidated. Possible contamination by PCDF was not reported.

#### 4.3.1.2 Oral

**Human.** Pertinent data were not located in the available literature.

**Animal.** Acute oral LD<sub>50</sub> values for the PCBs covered by this profile (Aroclors 1254, 1221, 1260, 1232, 1242, and 1248) are presented in Table 4.1. No values for Aroclor 1016 were found in the available literature. The lowest oral LD<sub>50</sub> in rats was 1.01 g/kg for Aroclor 1254 as reported by Garthoff et al. (1981). In mink, the lowest LD<sub>50</sub> was between 0.75 and 1.0 g/kg for Aroclor 1221 as reported by Aulerich and Ringer (1977). As seen from the data of Grant and Phillips (1974) and Linder et al. (1974), immature rats appear to be more sensitive than adult rats. The full range of LD<sub>50</sub> values for all PCBs is greater, with the lowest value of 0.5 g/kg for hexachlorobiphenyl in guinea pigs (McConnell and McKinney 1978) and the highest value of 11.3 g/kg reported for Aroclor 1262 in the rat (Fishbein 1974).

In mice maintained on diets that provided 1,000 ppm Aroclor 1254 for 14 days, 3/5 died of unspecified causes by day 15 (Sanders et al. 1974). All mice treated at 4,000 ppm died within 7 days after the onset of treatment. No deaths occurred in five mice that were similarly treated with 250 ppm.

For intermediate-exposure durations, the LC<sub>50</sub> for Aroclor 1254 fed to mink in the diet for 28 days ranged from 79 to 84 ppm and 47 to 58 ppm after a 7-day withdrawal period (Hornshaw et al. 1986). In mink fed Aroclor 1254 for 9 months, the LC<sub>50</sub> was 6.65 ppm (Ringer et al. 1981). Death generally was due to nonspecific hemorrhagic lesions.

Groups of 24 male rats that were fed diets containing 0, 25, 50, or 100 ppm Aroclor 1254 for 104 to 105 weeks experienced dose-related decreased survival (92, 83, 58, and 46%, respectively) (NCI 1978). The cause of death was not specified, and there was no effect on survival in similarly treated female rats. There was no attempt to identify or quantitate impurities. Decreased survival is not a universal finding in chronic PCB studies, as survival was unchanged or increased in rats treated with 100 ppm of 60% chlorine PCB mixtures (Aroclor 1260 and Clophen A-60) via diet (Norback and Weltman 1985, Schaeffer et al. 1984).

Table 4.1. Acute oral LD<sub>50</sub>s of Aroclors

Aroclor	Species/strain	Sex/age	LD <sub>50</sub> (g/kg)	References
1254	Rat/Wistar	M/30 days	1.3	Grant and Phillips 1974
		F/30 days	1.4	
		M/60 days	1.4	
		F/60 days	1.4	
		M/120 days	2.0	
		F/120 days	2.5	
	Rat/Sherman	M/weanling NR <sup>a</sup> /adult	1.295 4-10	Linder et al. 1974
Rat/Osborne-Mendel	M/adult	1.01 (single dose) 1.53 (5 doses over 2½ weeks) 1.99 (5 doses, 1 day/week)	Garthoff et al. 1981	
	Mink/pastel	NR/NR	4	Aulerich and Ringer 1977
1221	Rat/NR	NR/NR	3.98	Fishbein 1974
	Rat/Sherman	F/NR	4.0	Nelson et al. 1972
	Mink/pastel	NR/NR	>0.75 to <1.0	Aulerich and Ringer 1977
1260	Rat/Sherman	NR/adult	4-10	Linder et al. 1974
		M/weanling	1.315	
1232	Rat/NR	NR/NR	4.47	Fishbein 1974
1242	Rat/Sprague-Dawley	M/adult	4.25	Bruckner et al. 1973
	Rat/NR	NR/NR	8.65	Fishbein 1974
	Mink/pastel	NR/NR	>3	Aulerich and Ringer 1977
1248	Rat/NR	NR/NR	11	Fishbein 1974

<sup>a</sup>NR = not reported.

#### 4.3.1.3 Dermal

**Human.** Pertinent data were not located in the available literature.

**Animal.** Median lethal doses for single application of Aroclors to the skin of rabbits ranged from >1,269 mg/kg for Aroclors 1242 and 1248 in 50% corn oil to <3,169 mg/kg for undiluted Aroclor 1221 as reported by Nelson et al. (1972) and summarized by Fishbein (1974) (Table 4.2).

#### 4.3.2 Systemic/Target Organ Toxicity

##### 4.3.2.1 Liver

**Inhalation, human.** Epidemiological studies and clinical surveys indicate that occupational exposure to Aroclors has produced increases in serum liver-related enzymes, particularly GGTP and SGOT (Ouw et al. 1976; Alvares et al. 1977; Fischbein et al. 1979, 1985; Baker et al. 1980; Smith et al. 1981a,b,c; Brown and Jones 1981; Maroni et al. 1981a; Fischbein 1985; Emmett 1985; Lawton et al. 1985; Drill et al. 1981; Kreiss 1985; Guzelian 1985). These increases show generally inconsistent patterns, may be nonspecific, may be within the normal population range, and have not been shown to be associated with hepatic dysfunction. Alvares et al. (1977) found that the mean half-life of antipyrine disappearance from blood was significantly lower in five workers who were exposed to Aroclor 1016 (10.8 h) than in controls (15.6 h). Asymptomatic hepatomegaly was reported by Maroni et al. (1981a). The subjects of the aforementioned studies were primarily involved in electrical equipment (e.g., capacitors, transformers) manufacturing and repair, and many had measurable and often high serum levels of PCBs.

Monitoring data were reported only in some of the studies and do not adequately characterize exposure levels because of limitations and dissimilarities in sampling methods, durations, and locations; changes in workplace ventilation and Aroclor formulations during the exposure period; wide ranges in concentrations within and between studies without indications of average levels; emphasis on correlating effects with serum PCB concentrations rather than air concentrations of PCBs; and unknown contribution of dermal exposure to total exposure. It appears, however, that air concentrations of Aroclors were often <1 mg/m<sup>3</sup>.

Fischbein et al. (1979, 1985) reported that capacitor manufacturing plant workers who were exposed to various Aroclors (primarily 1242 and 1254) experienced 8-h time-weighted average (TWA) concentrations ranging from 0.007 to 11.0 mg/m<sup>3</sup>. Liver-related indices were evaluated in 280 of the workers; approximately 40% of the workers had been employed for >20 years. Of the workers with plasma levels of higher chlorinated PCBs >75 ppb, 8.3% had abnormally high SGOT levels compared with 1.6% of the workers with plasma levels of higher chlorinated PCBs ≤75 ppb. Of the workers with plasma levels of lower chlorinated PCBs >200 ppb, 10.8% had abnormally high SGOT levels compared with 1.2% of the workers with plasma levels of lower chlorinated PCBs ≤200 ppb. The differences were statistically significant, but remained significant only for females when sexes were analyzed separately. An increased prevalence of abnormal GGTP levels and weak but statistically significant correlations between serum concentrations of PCBs and GGTP were also reported. Greater than

**Table 4.2. Acute dermal LD<sub>50</sub> values of Aroclors in rabbits**

Aroclor	Vehicle	LD <sub>50</sub> (mg/kg)
1221	Undiluted	>2000 <3469
1232	Undiluted	>1260 <2000
1242	Undiluted	>794 <1269
1248	Undiluted	>794 <1269
1260	50% corn oil	>1260 <2000

*Source:* Fishbein 1974.

90% of the values for SGOT and other liver-associated enzymes were within normal laboratory limits and the prevalence of abnormal values was comparable to the general population. Limitations of this study, including broad exposure categories, lack of an unexposed control group, and lack of correction for confounding variables such as alcohol consumption, indicate that the data, while suggestive, should not be interpreted as demonstrating a relationship between SGOT levels and plasma levels of PCBs.

**Inhalation, animal.** Reversible degenerative lesions of the liver were observed in rats, mice, rabbits, cats, and guinea pigs exposed to 1.5 mg/m<sup>3</sup> (0.11 ppm) Aroclor 1254 vapor 7 h/day, 5 days/week for a 213-day period (Treon et al. 1956). Exposure to Aroclor 1242 for 7 h/day, 5 days/week at 1.9 mg/m<sup>3</sup> (0.18 ppm) for 214 days or 8.6 mg/m<sup>3</sup> (0.83 ppm) for 24 days did not produce histological effects in the liver or other viscera. It was necessary to heat the Aroclors to attain the concentrations used in this study.

**Oral, human.** Serum levels of PCBs and GGTP were positively correlated in Triana, Alabama, residents (Kreiss et al. 1981). Consumption of contaminated fish was the only known source of PCB exposure. The population was also exposed to DDT via consumption of fish and the strongest correlations were between serum levels of PCBs and DDT, but the effects of DDT residues on the metabolism or toxicity of PCBs are unknown.

**Oral, animal.** Carter (1985) exposed groups of 12 male weanling Charles River rats to 0, 4, 8 or 16 ppm of Aroclor 1254 in the diet for 4 days. Relative liver weights were significantly increased at >8 ppm, and serum levels of HDL cholesterol were significantly increased at 16 ppm. Histological examinations were not performed.

Litterst et al. (1972) exposed groups of six male Osborne-Mendel rats to Aroclors 1260, 1254, 1248, or 1242 in the diet at concentrations of 0, 0.5, 5.0, or 500 ppm for 4 weeks. Increased microsomal nitroreductase and demethylase activities occurred at ≥0.5 ppm, increased pentobarbital hydroxylation and relative liver weight occurred at ≥50 ppm, and increased liver triglycerides occurred at 500 ppm.

Dietary exposure to 5 or 25 ppm Aroclor 1242 for 2, 4, or 6 months produced increased hepatic microsomal hydroxylase activity and histochemically discernible lipid content of hepatocytes in groups of six male Sprague-Dawley rats (Bruckner et al. 1974). Increased relative liver weight was observed at 25 ppm at 4 and 6 months and at 5 ppm at 4 months.

Frank histological effects in the liver (e.g., fatty degeneration) occurred in rats exposed to ≥20 ppm Aroclor 1254 or 1260 for 28 days (Chu et al. 1977), rats exposed to ≥20 ppm Aroclor 1254 or 1260 for 8 months (Kimbrough et al. 1972), and mice exposed to 37.5 ppm but not 3.75 ppm Aroclor 1254 for 6 months (Koller 1977).

In a study in which 4 male and 18 female rhesus monkeys were fed diets containing Aroclor 1248, Barsotti et al. (1976) conducted autopsies on one female monkey that died after being fed 2.5 ppm of Aroclor 1248 3 days and on one female monkey that died after being fed 5.0 ppm of Aroclor 1248 for 310 days. Hepatic effects in both

monkeys included focal areas of necrosis, enlarged hepatocytes, and lipid droplets. Although only one animal per dose was examined, these effects must be regarded as treatment-related because of the characteristic nature of the hepatic response. Also, similar effects on the liver were observed in an earlier study by Allen (1975) in which the animals received Aroclor 1248 in the diet at levels of 100 and 300 ppm for 2 or 3 months.

Chronic dietary studies were conducted with rats exposed to 25 to 100 ppm Aroclor 1254 for 2 years (NCI 1978, Morgan et al. 1981, Ward 1985), 100 ppm Aroclor 1260 for 16 months followed by 50 ppm for 8 months, and then no treatment for 5 months (Norback and Weltman 1985) or 100 ppm Aroclor 1260 for 21 months (Kimbrough et al. 1975). Treatment-related nonproliferative liver lesions or nonproliferative liver lesions that did not progress to neoplasms after 1 year were not described in these studies.

The effects of chlorination and chemical composition of PCBs with regard to the dose effects relation of liver toxicity after subchronic exposure are indicated by the data of Biocca et al. (1981). In this study, hepatotoxic effects were observed in mice after 5 weeks of maintenance on diets containing 0.3 ppm of 3,4,5-symmetrical hexachlorobiphenyl, while similar effects were observed only after 30 ppm of 2,4,5-symmetrical hexachlorobiphenyl and 100 ppm of 2,4,6-symmetrical hexachlorobiphenyl, and no effects were noted after 300 ppm of 2,3,6-symmetrical hexachlorobiphenyl. Similar dependence of liver toxicity on the chemical composition of the PCB mixture would be anticipated following chronic exposure in mice and other species.

None of the above studies reported possible contamination of the Aroclor with PCDF.

**Dermal, human.** A study of capacitor workers, already discussed under inhalation (Sect. 4.3.2.1: Systemic/Target Organ Toxicity, Liver, Inhalation, human), provided PCB exposure measurements of 48-275  $\mu\text{g}/\text{m}^3$  in workroom air and 2-28  $\mu\text{g}/\text{cm}^2$  of skin surface on the palms of the workers' hands (Maroni et al. 1981a,b). The authors concluded that much of the absorption of PCBs occurred through the skin. Of the 80 exposed workers, 16 had some evidence of liver involvement including asymptomatic hepatomegaly and/or elevated (to slightly above normal range) serum levels of GGPT, SGOT, or SGPT. No control group was included in the study. The findings were considered by the authors to be indicative of hepatic microsomal induction. Drill et al. (1981) concluded that the serum enzyme levels reflected random variations from normal, but did not discuss the finding of hepatomegaly.

**Dermal, animal.** Aroclor 1260 in isopropanol vehicle was applied to the shaved backs of groups of four female New Zealand rabbits daily 5 days/week at a dose of 118 mg/day for 38 days (Vos and Beems 1971) or 120 mg/day for 28 days (Vos and Notenboom-Ram 1972). Histological alterations were produced in the livers, including centrolobular degeneration and liver cell atrophy, focal hyalin degeneration of the cytoplasm of the hepatocyte, enlarged nuclei, and loss of glycogen. Aroclor 1260 used in these experiments was reported to be free of PCDF contamination.

**General discussion.** The liver is the organ most often implicated in the toxicity of Aroclors in animals. Hepatic effects have been observed in numerous studies with exposed rats, mice, guinea pigs, rabbits, dogs, and monkeys, but rats have been tested most extensively. The effects appear to be reversible at low doses (Treon et al. 1956), are similar among species, and include hepatic microsomal enzyme induction, increased serum levels of liver-associated enzymes indicative of possible hepatocellular damage, liver enlargement, fat deposition, and necrosis. Microsomal enzyme induction is the most sensitive indicator of hepatic alterations, but this effect is not necessarily adverse and few studies were designed to define minimum effective doses of Aroclors. The liver enlargement is associated with hepatocyte enlargement and an increase in smooth endoplasmic reticulum and/or increased enzymatic activity. Proliferative lesions in the liver have been attributed to Aroclor treatment (Sect. 4.3.6 on carcinogenicity in this section). The hepatic effects of Aroclors in animals appear to be typical of chlorinated hydrocarbons.

Histologically documented liver damage is a consistent finding among PCB-exposed animals. Studies of Aroclor-exposed workers provide inconsistent but suggestive evidence for subclinical increases in serum enzymes that are indicators of possible liver microsomal enzyme induction or possible hepatocellular damage (e.g., GGPT, SGOT) (EPA 1988a, Kreiss 1985, Drill et al. 1981). Hepatic dysfunction has not been demonstrated in PCB-exposed workers. That hepatic alterations have been inconsistently observed in humans may be related to the fact that many of the studies (particularly the earlier ones) did not account for confounding variables, such as alcohol consumption, exposure to additional chemicals, or previous medical histories, or may be an artifact of the relative insensitivity of the standard biochemical tests of liver damage (e.g., SGOT) as compared with biopsy evaluation (Letz 1983, Drill et al. 1981). Drill et al. (1981) concluded that SGOT and/or GGPT appear to be the most sensitive indicators of PCB exposure in humans, and that changes in liver enzymes may occur at levels below those at which chloracne occur. Abnormal liver function and some hepatomegaly have been documented in Yusho and Yu Cheng patients, but PCDFs, polychlorinated quaterphenyls, and perhaps other contaminants (e.g., chlorinated diphenyl ethers) are significant etiologic factors (Fischbein 1985).

Aroclors are commonly used to induce hepatic enzymes in animal studies with other chemicals. Exposures in these studies are not representative of realistic human exposures, as large doses are usually given by intraperitoneal injection or gavage to obtain maximal enzyme induction. Induction of enzymes by PCBs occurs in both the cytochrome P-450 and P-448 systems, has been observed in humans, and is not restricted to the liver (Letz 1983). Implications of enzyme induction for human health include the possibility of disease secondary to the increased metabolism of endogenous substances (such as hormones) and increased metabolic activation of exogenous substances, possible protective effects secondary to the increased metabolic detoxification of exogenous substances, and the interference with medical therapy due to increased metabolism of administered drugs (Letz 1983).

Safe et al. (1985a) reviewed data concerning the mechanism of PCB induction of liver microsomal enzymes. The activity of individual PCBs depends on their structure. The most active congeners are those substituted at both para and at two or more meta positions and include 3,4,4',5-tetra-, 3,3',4,4'-tetra-, 3,3',4,4',5-penta-, and 3,3',4,4',5,5'-hexachlorobiphenyl. The coplanar PCBs induce rat liver microsomal aryl hydrocarbon hydroxylase and cytochromes P-450a, P-450c, and P-450d, thus resembling 3-methylcholanthrene and 2,3,7,8-TCDD in their mode of microsomal enzyme induction. Mono-ortho- and di-ortho-chloro analogs of coplanar PCBs exhibit a mixed type of enzyme induction similar to Aroclor 1254. These PCBs induce aryl hydrocarbon hydroxylase, dimethylaminoantipyrine, *N*-demethylase, and cytochromes P-450a through P-450e. Results of quantitative structure-activity relationships showed a correlation between aryl hydrocarbon hydroxylase induction activity and binding affinity for the 2,3,7,8-TCDD cytosolic receptor protein, with the order of activity as follows: coplanar PCBs > 3,4,4',5-tetrachlorobiphenyl  $\approx$  mono-ortho coplanar PCBs > di-ortho coplanar PCBs. Support for the receptor-mediated mechanism of action was found when the coplanar and mono-ortho coplanar PCBs were administered to C57BL/6J and DBA/2J mice. C57BL/6J mice contain much higher concentrations of the Ah receptor than do DBA/2J mice. The PCBs induced aryl hydrocarbon hydroxylase in the responsive C57BL/6J mice but not in the unresponsive DBA/2J mice. Although there is general agreement regarding the role of the Ah receptor in microsomal enzyme induction, the role of Ah receptor binding in the toxicity of PCBs and other halogenated aromatic hydrocarbons is unclear.

#### 4.3.2.2 Cutaneous tissues

**Inhalation, human.** Effects such as chloracne, skin rashes, and burning eyes and skin have been associated with occupational exposure to Aroclors (Meigs et al. 1954; Ouw et al. 1976; Fischbein et al. 1979, 1982, 1985; Baker et al. 1980; Smith et al. 1981a,b,c; NIOSH 1977a; EPA 1988a; Drill et al. 1981; Kimbrough 1987a). Monitoring data do not adequately characterize exposure levels for the reasons indicated in Sect. 4.3.2.1 on liver effects in humans after inhalation exposure. Correlations between chloracne and duration of exposure or blood concentrations of PCBs are poor or nonexistent, and the actual incidence of chloracne is unknown but appears to be low. Drill et al. (1981) concluded that individuals with blood PCB levels >200 ppb have an increased risk of chloracne and that chloracne may occur more frequently among workers exposed to PCBs that have been heated and to PCBs that have >54% chlorination. The available evidence, however, cannot be used to conclude that 200 ppb represents a threshold for chloracne. The conclusions of Drill et al. (1981) are based on Kanechlors as well as Aroclor toxicity data. As chloracne is reported frequently among workers who were exposed to Kanechlors, the higher chloracnegenic potential of Kanechlors and heated Aroclors may be related to higher levels of PCDFs and polychlorinated quaterphenyl contaminants (Drill et al. 1981).

Fischbein et al. (1979, 1982) conducted a clinical survey of 289 capacitor manufacturing workers (153 male, 136 female) who were exposed to 0.007-11 mg/m<sup>3</sup> concentrations of various Aroclors; 20% of the workers had been employed for 5-10 years and 39% for >20 years. Sixty-nine (45%)

male and 75 (55%) female workers had a history of dermatological complaints. Physical examination revealed that 59 males (39%) and 48 females (35%) had abnormal dermatological findings. The most prevalent skin abnormalities were erythema, dryness, thickening, and eye abnormalities (conjunctival redness, palpebral hyperpigmentation, and edema); nonadolescent acneform eruptions were observed in 16 individuals [7 males (5%) and 9 females (7%)]. A subgroup of 42 workers (22 males, 20 females) with skin effects that clinically were thought to be related to PCB exposure in particular (e.g., hyperpigmentation, comedones, chloracne) was compared with an unspecified population; a difference was found between the mean plasma concentrations of higher chlorinated PCBs in males with and without skin abnormalities. The difference was statistically significant using a Student's t-test adjusting for unequal variances ( $P = 0.03$ ), but not using the t-test to compare mean log plasma concentrations ( $P = 0.07$ ) or using nonparametric tests. These data suggest an association between dermatologic effects and plasma levels of higher chlorinated PCBs.

Thirty-four workers who were exposed to Aroclor 1242 at concentration between 0.32 and 2.22 mg/m<sup>3</sup> for 5 to 23 years in an electrical plant complained of burning of the eyes, face, and skin; five had eczematous rashes on the hands and legs (Ouw et al. 1976). The Aroclor 1242 was reported to be free of impurities.

**Inhalation, animal.** Pertinent data were not located in the available literature.

**Oral, human.** Pertinent data were not located in the available literature.

**Oral, animal.** Cutaneous effects occurred in rhesus monkeys fed diets that contained Aroclors for subchronic durations (Allen and Norback 1973, Allen et al. 1974a, Allen 1975, Barsotti and Allen 1975, Barsotti et al. 1976, Thomas and Hinsdill 1978, Becker et al. 1979, Allen et al. 1979, McNulty et al. 1980). These include facial (particularly periorbital) edema, purulent discharge from the eyes, chloracne, and alopecia. The effects appear to be reversible and have been produced by diet exposures as low as 2.5 ppm Aroclor 1248 for 1 to 6 months (Barsotti and Allen 1975) and 3 ppm Aroclor 1242 for 6 months (Becker et al. 1979). NOAELs were not identified in the available studies.

In the Barsotti and Allen (1975) study, rhesus monkeys were fed diets containing 2.5 or 5.0 ppm Aroclor 1248 for 1 year. The animals exposed to 2.5 ppm (all females) developed periorbital edema, alopecia, erythema, and acneform lesions of the face and neck within 1 to 2 months. The males treated at 5.0 ppm had only moderate periorbital edema and erythema.

Thomas and Hinsdill (1978) fed 0, 2.5, and 5.0 ppm Aroclor 1248 to adult female rhesus monkeys. All eight monkeys in each Aroclor-treated group developed alopecia, chloracne, and facial edema after 6 months of treatment.

In the Becker et al. (1979) study, six young (7 to 8 months old) monkeys were fed diets containing 0, 3, 10, 30, or 100 ppm Aroclor 1242 (two were fed 10 ppm). Facial changes (palpebral swelling and erythema

but no loss of hair) were evident by the end of the second month at  $\geq 10$  ppm and in the sixth month at 3 ppm; mortality was 4/6 by day 245, including the monkey fed 3 ppm.

Rats exposed to Aroclor 1254 in the diet developed alopecia, facial edema, and exophthalmos after 104 weeks of 50 ppm and 72 weeks of 50 ppm (NCI 1978); these effects did not occur after 104 weeks of 25 ppm.

In a single-dose study, thickening and erythema of the pinna of the ear occurred in mice exposed to 200 ppm of Aroclor 1254 in the diet for 23 weeks (Bell 1983).

All of the above studies did not report possible impurities.

**Dermal, human.** Pertinent data were not located in the available literature.

**Dermal, animal.** Daily application of 118 mg Aroclor 1260 (free of PCDF) in isopropanol vehicle to the shaved backs of four female New Zealand rabbits 5 days/week for 38 days produced thickening of the skin and acneform lesions resulting from hyperplasia and hyperkeratosis of the epidermal and follicular epithelium (Vos and Beems 1971). These results were verified in another similarly designed study (Vos and Notenboom-Ram 1972).

**General discussion.** Relatively small groups of animals were tested in most of the studies, but the cutaneous effects are well characterized. The cutaneous effects in occupationally exposed humans are generally consistent with the animal data, but effect levels cannot be ascertained and the contribution of direct skin exposure or contaminants cannot be evaluated with the information reported in the papers.

#### 4.3.2.3 Immunological effects

**Inhalation, human.** Significant alterations in various globulin fractions have not been observed in Aroclor-exposed workers (Ouw et al. 1976; Smith et al. 1981a,b,c). No difference in the incidence of positive responses was found during skin hypersensitivity testing with mumps and trichophyton in Aroclor-exposed switchgear workers and unexposed workers (Mosley and Emmett 1984). Elevations in total white blood cells associated with decreased polymorphonuclear cells and increased lymphocytes, monocytes, and eosinophils were measured in capacitor workers 1 year before discontinuance of Aroclor use in the operation (Lawton et al. 1985). The findings were difficult to interpret because they were also associated with dichlorodiphenyldichloroethylene (DDE) exposure.

**Inhalation, animal.** Pertinent data were not located in the available literature.

**Oral, human.** Pertinent data were not located in the available literature.

**Oral, animal.** Female guinea pigs maintained on diets that contained 50 ppm of Aroclor 1260 for 6 weeks had significantly lowered tetanus autotoxin titers, circulating leukocytes and lymphocytes, and

thymus atrophy (Vos and van Genderen 1973). Exposure to 10 ppm Aroclor 1260 in the diet for 8 weeks produced splenic atrophy in guinea pigs (Vos and de Roij 1972). NOAELs were not identified in these studies. The Aroclor 1260 used in these studies was reported to be free from PCDF impurities.

Thomas and Hinsdill (1978) exposed groups of 5 to 8 female rhesus monkeys to 0, 2.5, or 5.0 ppm Aroclor 1248 in the diet for 11 months. Significantly lower antibody response to sheep red blood cells occurred at 5.0 ppm. There was no treatment-related effect on antibody response to tetanus toxoid.

Barsotti et al. (1976) also found evidence of an immunological effect in rhesus monkeys fed 2.5 or 5.0 ppm Aroclor 1248 in the diet for 7 months prior to mating and during pregnancy. Monkeys developed shigellosis during and after treatment, indicating an increased susceptibility to infection.

Thomas and Hinsdill (1978) also fed Aroclor 1248 to mice at 100 or 1,000 ppm in the diet for 3 to 5 weeks. The mice had enhanced sensitivity to *Salmonella typhimurium* and endotoxin, indicating lowered resistance to infection.

**Dermal, human.** Pertinent data were not located in the available literature.

**Dermal, animal.** Dermal application of 120 mg/day Aroclor 1260 (free of PCDF impurities) in isopropanol 5 days/week for 4 weeks produced moderate thymic atrophy in rabbits (Vos and Notenboom-Ram 1972). Similar application of 118 mg/day Aroclor 1260 for 38 days produced histological atrophy of the thymus cortex and a reduction in the number of germinal centers in the spleen and lymph nodes in rabbits (Vos and Beems 1971).

**General discussion.** Immunotoxic effects of PCBs in humans have not been clearly demonstrated. Studies in animals, however, have shown effects on the immune system. Immunosuppression was observed in monkeys that received Aroclor 1248 in the diet at concentrations as low as 5.0 ppm (Thomas and Hinsdill 1978). Treatment of rodents with oral or dermal doses of Aroclors, non-Aroclor PCBs, and/or individual PCB congeners that have a different composition than those covered by this profile has also produced effects on the immune system. This is illustrated in the study by Biocca et al. (1981) in which a decrease in thymus weight was observed in mice exposed to 3,4,5-symmetrical hexachlorobiphenyl for 5 weeks in the diet at 10 ppm, compared with similar effects produced at levels of 300 ppm for 2,4,5- or 2,4,6-symmetrical hexachlorobiphenyl or at 167 ppm Aroclor 1242 in the diet of mice in a 6-week study (Loose et al. 1978a,b). These effects include immunosuppression as measured by increased mortality to *Salmonella typhosa* endotoxin and *Plasmodium berghei* in mice given 167 ppm Aroclor 1016 or 1242 in the diet for 6 weeks (Loose et al. 1978a,b), and increased mortality caused by *S. typhimurium* endotoxin in mice that were given 100 or 1,000 ppm Aroclor 1248 in the diet for 5 weeks (Thomas and Hinsdill 1978). PCBs also caused splenic, thymic, and lymph node atrophy in rats (Allen et al. 1975, Allen and Abrahamsom 1973, Parkinson et al. 1983).

Although PCBs appear to be immunosuppressive in animals, the effect of PCBs on immune system function in humans has not been adequately evaluated. Based on animal splenic and lymphoid system histological alterations, Drill et al. (1981) speculated that significant immunosuppression in humans may occur only at high dosages secondary to malnutrition (i.e., via general toxic responses such as decreased food intake, decreased body weight, or decreased body weight gain). From their results in monkeys, Thomas and Hinsdill (1978) concluded that the occasional ingestion of food contaminated with 5 ppm PCBs by humans would probably not result in immunosuppressive effects measured by decreased antibody titers.

Immunotoxicity of PCBs appears to be dependent upon expression of the aromatic hydrocarbon receptor and on the ability of PCBs to bind to the receptor (EPA 1988a). The receptor binding affinity of PCBs is dependent on the molecular conformation that is determined by the chlorine substitution pattern.

#### 4.3.2.4 Thyroid

**Inhalation.** Pertinent data were not located in the available literature.

**Oral, human.** Pertinent data were not located in the available literature.

**Oral, animal.** Rats exposed to Aroclor 1254 for 4 to 12 weeks experienced thyroid alterations that included enlargement, reduced follicular size, follicular cell hyperplasia, and accumulation of colloid droplets and large, abnormally shaped lysosomes in the follicular cells (Collins et al. 1977; Collins and Capen 1980b,c; Kasza et al. 1978). The thyroid alterations resulted in reduced serum thyroxine levels and appear to be reversible after cessation of exposure. None of these studies reported the purity of the Aroclor 1254 sample used.

Collins and Capen (1980b) exposed groups of six male Osborne-Mendel rats to 0, 5, 50, or 500 ppm Aroclor 1254 in the diet for 4 weeks. Histological and ultrastructural effects consistent with those described above occurred at  $\geq 5$  ppm, and reduced serum thyroxine occurred at  $\geq 50$  ppm. A NOAEL for thyroid alterations cannot be discerned from the available studies.

**Dermal.** Pertinent data were not located in the available literature.

**General discussion.** Although effects of Aroclor exposure on the thyroid have been investigated in only a few studies, this gland is an unequivocal target of Aroclor in rats. The lowering of serum thyroxine by Aroclors appears to be the combined result of a direct effect on thyroid follicular cells with an interference in hormone secretion plus an enhanced peripheral metabolism of thyroxine (Collins et al. 1977).

Ultrastructural lesions in thyroid follicular cells and reductions in serum levels of thyroid hormones (thyroxine and triiodothyronine) occurred in neonatal and weanling rats whose dams were fed diets containing 50 or 500 ppm Aroclor 1254 throughout gestation and lactation

(Collins and Capen 1980a). These authors also reported that other studies have found that decreased reproductive performance and interference in growth and development occurred in man and animals that were rendered hypothyroid and that PCBs enhance the peripheral metabolism and excretion of thyroxine-glucuronide in the bile. These findings and the thyroid effects in Aroclor-exposed adult rats summarized previously suggested to Collins and Capen (1980a) that some of the well-documented PCB-related disturbances in reproduction, growth, and development may be related to alterations in thyroid structure and function in the dam, fetus, or neonate.

#### 4.3.2.5 Stomach

Effects on the stomach have been studied only in animals exposed orally. Oral administration of Aroclor 1248 (Allen and Norback 1973; Allen et al. 1974a,b; Allen 1975; Barsotti and Allen 1975) and Aroclor 1242 (Becker et al. 1979) to monkeys produced gastritis, which progressed to hypertrophy and hyperplasia of the gastric mucosa. Related effects include mucous-filled cysts that penetrate the muscularis mucosa. These effects were initiated by exposures as low and/or short as a single gavage dose of 1.5 g/kg of Aroclor 1248 (Allen et al. 1974a), 25 ppm of Aroclor 1248 in the diet for up to 1 year (Barsotti and Allen 1975), and 3 ppm of Aroclor 1242 for 71 days (Becker et al. 1979).

The Aroclor-induced gastric lesions occurred only along the greater curvature of the stomach (not in the cardiac or pyloric regions, which are more usual regions for gastric effects), did not occur in other sections of the gastrointestinal tract, and have not been observed in species other than monkeys (Becker et al. 1979, Drill et al. 1981). These gastric effects may therefore be species specific. Aroclor 1254-induced metaplasia and adenocarcinoma in the glandular stomach of F344 rats have been reported (Morgan et al. 1981) (Sect. 4.3.6 on carcinogenicity in this section). These studies did not report the purity of the Aroclor sample used.

#### 4.3.2.6 Porphyria

**Inhalation, human.** Exposure-related urinary porphyrin excretion, porphyrin-related disease, or cases of porphyria cutaneous tarda have not been reported in several clinical studies of Aroclor-exposed workers (Alvares and Kappas 1979; Fischbein et al. 1979; Smith et al. 1981a,b,c). A clinical study by Colombi et al. (1982), however, reported a marked increase in the excretion of urinary porphyrins by Aroclor-exposed workers whose blood levels of PCBs were at least ten times higher than expected in a population without occupational exposure to PCBs. The relative proportions of the urinary porphyrins did not differ from those in controls, indicating that the increase was due to a generalized increase in porphyrin synthesis by the liver, probably because of induction of liver microsomal enzymes. No evidence of porphyria was seen in these workers, but the investigators pointed out that a similar increase in urinary porphyrin excretion in experimental animals is followed by porphyria if administration of Aroclors continues.

**Inhalation, animal.** Pertinent data were not located in the available literature.

**Oral, human.** Pertinent data were not located in the available literature.

**Oral, animal.** Groups of six male Sprague-Dawley rats were treated with 0, 5, or 25 ppm of Aroclor 1242 (purity not reported) in the diet for 2, 4, or 6 months (Bruckner et al. 1974). Urinary coproporphyrin levels were increased in rats treated at both concentrations.

In rats fed 100 ppm Aroclor 1254 in the diet, Goldstein et al. (1974) found that liver microsomal P-450 concentrations and liver weight were increased maximally by 1 week, but that the onset of porphyria and induction of ALA synthetase was delayed until 2-7 months of treatment. A marked accumulation of uroporphyrins occurred in the liver, and urinary excretion of coproporphyrin and other porphyrins was increased, with the largest increase in uroporphyrins. The uroporphyrins in liver and urine of the treated rats consisted primarily of 8-carboxy- and 7-carboxyporphyrins. The disproportionate increase in hepatic and urinary uroporphyrins could have been due, in part, to a decrease in uroporphyrinogen decarboxylase activity (Goldstein et al. 1974, Hill 1985).

**Dermal, human.** Pertinent data were not located in the available literature.

**Dermal, animal.** Fecal coproporphyrin was elevated in female New Zealand rabbits that received a 120-mg application of Aroclor 1260 to shaved backs 5 days/week for 4 weeks (Vos and Notenboom-Ram 1972). Fecal coproporphyrin and protoporphyrin were increased in rabbits similarly treated with 118 mg/day Aroclor 1260 5 days/week for 36 days (Vos and Beems 1971). The Aroclor 1260 used in these studies was free of PCDF.

**General discussion.** Induction of ALA synthetase (a rate-limiting enzyme in heme synthesis) and inhibition of uroporphyrinogen decarboxylase are the mechanisms of porphyrogenic action of other polyhalogenated aryl hydrocarbons (Colombi et al. 1982, Drill et al. 1981, Hill 1985). It has been suggested that the changes in porphyrin metabolism are triggered by the induction of liver microsomal enzymes (Colombi et al. 1982). The results of Goldstein et al. (1974) in rats fed Aroclor 1254 in the diet suggest that Aroclors may produce porphyria in a similar manner. Although porphyria has not been reported in Aroclor-exposed humans, increased urinary excretion of porphyrins has been observed in one study of occupationally-exposed humans (Colombi et al. 1982), and evidence of induction of hepatic microsomal enzymes has also been observed (Sect. 4.3.2.1 on Systemic/Target Organ Toxicity, Liver). There are no data to indicate that a progression from these alterations to porphyria would occur as a consequence of continued occupational exposure to Aroclors, but such a progression has been demonstrated in orally exposed animals (Goldstein et al. 1974). Drill et al. (1981) raised the possibility that PCBs, via induction of ALA synthetase, might be capable of precipitating an attack of porphyria in patients suffering from acute, intermittent porphyria. Chronic hepatic porphyria and porphyria cutanea tarda are associated with exposure to

other polyhalogenated aryl hydrocarbons, including polybrominated biphenyls and 2,3,7,8-TCDD (Hill 1985).

#### 4.3.2.7 Kidney

The only study that reported effects on the kidneys was Vos and Beems (1971). In this study, Aroclor 1260 in isopropanol vehicle was applied to the shaved backs of New Zealand rabbits for 5 days/week at a dose of 118 mg/day for 38 days. Hydropic degeneration of the convoluted tubules, destruction of tubular epithelial cells, tubular dilation, and proteinaceous casts were observed. No mention of kidney effects was made in the study by Vos and Notenboom-Ram (1972), in which Aroclor 1260 was applied to the shaved backs of rabbits at 120 mg/day, 5 days/week for 28 days.

### 4.3.3 Developmental Toxicity

#### 4.3.3.1 Inhalation

**Human.** Fifty-one infants born to women employed at two capacitor-manufacturing facilities with a history of high exposure to Aroclors 1254, 1242, and/or 1016 had mean birth weights and mean gestational ages that were lower than infants born to women who had worked in low-exposure areas (Taylor et al. 1984). The differences were small (153 g and 6.6 days), and the birth weight difference appears to have resulted from the shortened gestation rather than from a retardation of intrauterine growth. The high-exposure workers were directly exposed to Aroclors during the manufacturing process for at least 1 year prior to birth of the infant; the workers with low exposure were employed in areas where Aroclors were not used directly. The results of this study are considered to be suggestive but inconclusive because the effects were small and confounding factors such as smoking and alcohol consumption, prenatal care, underlying medical conditions, maternal height, and previous history of low birth weight were not considered.

**Animal.** Pertinent data were not located in the available literature.

#### 4.3.3.2 Oral

**Human.** Birth weight, length, head circumference, gestational age, and neonatal behavior were evaluated in 313 newborn infants (Fein 1984, Fein et al. 1984, Jacobson et al. 1984a). Of these infants, 242 were born to mothers who had consumed moderate to large quantities of Lake Michigan fish sometime during their lives, and 71 were born to mothers who did not consume Lake Michigan fish. Mean ( $\pm$  standard deviation) fish consumption and duration of consumption were  $6.7 \pm 5.8$  kg/year and  $15.9 \pm 9.1$  years, respectively; consumption during pregnancy was  $4.1 \pm 4.4$  kg/year. Maternal serum PCB concentrations averaged  $5.5 \pm 3.7$  ng/mL, which reportedly is comparable to those for other midwestern area samples, and umbilical cord serum PCB levels averaged  $2.5 \pm 1.9$  ng/L. Both maternal consumption of fish and levels of PCBs in cord serum were positively correlated with lower birth weight, smaller head circumference, and shorter gestation (Fein et al. 1984). Infants of

mothers who had consumed contaminated fish were, on the average, 190 g lighter, had head circumferences 0.6 cm less, and were born 4.9 days earlier than infants of mothers who had not consumed contaminated fish. Similar values were determined when infants with cord serum levels  $\geq 3$  ng/mL were compared with infants whose cord levels were  $< 3$  ng/mL (the analytical quantification limit) (160 g lighter, 0.6 cm less in head circumference, 8.8 days less in gestational age). Head circumference was significantly smaller in both analyses even after birth weight and gestational age were statistically controlled. Contaminated fish consumption was also positively correlated with impaired autonomic maturity, increased numbers of abnormal reflexes, and decreased range of state (Jacobson et al. 1984b). Range of state is a neurological category that includes peak of excitement, rapidity of buildup, irritability, and lability of state.

Jacobson et al. (1985) studied the effect of intrauterine exposure or exposure through breast milk to PCBs on visual recognition memory and preference for novelty in 123 infants. Measures of exposure included reports by mothers of contaminated fish consumption and analysis of cord serum levels and breast milk levels of PCBs. Reports of fish consumption and cord serum levels were predictors of poor visual recognition memory, while breast milk levels were not. There was a dose-related decrease in fixation to novelty: cord serum levels of 0.2 to 1.1 ng/mL were associated with mean scores of 61%, 1.2 to 2.2 ng/mL with mean scores of 60%, 2.3 to 3.5 ng/mL with scores of 57%, and 3.6 to 7.9 ng/mL with scores of 50%.

Limitations of these studies include lack of analysis for chemicals other than PCBs, failure to report maternal and cord serum PCB levels based on fish consumption, correlation of effects with fish consumption but not cord serum PCB levels, PCB blood levels within the range of the general population, and/or unknown effects of maternal genetic makeup, lifestyle, and acute illness.

Rogan et al. (1986) examined birth weight, head circumference, and the results of behavioral tests in 930 children. At birth, samples of placenta, maternal and cord serum, and milk were collected and analyzed for PCBs. There was no correlation between birth weight or head circumference with PCB levels. Levels of PCBs in milk fat at birth of 3.5 to  $>4$  ppm, but not  $< 3.49$  ppm, were significantly correlated with less muscle tone, decreased activity, and abnormal reflexes. The levels of PCBs to which these infants were exposed were probably as high as those encountered in the general population. Follow-up evaluation of the same children showed no adverse effects on weight or frequency of physician visits for various illnesses (Rogan et al. 1987). Because of confounding exposure to DDE, the effects on neonatal behavior cannot be attributed solely to PCBs.

Although these studies have several limitations, they provide strongly suggestive but not yet conclusive evidence of behavioral effects of PCBs in humans.

**Animal.** Rabbits were exposed to 0, 1.0, or 10.0 mg/kg/day and 12.5, 25.0, or 50 mg/kg/day Aroclor 1254 (purity not reported) by gavage on days 1 to 28 of pregnancy in separate experiments (Villeneuve et al. 1971). Abortions, stillbirths, and maternal deaths occurred at

$\geq 12.5$  mg/kg/day, but there were no treatment-related teratogenic effects at any dose level. It was noted that unpublished data from the same laboratory showed that administration of Aroclor 1221 at doses  $\leq 25$  mg/kg/day was not fetotoxic to rabbits (Villeneuve et al. 1971).

Doses of 0, 6.25, 12.5, 25, 50, or 100 mg/kg/day of Aroclor 1254 were administered by gavage on days 6 to 15 of gestation to rats (Villeneuve et al. 1971). Average pup weights were reduced at 100 mg/kg/day, although total litter weight (average weight times number of fetuses) did not differ from controls. There were no skeletal or visceral abnormalities or effects on conception, resorptions, litter size or number, or average litter weight in any of the treated groups. In other rat studies with Aroclor 1254 (purity not reported), reduced average fetal weight per litter (Spencer 1982) and reduced pup survival and body weight at weaning (Linder et al. 1974) resulted from 100 mg/kg/day gavage exposure on days 6 or 7 to 15 of gestation.

Collins and Capen (1980a) fed diets containing 0, 50, or 500 ppm Aroclor 1254 (purity not reported) to groups of 15 female Osborne-Mendel rats throughout pregnancy and lactation. There was a statistically significant ( $P < 0.001$ ) reduced litter size in the 500-ppm groups compared with controls. Statistically significant decreases in pup body weight were observed at 50 and 500 ppm in 21-day-old pups, but not at 7 or 14 days or at parturition. Ultrastructural lesions in thyroid follicular cells and reduction in serum levels of thyroid hormone (thyroxine and triiodothyronine) occurred in the neonatal and weanling rats at 50 and 500 ppm. Although pups are not usually examined for effects on the thyroid in developmental studies, the observation of thyroid effects in the neonates can be considered a fetotoxic effect because the thyroid is a target organ of Aroclor 1254 toxicity. Assuming that a rat consumes a daily amount of food equal to 5% of its body weight (EPA 1986a), the 50- and 500-ppm levels are equivalent to doses of 2.5 and 25 mg/kg/day, respectively; therefore, 2.5 mg/kg/day is the LOAEL for fetotoxicity in rats.

Haake et al. (1987) reported that treatment of pregnant C57BL/6 mice with Aroclor 1254 by gavage at 244 mg/kg on day 9 of gestation did not result in any fetuses with cleft palate.

Groups of eight female monkeys were maintained on diets containing 0, 0.25, or 1.0 ppm of Aroclor 1016 (free of PCDF) in the diet for approximately 7 months prior to mating and during pregnancy (total duration  $87 \pm 9$  weeks) (Barsotti and Van Miller 1984). Mean birth weight in the 1.0-ppm group was significantly ( $P < 0.01$ ) less than controls, but head circumference and crown-to-rump length were unaffected. All females conceived, carried their infants to term, and delivered viable offspring. More pronounced fetotoxic effects (early abortions or resorption, stillbirths, and/or reduced birth weight), lengthened menstrual cycles, and lowered serum progesterone levels occurred in monkeys exposed to 2.5 or 5.0 ppm Aroclor 1248 (purity not reported) in similarly designed studies (Allen and Barsotti 1976; Allen et al. 1979, 1980).

#### 4.3.3.3 Dermal

Pertinent data were not located in the available literature.

#### 4.3.3.4 General discussion

Comprehensive teratological examinations have not been conducted; however, the above studies and others (EPA 1988a) indicate that Aroclors were not teratogenic in rats and nonhuman primates when tested via the oral route during the critical periods of organogenesis at doses that produce fetotoxicity and/or maternal toxicity. Although fetotoxicity of Aroclors is documented in several species of animals, the possibility that contaminants (e.g., PCDFs) may be responsible for the effects should be recognized.

The reports of reduced birth weight, gestational age, and behavioral effects in infants of mothers with environmental and occupational exposure to PCBs are inconclusive for the reasons indicated in Sects. 4.3.3.1 and 4.3.3.2, but provide suggestive evidence for PCB-related developmental effects in humans. Infants born to mothers who were exposed to Kaneclor PCBs during the Yusho incident had signs of toxicity and delayed development (e.g., abnormal skin pigmentation, ocular discharge, small size), but no developmental abnormalities (EPA 1988a, Miller 1985). These effects did not persist. As discussed earlier in this profile, the Yusho incident was a unique event in which effects may not be related entirely to PCBs given that dibenzofurans were also present.

Higher concentrations of PCBs in breast milk than in cord serum and in suckling animals than in fetuses have led some investigators to assume that postnatal lactation exposure poses a greater threat to infants than intrauterine exposure. Jacobson et al. (1985) indicated that this assumption may be inappropriate because fetuses may be particularly sensitive to toxic insult due to factors such as lack of protective barriers (i.e., blood-brain) and metabolizing capacities that are found postnatally. That intrauterine exposure may be more harmful than postnatal exposure is suggested by the results of the Jacobson et al. (1985) study, which indicated that behavioral effects were correlated more with prenatal exposure (cord serum PCBs) than with exposure via breast milk.

#### 4.3.4 Reproductive Toxicity

Data for reproductive effects in animals were available only for oral exposure.

Groups of 12 female and 4 male mink were maintained on diets that provided 0, 1, 5, or 15 ppm Aroclor 1254 (purity not reported) for 4 months and were mated (Aulerich and Ringer 1977). Dose-related impaired reproduction (reduced number of females whelped and reduced kit/female ratio) occurred at  $\geq 5$  ppm, with total inhibition of reproduction at 15 ppm. These effects were also produced at 2 ppm Aroclor 1254 in a similarly designed single-dose level study; however, these effects did not appear to result from adverse effects on spermatogenesis (Aulerich and Ringer 1977). Complete reproductive failure occurred in mink exposed to  $\geq 5$  ppm Aroclor 1242, and

Aroclor 1016 reduced but did not completely eliminate mink reproduction at 20 ppm (Bleavins et al. 1980). The rat appears less sensitive, with fetal mortality and maternal toxicity reported after daily consumption for 9 weeks of Aroclor 1254 at a level of 6.4 mg/kg/day (Baker et al. 1977). The purity of the Aroclors was not reported.

Rats were exposed to 0, 1, 5, 20, 100, or 500 ppm of Aroclor 1254 (purity not reported) in the diet in one- and two-generation reproduction studies (Linder et al. 1974). Reduced litter sizes occurred in the F1b and F2 generations at  $\geq 20$  ppm.

In longer-term studies (Allen et al. 1979, 1980; Barsotti et al. 1976), monkeys were exposed to Aroclor 1248 in the diet at levels of 2.5 and 5.0 ppm for 18 months. Maternal toxicity that included lengthened menstrual cycles was observed. At the high-dose level, there was nearly complete inhibition of reproduction, while at the low-dose there were early abortions and fetal resorptions, although some live births did occur. Although this indicates that the monkey was very sensitive to the reproductive toxicity of Aroclor 1248, it should be noted that chemical analyses indicated that the PCBs were contaminated with approximately 1.7 ppm of PCDFs, which may have contributed to the observed toxicity.

Reproductive effects resulting from higher oral doses of Aroclor prior to and during gestation include prolonged estrous cycle and decreased sexual receptivity in rats (Brezner et al. 1984), reduced conception rate in mice (Welsch 1985), and reduced litter size in rats (Linder et al. 1974). Lactation exposure produced decreased reproductive capacity in male rats (Sager 1983) and premature vaginal opening and delayed first estrus in female rats (Brezner et al. 1984).

#### 4.3.5 Genotoxicity

##### 4.3.5.1 Human

No data were located in the available literature.

##### 4.3.5.2 Animal

Results of mutagenicity assays with PCBs in in vitro systems are summarized in Table 4.3. Results of studies using PCB mixtures other than Aroclors are included to provide additional information. PCBs gave generally negative results in *Salmonella typhimurium*, with and without metabolic activation.

PCBs gave generally negative results in in vivo assays with rats and mice (Table 4.4). Equivocal results (chromosomal aberrations) were obtained in ring dove (*Streptopelia risoria*) embryos from doves fed Aroclor 1254 at 10 ppm in the diet (Peakall et al. 1972).

Table 4.3. Genotoxicity of PCBs in vitro

End point	Species (test system)	Result with activation/without activation	References
Gene mutation	<i>Salmonella typhimurium</i>	-/-	Schoeny et al. 1979, Schoeny 1982, Heddle and Bruce 1977, Wyndham et al. 1976, Safe 1980, Harbison 1986, Bruce and Heddle 1979
	Chinese hamster V79 cells	-/-	Hattula 1985
Chromosomal aberrations	Human lymphocytes	-	Hoopingarner et al. 1972

Table 4.4. Genotoxicity of PCBs in vivo

End point	Species (test system)	Result <sup>a</sup>	References
Chromosomal aberration	<i>Drosophila melanogaster</i>	-	Nilsson and Ramel 1974
	Ring dove ( <i>Streptopchia risoria</i> )	±	Peakall et al. 1972
	Chicken	-	Blazak and Marcun 1975
	Mouse	-	Watanabe and Sugahara 1981
	Rat	-	Green et al. 1975a Garthoff et al. 1977, Dikshith et al. 1975
Micronucleus test	Mouse	-	Bruce and Heddle 1979
Sperm abnormality	Mouse	-	Bruce and Heddle 1979
Dominant lethal	Mouse	-	Green et al. 1975b, Keplinger et al. 1971, Calandra 1976

<sup>a</sup> - negative  
± equivocal

### 4.3.6 Carcinogenicity

#### 4.3.6.1 Inhalation

**Human.** Two brief reports of a study of 31 research and development employees and 41 refinery plant employees at a New Jersey petrochemical facility (Bahn et al. 1976, 1977; Lawrence 1977) and an update of the same study (NIOSH 1977b) are available. Aroclor 1254 had been used at the plant during a 9-year period ending in the late 1950s. Malignant melanomas were found in 2 of the 31 research and development workers and 1 of the 41 refinery plant workers; the incidence in the research and development workers was significantly ( $P < 0.001$ ) greater than expected. NIOSH (1977b) found that there were 8 cancers in the total study population (5.7 expected). Of these 8 cancers, 3 were melanomas and 2 were pancreatic cancer; these were significantly different from calculated expectations (data not reported). The data from this study should be regarded as inconclusive because PCB exposure was not quantified, exposure to other potential and known carcinogens was not evaluated although believed to be present, the number of cases and the cohort size are small, and the expected cancer rates were based on U.S. population data rather than on local rates.

Davidorf and Knupp (1979) found no relationship between possible PCB exposure and increased annual occurrence of ocular melanoma in Ohio during 1967-1977.

Brown and Jones (1981) conducted a retrospective cohort mortality study of 2,567 workers who had completed at least 3 months of employment during the years 1940-1976 (39,018 total person-years) in two capacitor factories where PCBs were used. Aroclor 1254 was used first, but this changed during the years to Aroclor 1242 and finally to Aroclor 1016. Historical exposure data were not available, but personal TWA PCB (Aroclor 1016) concentrations in 1977 ranged from 24-393  $\text{mg}/\text{m}^3$  at plant 1 and 170-1,260  $\mu\text{g}/\text{m}^3$  at plant 2. Mortality from all causes and all cancers was lower than expected. Excess mortality was noted for liver cancer (3 observed deaths versus 1.07 expected) and rectal cancer (4 observed versus 1.19 expected), but neither excess was statistically significant. There were no deaths due to malignant melanoma.

An unpublished update of the Brown and Jones (1981) study evaluated an additional 7 years of follow-up (Brown, 1986). Mortality from all causes and all cancers was still lower than expected, but a statistically significant ( $P < 0.05$ ) excess risk of cancer of the liver and biliary passages (5 observed versus 1.9 expected) was found. Four of the 5 deaths due to liver cancer occurred in women who were employed in plant 2; female employees at plant 2 contributed 41% of the total person-years to the analysis. The author indicated that the liver cancer can only be associated tentatively with PCB exposure because of the small number of deaths and other limitations of the study.

Gustavsson et al. (1986) performed a cohort study of 142 male Swedish capacitor-manufacturing workers who had been exposed to PCBs for an average of 6.5 years between 1965 and 1978. Airborne PCB levels measured in 1973 were 0.1  $\text{mg}/\text{m}^3$ . It is not clear if this level

represents an average for 1965-1978. Skin contamination had occurred in some of the workers. Seven cancers had occurred in these workers, which was in agreement with national statistics. One person had two rare tumors, a slow-growing mesenchymal tumor and a malignant lymphoma. The authors concluded that this study did not indicate any excess mortality or cancer incidence among PCB workers, but that such effects could not be ruled out because of the small cohort and relatively short follow-up period.

Bertazzi et al. (1987) conducted a retrospective prospective mortality study of 544 male and 1,556 female workers who were engaged in the manufacture of PCB-impregnated capacitors in an Italian plant during 1946-1982. The workers were employed for a minimum of 1 week between 1946-1978 (41,010 person-years total) and examined for the period 1946-1982. PCB mixtures containing 54% chlorine (Aroclor 1254 and Pyralene 1476) were used until 1964; these were progressively replaced by mixtures containing 42% chlorine (Pyralene 3010 and 3011) until 1970, when only Pyralene 3010 and 3011 were used. The maximum quantities of PCBs were used in 1967-1968 and the use of PCBs has been abandoned completely since 1980. Area samples taken in 1954 and 1977 showed air PCB concentrations ranging from 5,200-6,800  $\mu\text{g}/\text{m}^3$  (Aroclor 1254) and 48-275  $\text{mg}/\text{m}^3$  (Pyralene 3010). Measurements of unspecified PCBs on workers' hands in 1977 and 1982 showed concentrations ranging from 0.3-9.2  $\mu\text{g}/\text{cm}^2$  and 0.09-1.5  $\mu\text{g}/\text{cm}^2$ , respectively. Mean blood concentrations determined in 1977 and 1982 from the same 37 workers were 282.8 and 202.8 ppb for 54% chlorine PCBs, respectively, and 142.8 and 42.9 ppb for 42% chlorine PCBs, respectively. Relatively few deaths were recorded by 1982 [30 males (5.5%) and 34 females (2.2%)]. Overall mortality was not significantly different from expected in males when compared with national or local rates but was significantly ( $P < 0.05$ ) higher than expected in females when compared with local rates. Mortality from all cancers was significantly higher than expected in males when compared with both national and local rates (14 observed versus 1.7 national and 2.2 local), and in females when compared with local rates (12 observed versus 5.3 expected). Deaths from gastrointestinal tract cancer were significantly increased in the males when compared with national and local rates, and deaths from hematologic neoplasms were increased in both sexes but only significantly in females when compared with local rates. Clear site-specific risks of cancer cannot be identified because of the small number of cases and limited follow-up.

**Animal.** No data were located in the available literature.

#### 4.3.6.2 Oral

**Human.** Appropriate data were not located in the available literature. Information regarding cancer in people exposed to PCBs during the Yusho incident is discussed in Sect. 4.3.6.4.

**Animal.** Kimbrough et al. (1975) fed groups of 200 female weanling Sherman rats diets containing 0 or 100 ppm Aroclor 1260 (purity not reported). Aroclor treatment was discontinued 6 weeks before the rats were killed at 23 months of age. Mean final body weights and body weight gain were significantly ( $P < 0.001$ ) reduced in the treated group, but

food consumption in the two groups was comparable. Actual PCB intake in the treated rats was 11.6 mg/kg/day during the first week of exposure, 6.1 mg/kg/day at 3 months, and 4.3 mg/kg/day at 20 months. Almost all treated rats (170/184) exhibited a few to multiple tan nodules on the surface of the liver and more on sectioning. Only one control animal had gross abnormalities of the liver. Hepatocellular carcinomas were found in 1/173 (0.58%) controls and 26/184 (14%) treated rats. Neoplastic nodules were found in the livers of 0/173 controls and 144/184 treated rats. The total incidence of neoplastic liver lesions was 1/173 (<1%) in controls and 170/184 (92%) in treated rats.

In a shorter preliminary study, Kimbrough et al. (1972) exposed groups of 10 male and female Sherman rats to 0, 100, 500, or 1,000 ppm Aroclor 1254 (purity not reported) or 1260 in the diet for <1 year. No neoplastic nodules or hepatocellular carcinomas were found.

Norback and Weltman (1985) fed a group of Sprague-Dawley rats (70 per sex) a diet containing Aroclor 1260 (purity not reported) at a concentration of 100 ppm for 16 months, and 50 ppm for an additional 8 months, followed by a control diet for 5 months. A control group consisted of 63 rats per sex. In the treated rats examined after 18 months, 95% of the 47 females and 15% of the 46 males had hepatocellular neoplasms. This indicated a gender-related effect. Among treated females, 43/47 had trabecular carcinomas and/or adenocarcinomas, and another 2 females had neoplastic nodules only. Two of 46 treated males had trabecular carcinomas, and another 5 had neoplastic nodules. Incidences of hepatocellular neoplasms in control rats were 0/32 males and 1/49 females, the one female having a single neoplastic nodule. The progression of hepatocellular lesions was as follows: centrolobular cell hypertrophy at 1 month, foci of cell alteration at 3 months and areas at 6 months, neoplastic nodules at 12 months, trabecular carcinoma at 15 months, and adenocarcinoma at 24 months. The authors noted that while the tumors met morphologic criteria for malignancy, they were relatively unaggressive as they did not metastasize to distant organs or invade blood vessels. Mortality was not affected, probably because of the late appearance and slow growth of the tumors. Both treated and control rats developed cholangioma, cystic cholangioma, and adenofibrosis, but the incidence was greater in the treated group.

EPA (1988a) used the Norback and Weltman (1985) study as the basis for a carcinogenic risk assessment of PCBs using combined incidences of neoplastic nodules and hepatocellular carcinomas. Because this study demonstrated the progression of hepatocellular lesions through neoplastic nodules to carcinomas, it provides justification for using the combined incidences for quantitative risk assessment.

NCI (1978) exposed groups of 24 Fischer 344 rats per sex per dose to 0, 25, 50, or 100 ppm Aroclor 1254 in the diet for 104 to 105 weeks. Mean body weights of mid- and high-dose males and low-dose females were below those of controls from week 10 onward. There was a significant dose-related reduction in survival among treated males. There was a significant dose-related trend in combined incidences of lymphomas and leukemias in males, but incidences in each dose group were not significantly different from matched controls. NCI (1978) concluded that these tumors could not clearly be related to administration of Aroclor

1254. Hepatocellular adenomas and carcinomas were found in treated groups but not controls (males: mid-dose 1/24, high-dose 3/24; females: mid-dose 1/24, high-dose 2/24). Nonneoplastic hyperplastic nodules also occurred at a high incidence in treated animals but not controls. The tumor incidences were not significant, but the hyperplastic nodules appeared to be treatment related. Adenocarcinomas were found in the stomach, jejunum, or cecum of two treated males and two treated females, and a carcinoma was found in one treated male. Although their incidence was not statistically significant, the low historical incidences of these lesions suggest that they might have been treatment related. NCI (1978) concluded that the high incidence of hepatocellular proliferative lesions in male and female rats was related to treatment, but that Aroclor 1254 was not carcinogenic in this bioassay. There was no attempt to identify or quantitate impurities.

Morgan et al. (1981) reexamined the NCI (1978) data with respect to gastric adenocarcinomas. Stomachs from rats used in that study were available for further sectioning and examination. Incidences of focal stomach lesions, mostly metaplasia, were 6, 10, 17, and 35% in rats receiving 0, 25, 50, and 100 ppm, respectively. Adenocarcinomas were found in six treated rats. When compared with incidences of stomach adenocarcinomas in historical controls (1/3,548), the incidence 6/144 was significant at  $P < 0.001$ . The authors commented that adenocarcinoma and intestinal metaplasia appeared to be related and might have the same initiating mechanism. They concluded that Aroclor 1254 led to induction of intestinal metaplasia and probably to induction of adenocarcinoma in the glandular stomachs of F344 rats.

Ward (1985) also reexamined data from the NCI (1978) bioassay. He noted that hepatocellular adenomas, carcinomas, and eosinophilic and vacuolated hepatocellular foci usually occurred only in treated rats. It appeared that eosinophilic hepatocellular foci and tumors arose de novo rather than from naturally occurring basophilic foci. He suggested that Aroclor 1254 induced or initiated these unique lesions rather than promoted the growth of naturally occurring lesions. Ward (1985) also discussed the intestinal metaplasia and adenocarcinomas in treated rats. He noted that the metaplastic lesions were similar to those seen in monkeys, but differed in being focal and singular, while monkey lesions were diffuse. The appearance of the few metaplastic lesions in the stomachs of controls was different from those in treated rats, which resembled precancerous lesions induced by gastric carcinogens. Ward (1985) concluded that the effects of PCBs on the glandular stomach of rats should be studied further.

Kimbrough and Linder (1974) fed groups of 50 male Balb/cJ mice diets containing 0 or 300 ppm Aroclor 1254 (purity not reported) for 11 months or for 6 months followed by a 5-month recovery period. Treated mice had enlarged livers and adenofibrosis, a possible premalignant lesion (EPA 1988a). Incidences of hepatomas were: 0/34 and 0/24 in two control groups, 9/22 in the 11-month exposure group, and 1/24 in the 5-month exposure group. This study provided evidence of the potential hepatocarcinogenicity of PCBs in mice.

Ito et al. (1974) observed hepatocellular carcinomas (5/12 mice) and liver nodules (7/12) in dd mice fed 500 ppm of Kanechlors 500 for

32 weeks. This study provides supporting evidence for the hepatocarcinogenicity of PCB mixtures.

Because PCB mixtures are often contaminated with PCDFs, it is possible that the carcinogenic response of some PCB mixtures is due to or augmented by these contaminants. Schaeffer et al. (1984) fed male Wistar rats diets containing 100 ppm Clophen A-30 (30% chlorines by weight) or Clophen A-60 (60% chlorines by weight) until they died (approximately 800 days). These PCB mixtures were reported to be free of furans. The treated rats displayed better survival than did controls. Hepatocellular carcinomas developed in 61% of the rats fed Clophen A-60. Only 3% of the Clophen A-30 treated rats developed hepatocellular carcinomas, while 89% had preneoplastic lesions. None of controls developed hepatocellular carcinomas. This study demonstrates that PCB mixtures free from contamination with furans elicit a carcinogenic response.

#### 4.3.6.3 Dermal

**Human.** Human exposures to PCBs via both the dermal and inhalation routes are discussed under the inhalation data.

**Animal.** DiGiovanni et al. (1977) reported that Aroclor 1254 (purity not reported) showed weak initiator activity when applied to the skin of CD-1 mice as a single 0.1-mg dose, followed by promotion with the phorbol ester TPA (12-O-tetradecanoylphorbol-13-acetate). Interpretation of this study is confounded by the lack of a control group treated only with TPA; TPA and other phorbol esters have been shown to produce low incidences of skin tumors (Berry et al. 1978, 1979; Van Duuren 1981). Berry et al. (1978, 1979) reported that Aroclor 1254 was not a skin tumor promoter in female CD-1 mice that had been initiated with dimethylbenzanthracene (DMBA), nor did it produce tumors when tested without DMBA initiation at a level of 0.1 mg administered twice weekly.

#### 4.3.6.4 General discussion

The study by Kimbrough et al. (1975) demonstrated the hepatocarcinogenicity of Aroclor 1260 in female Sherman rats. A preliminary experiment using smaller groups of animals of the same sex and strain exposed for <1 year did not result in neoplastic nodules or hepatocellular carcinomas (Kimbrough et al. 1972). These results suggest that hepatocellular carcinomas caused by PCBs can be detected only in long-term experiments at doses low enough to prevent interfering toxicity (EPA 1985a). In addition, because the large long-term experiment only produced a 14% incidence of carcinomas, relatively large numbers of animals must be used to detect a significant increase in tumor incidence. Similarly, the NCI (1978) rat study with group sizes of 24 rats per sex was considered not sensitive enough to identify as significant an increase in tumor incidence of this magnitude (14%). The NCI (1978) study found hepatocellular carcinomas in 2/24 (8%) male rats fed 100 ppm Aroclor 1254. If incidences are expressed as the number of animals with tumor per number of animals at risk, as is more commonly done, the incidence is 2/20 or 10%. The 8 to 10% incidence is not detected as statistically significant with group sizes of 24 rats, nor

would a 14% incidence, as was observed in the Kimbrough et al. (1975) study, be detected as statistically significant. The studies of Aroclor 1260 and Clophen A-60 indicate that liver tumors induced by these 60% chlorine PCB mixtures are relatively unaggressive, nonmetastasizing and not life-shortening, and that incidences of extrahepatic tumors are decreased (Kimbrough et al. 1975, Schaeffer et al. 1984, Young 1985, Norbeck and Weltman 1985). In the studies by Kimbrough et al. (1975), the rats were killed at 23 months of age, a substantial portion of their life span, and apparently, there was no significant difference in mortality between the control and treated group, although the treated rats had very significant increased incidences of liver tumors compared with controls. In the study by Norbeck and Weltman (1985), the treated and control rats were maintained for a total of 29 months. While the treated rats developed highly significant increased incidences of liver tumors compared with controls, there was no effect on mortality. In the study by Schaeffer et al. (1984), the rats were followed until they died; the treated animals, which had increased incidences of liver tumors, actually survived longer than the controls.

EPA (1985a) discussed the difficulties in using data from assays with commercial PCB mixtures for quantitative risk assessment. The composition of these mixtures is highly variable. Different lots of the same Aroclor, while having the same average chlorine content, can differ substantially in content of individual isomers. The metabolic and pharmacokinetic behavior of the pure isomers varies greatly with the degree and position of chlorine substituents. Analysis of an Aroclor 1254 lot indicated a predominance of pentachloro biphenyl isomers, which are relatively rapidly metabolized and excreted. An Aroclor 1260 lot was primarily hexa- and heptachloro isomers, which would be retained in adipose and skin storage depots for long periods. These storage depots might be considered effective removal of carcinogens from the target organs or, conversely, a carcinogen pool capable of mobilization and adding to target organ exposure. Different Aroclors administered at the same dosage could result in completely different tissue-specific exposure levels for the various pure isomers and metabolites. A potency estimate based only on administered dosage is therefore inappropriate. EPA (1985a) concluded that the potency of any commercial PCB mixture is probably higher than any estimate that would be derived by using dietary levels of exposure as a basis for calculation.

EPA (1988b) concluded that the level of carcinogenic evidence in rats and mice for some commercial PCBs (Aroclor 1260, Kanechlor 500, and Aroclor 1254) constitutes a "sufficient" level of carcinogenic evidence for PCBs in animals. The multiple studies with Aroclor 1260 and one study with Clophen A-60 provide sufficient animal cancer evidence, and the studies with Aroclor 1254, Kanechlor 500, and Clophen A-30 provide limited animal cancer evidence. Taken collectively, this evidence, along with an argument for a hypothesis that structure-activity relationship provides a basis for recommending that PCB mixtures of any composition should be regarded as having the potential to be probable human carcinogens, is used to classify PCBs in the EPA weight-of-evidence category Group B2 (EPA 1988b). The EPA (1988b) decision to regard all PCBs as Group B2 compounds has uncertainty since it cannot be verified with present knowledge.

EPA (1985a) selected the Kimbrough et al. (1975) study as the basis for the carcinogenicity risk assessment for PCBs. More recently, the Norback and Weltman (1985) study was used for quantitative risk assessment in EPA (1988a,b), which supersedes the aforementioned assessment. The Norback and Weltman (1985) study was preferred because the strain of rats used (Sprague-Dawley) has a low incidence of spontaneous liver neoplasia, the duration of the study was for the life span of the rats, and there was a sequential progression of liver lesions to hepatocellular carcinomas.

Available epidemiological data do not indicate a consistent tumorigenic effect among people exposed to PCBs. As indicated in Sect. 4.3.6.1, occupational studies (Brown 1986, Bertazzi et al. 1987) suggest possible carcinogenicity of PCBs by the inhalation route. A statistically significant excess risk of liver cancer has been reported in Yusho patients who were studied for a follow-up period of >16 years (Amano et al. 1984, Kuratsune 1986). Because the excess cancer was found in only one prefecture and the victims also consumed PCDFs and polychlorinated quaterphenyls, these findings are considered to be suggestive of a possible carcinogenic effect of PCBs by the oral route. Because of the tentative nature of the inhalation and oral data, EPA (1988b) has concluded that the evidence for carcinogenicity in humans is inadequate but suggestive.

#### 4.4 INTERACTIONS WITH OTHER CHEMICALS

Many of the interactive effects of PCBs with other chemicals are related to the capacity of PCBs for enzyme induction. Therefore, the effects of PCBs on toxicity of other compounds depend on the role of oxidative metabolism in the toxicity of those compounds. Reported effects of PCB pretreatment include increased metabolism and excretion of pentobarbital and decreased pentobarbital sleeping times (Chu et al. 1977, Villeneuve et al. 1972), increased mutagenicity of B(a)P (Hutton et al. 1979), and increased hepatotoxicity of halothane and vinylidene fluoride (Sipes et al. 1978, Conolly et al. 1979).

Increased dietary ascorbic acid may protect against some of the toxic effects of PCBs, such as altered enzyme activity and liver histopathology, perhaps by inhibiting lipid peroxidation (Chakraborty et al. 1978, Kato et al. 1981). The exact mechanism is not known.

PCBs have had mixed effects on tumor development. Aroclor 1254 pretreatment protected mice from lung tumors but increased the number of mice with liver tumors 18 months after administration of *N*-nitrosodimethylamine (Anderson et al. 1983). Pretreatment with Aroclor 1254 gave slight protection against skin tumor development in mice initiated with 7,12-dimethylbenz(a)anthracene and promoted with TPA (Berry et al. 1979). Makiura et al. (1974) reported that Kanechlor 500 inhibited hepatocarcinogenicity of 3'-methyl-4-dimethylaminoazobenzene, *N*-2-fluorenylacetamide, and *N*-nitrosodiethylamine when administered orally to rats. Nagasaki et al. (1975) found that Kanechlor 400 and 500 enhanced the hepatocarcinogenicity of  $\alpha$ -BHC in mice. PCBs promoted the development of enzyme-altered foci or hyperplastic nodules following treatment with nitrosamines (Oesterle and Deml 1983, Pereira et al. 1982) or *N*-2-fluorenylacetamide (Tatematsu et al. 1979).

Birnbaum et al. (1985) found that 2,3,3',4,4',5-hexachlorobiphenyl, but not 2,2',4,4',5,5'-hexachlorobiphenyl, when coadministered with 2,3,7,8-TCDD to mice during gestation resulted in a dose-related enhancement of the TCDD-induced hydronephrosis in mouse fetuses, but 2,3,3',4,4',5-hexachlorobiphenyl alone caused hydronephrosis in the mouse fetuses. 2,2',4,4',5,5'-Hexachlorobiphenyl did not induce hydronephrosis.

Haake et al. (1987) found that Aroclor 1254 antagonized the teratogenicity of 2,3,7,8-TCDD in mice. In this study, treatment of pregnant mice by gavage with Aroclor 1254 at 244 mg/kg on day 9 of gestation followed by 2,3,7,8-TCDD at 20 mg/kg on day 10 resulted in an 8.2% incidence of cleft palate. Treatment with 2,3,7,8-TCDD alone resulted in a 62% incidence of cleft palate. Aroclor 1254 alone was not teratogenic.

Bannister et al. (1987) found that Aroclor 1254 partially antagonized the 2,3,7,8-TCDD-induced microsomal enzyme induction and immunotoxicity in mice.

## 5. MANUFACTURE, IMPORT, USE, AND DISPOSAL

### 5.1 OVERVIEW

PCBs are no longer produced or used in the United States; however, many of the transformers and capacitors which were produced with PCBs, and contain PCBs, are still in service. Therefore, these products constitute a potential source of exposure to the environment and to humans. Disposal of PCB materials is controlled by federal regulations.

### 5.2 PRODUCTION

PCBs have been commercially produced in the United States since 1929. Annual U.S. production of PCBs peaked in 1970 when 85 million pounds were produced. It was estimated that approximately 1,000 million pounds of PCBs had been sold in North America by 1970. Manufacture of PCBs (Aroclors) in the United States was terminated in October 1977 because these products accumulated and persisted in the environment and because of their toxic effects. Monsanto, the sole U.S. manufacturer at that time, had been producing Aroclors 1016, 1221, 1242, and 1254. In 1974, Monsanto produced just over 40 million pounds of the Aroclor mixtures. Production had been approximately 40 million pounds annually since 1971. Monsanto produced PCB Aroclor products at a facility in Sauget, Illinois, but production was stopped in October 1977. Of the total PCBs sold in the United States since 1970, over 98% were Aroclor 1260, 1254, 1248, 1242, 1232, 1221, and 1016 and less than 2% were Aroclor 1268 and Aroclor 1262. Therefore, 98% of PCBs sold in the United States since 1970 have been covered in this document (IARC 1978, Hatton 1979, Durfee 1976, EPA 1976).

The Aroclors were prepared industrially by the chlorination of biphenyl with anhydrous chlorine in the presence of a catalyst such as iron filings or ferric chloride. The degree of chlorination, which determined which Aroclor was produced, was controlled by the anhydrous chlorine contact time in the reactor (EPA 1976).

### 5.3 IMPORT

Imports of PCBs through principal U.S. custom districts in recent years have been reported as follows (USITC 1978, 1979, 1980, 1982):

Year	Import volume (lb)
1981	11,000
1979	357,147
1978	483,074
1977	280,867

No data were located to indicate that PCBs have been imported after 1981.

Section 6(e)(3)(A) of TSCA (Pub. L. 94-469, 90 stat. 2003, 15U.S.C.2601 et seq) prohibits all manufacture and importation of PCBs as of January 1, 1979. As of January 2, 1979, EPA announced that companies that had filed petitions for exemptions from the PCB manufacturing/importation ban could continue the manufacturing or importation activity until EPA has acted on the application petition (EPA 1979).

#### 5.4 USES

A thorough review of PCB use in the United States can be found in EPA (1976). By 1974, all U.S. use of PCBs was in closed systems for the production of capacitors and transformers. As of 1976, 70% of Monsanto's domestic sales of Aroclors was used in capacitor production and 30% in transformer production. Aroclors are no longer used in the production of capacitors and transformers; however, many of the devices manufactured with Aroclors are still in service today. The life expectancy of transformers containing PCBs is >30 years, and the life expectancy of capacitors can range from 10 to >20 years, depending upon electrical application. PCBs were used in capacitors and transformers because of their excellent dielectric properties and fire resistance. Production of a large capacitor involved filling the capacitor with the Aroclor oil (typically over 2 to 3 lb of PCB) through a small hole and then sealing. Transformers were similarly filled, but may contain many times the amount of PCBs, depending on size. As of 1976, only 5% of the transformers produced in the United States were filled with PCBs, but 95% of the capacitors used PCBs (Durfee 1976). As of 1981, an estimated 131,200 PCB transformers were still in service in the United States, representing approximately 1% of all operational transformers (Orris et al. 1986). PCBs (Aroclors 1260 and 1262) have been used as a slide-mounting medium for microscopes (IARC 1978) and are still used occasionally for this purpose since this use has been exempted from federal use restrictions.

#### 5.5 DISPOSAL

On April 18, 1978, regulations became effective in the United States concerning the storage and disposal of PCBs. These regulations specified incineration of the waste or contaminated material as the only acceptable method of PCB disposal unless, if this method is not possible, clearance is obtained from the EPA to dispose of the materials in another way. In March 1983, the EPA issued a procedural amendment to the PCB rule to enable new disposal technologies to receive approval on a nationwide basis. At present, EPA's PCB disposal rules typically require that various types of PCBs and PCB materials be disposed of in chemical-waste landfills or destroyed in high-temperature incinerators or high-efficiency boilers. The disposal rules are published in the July 1984 Code of Federal Regulations, 40CFR, Part 761 (Kokoszka and Flood 1985, Hatton 1979).

## 6. ENVIRONMENTAL FATE

### 6.1 OVERVIEW

At present, the major source of PCB exposure in the general environment appears to be environmental cycling of PCBs previously introduced into the environment. This cycling process involves volatilization from ground surfaces into the atmosphere with subsequent removal from the atmosphere via wet/dry deposition and then revolatilization. The environmental persistence of PCBs generally increases with an increase in the degree of chlorination of the congener. The Aroclors with a high degree of chlorination (1248, 1254, and 1260) are resistant to biodegradation and appear to be degraded very slowly in the environment. The chemical composition of the original commercial Aroclor mixtures which were released to the environment has changed over time since the individual congeners degrade and partition at different rates. Reviews of the environmental fate processes of PCBs are available (EPA 1988a, Leifer et al. 1983, Callahan et al. 1979).

### 6.2 RELEASES TO THE ENVIRONMENT

Since the Aroclors are no longer produced or used in the production of new products in the United States, industrial effluent discharges from production sources no longer occur. Current sources of PCB release to the environment include releases from landfills containing transformers, capacitors, and other PCB wastes; waste incineration of PCB materials; spills; and improper (or illegal) disposal to open areas (Weant and McCormick 1984, Murphy et al. 1985). In addition, explosions or overheating of transformers containing PCBs may release significant amounts of these materials into the local environment.

PCB emissions from landfills and incinerator stacks have been monitored (Murphy et al. 1985). Landfills are expected to be a continuous source of PCB release into the atmosphere because methane and carbon dioxide, which are generated from anaerobic degradation of organic waste, are released and expected to carry PCBs and all other volatile compounds with them. Incinerator stacks are expected to be a source of PCBs, which would volatilize in the upper levels of the incinerator before combustion occurred, because PCBs are resistant to oxidation but reasonably volatile. This monitoring has indicated that the amount of PCBs released from these sources (10-100 kg/year from landfills and 0.25 kg/stack/year for incinerators) may not be significant when compared to the quantities of PCBs estimated to cycle annually through the atmosphere over the U.S. (900,000 kg/year).

Atmospheric fallout and washout have been identified as nonpoint sources of PCB exposure to the environment (Kleinert 1976, Weant and McCormick 1984, Swackhamer and Armstrong 1986, Larsson 1985). Although

additional research is required for a definitive answer, evidence suggests that the current major source of PCB release to the environment is an environmental cycling process (Swackhamer and Armstrong 1986, Larsson 1985, Murphy et al. 1985). This cycling process involves volatilization of PCBs from bodies of water or from soil surfaces into the atmosphere. Once in the atmosphere, the PCBs are returned to earth via washout/fallout where the cycle is subsequently repeated with revolatilization. Since the volatilization and degradation rates of PCBs vary among the congeners present, this cycling process causes an alteration of the PCB ratio in water and air relative to the original source.

### 6.3 ENVIRONMENTAL FATE

#### 6.3.1 Transport and Partitioning

In water, adsorption to sediments or other organic matter is a major fate process for the PCBs (EPA 1988a, Callahan et al. 1979). Experimental and monitoring data have shown that PCB concentrations are higher in sediment and suspended matter than in the associated water column. Based on their water solubilities and octanol-water partition coefficients, the lower chlorinated components of the Aroclors will sorb less strongly than the higher chlorinated isomers. Although adsorption can immobilize PCBs for relatively long periods of time in the aquatic environment, resolution into the water column has been shown to occur on an environmental level (Swackhamer and Armstrong 1986, Baker et al. 1985). The substantial quantities of PCBs contained in aquatic sediments can therefore act as an environmental sink for environmental redistribution of PCBs. Environmental redistribution from aquatic sediments should be most important for the PCBs contained in the top layers of the sedimentary deposit. PCBs reaching the lower layers of sedimentary deposits may be effectively sequestered from environmental redistribution.

Volatilization is also an important environmental fate process for the PCBs that exist in natural water in the dissolved state. The values of the estimated Henry's law constants for the Aroclors (although they occur as a mixture in natural water) (see Table 3.2) are indicative of significant volatilization from environmental waters (Lyman et al. 1982). A study conducted on Lake Michigan has indicated that volatilization may be the major removal mechanism of PCBs from lakes (Swackhamer and Armstrong 1986). Strong PCB adsorption to sediment, however, significantly decreases the rate of volatilization, with the higher chlorinated Aroclors having longer volatilization half-lives than the lower chlorinated Aroclors (EPA 1985a). However, eventual resolution of PCBs from sediment into the water column can then result in volatilization.

The low water solubility, high octanol-water partition coefficients (see Chapter 3) of the PCBs and demonstrated strong adsorption of PCBs to soils and sediment (EPA 1988a, Callahan et al. 1979, Sklarew and Girvin 1987) indicate that significant leaching should not occur in soil under most conditions. The tendency of the lower chlorinated PCBs to leach will be greater than the highly chlorinated PCBs. In the presence

of organic solvents, PCBs can leach significantly in soil (Griffin and Chou 1981).

Organics having vapor pressures  $>10^{-4}$  mm Hg should exist almost entirely in the vapor phase in the atmosphere, while organics having vapor pressures  $<10^{-8}$  mm Hg should exist almost entirely in the particulate phase (Eisenreich et al. 1981). The vapor pressures of the Aroclors (see Table 3.2) indicate that they should therefore exist primarily in the vapor phase in the atmosphere. Monitoring data have shown that between 87 and 100% of the PCBs in air are operationally in the vapor phase (Eisenreich et al. 1981). The tendency of PCBs to adsorb to particulates will increase as the degree of chlorination increases.

PCBs in the atmosphere are physically removed by wet and dry deposition (Eisenreich et al. 1981). Dry deposition occurs only for the PCBs associated in the particulate phase. The PCB concentration of rain anywhere in the world may typically range between 1 and 250 ng/L (Eisenreich et al. 1981), which is an indication of the importance of wet deposition.

### 6.3.2 Transformation and Degradation

The ability of PCBs to be degraded or transformed in the environment is dependent upon the degree of chlorination of the biphenyl molecule (EPA 1988a, Leifer et al. 1983, Callahan et al. 1979). In general, the persistence of PCB congeners increases as the degree of chlorination increases.

In the atmosphere, the vapor phase reaction of PCBs with hydroxyl radicals (which are photochemically formed by sunlight) may be the dominant transformation process. The estimated half-lives for this reaction in a typical atmosphere with various PCB isomers are as follows (EPA 1987b): monochlorobiphenyl, 12.9 days; dichlorobiphenyl, 27.8 days; trichlorobiphenyl, 1.43 months; tetrachlorobiphenyl, 3.1 months; pentachlorobiphenyl, 4.75 months; hexachlorobiphenyl, 10.3 months; and heptachlorobiphenyl, 1.31 years.

In the aquatic environment, transformation processes such as hydrolysis and oxidation do not significantly degrade PCBs (Mabey et al. 1981; Callahan et al. 1979). Photolysis appears to be the only viable chemical degradation process in water; however, sufficient experimental data are not available to determine its relative rate or importance in the environment (Leifer et al. 1983).

Reviews of the biodegradability of PCBs are available (EPA 1988a, Leifer et al. 1983). Biodegradation rates depend on a number of factors, such as the amount of chlorination, concentration, type of microbial population, available nutrients, and temperature; therefore, the rates are highly variable. However, the results generally show that mono-, di-, and trichlorinated biphenyls (major components in Aroclors 1221 and 1232) biodegrade relatively rapidly; tetrachlorinated biphenyls (major components in Aroclors 1016 and 1242) biodegrade slowly; and the higher chlorinated biphenyls (major components in 1248, 1254, and 1260) are resistant to biodegradation. In addition to the degree of chlorination, chlorine positions on the biphenyl ring appear to be important in determining the biodegradation rate. For example, PCBs containing all of

the chlorines on one ring are degraded faster than PCBs containing the chlorines distributed between both rings, and PCBs containing chlorines in the ortho positions are more resistant (Leifer et al. 1983). A study of subsurface aquatic sediments has shown that PCBs containing chlorines in the para positions are preferentially biodegraded as compared to other ring positions (Brown et al. 1987). This study of subsurface sediments, primarily from spill sites, has also shown that the higher chlorinated congeners are biotransformed by a reductive dechlorination to lower chlorinated PCBs which are biodegradable by aerobic processes. This is important since PCBs in soil systems or in aquatic sediments have not been shown to degrade by processes other than biodegradation. Therefore, biodegradation is probably the ultimate degradation process in soils and in sediments.

A summary of experimentally determined bioconcentration factors of various Aroclors (1016, 1248, 1254, and 1260) in aquatic species (fish, shrimp, oyster) has found Aroclor bioconcentration factors ranging from 26,000 to 660,000 (Leifer et al. 1983).

## 7. POTENTIAL FOR HUMAN EXPOSURE

### 7.1 OVERVIEW

PCBs partition significantly from water to aquatic organisms such as fish and can result in extremely high bioconcentration factors. Consumption of contaminated fish then results in human exposure to PCBs. Consumption of fish has been identified as a primary route of human exposure to PCBs. The general population is also exposed, on a continual basis, to PCB levels in the breathable air. PCBs have been found in at least 216 of 1,177 sites on the National Priorities List (View 1989). A review of environmental PCB monitoring data is available (EPA 1988a).

### 7.2 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

#### 7.2.1 Air

Eisenreich et al. (1981) completed the following list of typical atmospheric concentrations of PCBs:

Location	Concentration range (ng/m <sup>3</sup> )	Mean
Urban	0.5 to 30	5-10
Rural	0.1 to 2	0.8
Great Lakes	0.4 to 3	1
Marine	0.05 to 2	0.5
Remote	0.02 to 0.5	0.1

These values were derived from a large volume of monitoring data reported in the literature.

Ambient atmospheric PCB concentrations of 7.1 and 4.4 ng/m<sup>3</sup> were detected in Boston, Massachusetts, and Columbia, South Carolina, respectively, during the summer of 1978 (Bidleman 1981). These concentrations are a composite for Aroclors 1016, 1242, and 1254. Analysis of ambient air in Antarctica between 1981 and 1982 found PCB levels of 0.02 to 0.18 ng/m<sup>3</sup> (Tanabe et al. 1983).

The average PCB concentration (Aroclors 1242 and 1260) emitted from gas vents at a hazardous waste landfill in North Carolina was found to be 0.126 mg/m<sup>3</sup> (Lewis et al. 1985). PCB concentrations of 0.01 to 1.5 ppm were detected in the fly ash from five municipal incinerators operating under different technological and working conditions (Morselli et al. 1985). Stack effluents from several midwest municipal refuse and sewage incinerators contained PCB levels of 300 to 3,000 ng/m<sup>3</sup> (Murphy et al. 1985). The total PCB concentration measured in the flue gas effluent from a municipal waste incinerator in Ohio was 260 ng/m<sup>3</sup> (Tiernan et al. 1983). PCBs were detected in effluents from combustion

of coal and refuse at Ames, Iowa, at levels of 2 to 10 ng/m<sup>3</sup> (EPA 1988a).

The average adult male inhales approximately 20 m<sup>3</sup> of air per day. Assuming the breathable outdoor air at a typical urban location contains an average PCB concentration of 5 ng/m<sup>3</sup>, the average daily intake via inhalation would be 100 ng. This estimate pertains to background levels of PCBs in outdoor air. As reported in Sect. 7.4 (populations at high risk), PCB levels in certain indoor air may be an order of magnitude higher than in outdoor air.

### 7.2.2 Water

The concentration of PCBs in the open waters of the oceans can be an indication of the environmental background level in water. Concentrations reported for various seawaters include 0.04 to 0.59 ng/L in the north Pacific, 0.035 to 0.069 ng/L in the Antarctic, and 0.02 to 0.20 ng/L in the north Atlantic (Tanabe et al. 1983, 1984; Giam et al. 1978). PCB concentrations of 0.3 to 3 ng/L, which are higher than the seawater levels reported above, have been detected in seawater from the North Sea; however, the seawaters sampled were receiving an anthropogenic influence (Boon and Duinker 1986).

Mean PCB concentrations of 0.63 to 3.3 ng/L were detected in the waters of western Lake Superior during 1978 to 1983 monitoring (Baker et al. 1985). Mean levels of 3.0 to 9.0 ng/L (1974 to 1976) and 0.49 to 17.15 ng/L (1979 to 1981) were found in the water columns of Lake Michigan and Lake Huron, respectively (Rodgers and Swain 1983). Analysis of water from eight sites in Galveston Bay resulted in an average PCB level of 3.1 ng/L between 1978 and 1979 (Murray et al. 1981). Thirty-two of 163 wells monitored in industrialized areas of New Jersey were found to contain PCB levels ranging from 60 to 1,270 ng/L (EPA 1988a). Mean PCB levels of 25 to 38 ng/L were detected in waters collected from 11 agricultural watersheds in Ontario during 1975 to 1977 (Frank et al. 1982). A discussion of a number of PCB monitoring studies conducted on the Hudson River can be found in EPA (1988a).

Although PCBs are widespread in the aquatic environment, their low solubility generally prevents them from reaching high concentrations in drinking water supplies (EPA 1980a). The National Organic Monitoring Survey (NOMS) was conducted by the EPA to determine the frequency of occurrence of specific organic chemicals (including PCBs) in finished water supplies of 113 cities nationwide (EPA 1988a). Data from the three phases (referred to as NOMS I, II, and III) of the study were collected between March 1975 and January 1977. PCBs were not found in groundwater supplies sampled in NOMS I (minimum quantifiable limit of 0.12 ppb). Only a single finished groundwater sample in each of NOMS I and II contained detectable levels of PCBs; the concentration of each was reported to be 0.1 ppb (detection limits of 0.1 to 0.2 ppb). PCBs were detected in two finished surface water supplies in each of NOMS I and II and in one surface water in NOMS III; the concentrations of the five positive samples ranged from 0.1 to 1.4 ppb. A total mean PCB level of 0.12 to 0.8 ppb was found in tap water from the Waterford Water Co. (Hudson River source) in 1976 and 1977 (EPA 1988a, Kim and Stone n.d.).

### 7.2.3 Soil

An analysis of 99 soil samples from rural and urban sites throughout Great Britain was conducted to determine background levels of PCBs in British soils (Creaser and Fernandes 1986). PCBs were identified in all samples within the range of 2.3 to 444 ppb ( $\mu\text{g}/\text{kg}$ ). The mean and median values found for all samples were 22.8 and 7.2 ppb, respectively. PCB levels ranging from 4.5 to 47.7  $\mu\text{g}/\text{kg}$  have been detected in soil samples collected in the vicinity of incineration facilities in South Wales and Scotland during 1984 to 1985 (Edujee et al. 1985, 1986). An analysis of Japanese soils detected PCB levels as high as 100  $\mu\text{g}/\text{kg}$ ; however, 40% of the samples had levels  $<10$   $\mu\text{g}/\text{kg}$  (Creaser and Fernandes 1986).

PCB concentrations ranging from  $<1$  to 33 ppb have been detected in the soils of the Everglades National Forest in Florida (Requejo et al. 1979), which is consistent with the monitoring data from Great Britain. Carey et al. (1979a) analyzed soils from 37 states in 1972 as part of the National Soils Monitoring Program and found PCB in only 2 of 1,483 soil samples; however, the analytical technique used had a minimum detectable limit of only 0.05 to 0.1 ppm, which was not low enough to detect the mean and median levels reported in Great Britain. Carey et al. (1979b) used the same analytical technique to analyze soils from five U.S. urban areas (43-156 samples per site) in 1971; positive detections were reported for three areas with PCB levels ranging from 0.02 to 11.94 ppm. The highest level (11.94 ppm) was detected in 1 of 55 samples from Gadsden Alabama.

PCB levels of 0.098 to 0.54 mg/kg have been detected in the sediments from four remote high-altitude lakes in the Rocky Mountain National Park (Heit et al. 1984), which indicates levels of PCBs that can accumulate in sediments from natural deposition. Sediment core samples from the Milwaukee harbor, which has received industrial effluents of PCBs, have been found to contain levels of 1.03 to 13.4 mg/kg (Christensen and Lo 1986). Analysis of sediments from 13 selected streams in the Potomac River Basin found a maximum PCB level of 1.2 mg/kg in one stream (Feltz 1980). In seven of the streams, zero or trace amounts of PCBs were detected, but the rest contained 10-80  $\mu\text{g}/\text{kg}$ . Upper sediment layers from the Hudson River and New York Harbor in 1977 contained Aroclor 1254 levels of 0.56 to 1.95 ppm and Aroclor 1242 levels of 3.95 to 33.3 ppm (Bopp et al. 1982). Analysis of surficial sediments from the Great Lakes and various associated waters found Aroclor 1254 levels of 2.5 to 251.7 ng/g, with the higher levels detected in Lake Erie (Thomas and Frank 1981). An average Aroclor 1260 concentration of 120 ng/g has been detected in sediment samples from eight sites along the coast of Maine (Ray et al. 1983).

### 7.2.4 Other

#### 7.2.4.1 Foodstuffs

Table 7.1 lists the amounts of PCBs detected in raw domestic agricultural commodities during fiscal years 1970 to 1976. These commodities were analyzed as part of federal monitoring programs conducted by the U.S. Food and Drug Administration (FDA) and the

**Table 7.1. Aroclor residues in raw domestic agricultural commodities for fiscal years 1970–1976**

Commodity	Number of samples analyzed	Percent with positive detections	Average concentration (ppm) <sup>a</sup>
Fish	2,901	46.0	0.892
Shellfish	291	18.2	0.056
Eggs	2,303	9.6	0.072
Red meat <sup>b</sup>	15,200	0.4	0.008
Poultry	11,340	0.6	0.006
Fluid milk	4,638	4.1	0.067
Cheese	784	0.9	0.011

<sup>a</sup>Average fall samples, both positive and negative.

<sup>b</sup>Fiscal years 1973–1976.

Source: Duggan et al. 1983.

U.S. Department of Agriculture. It appears from Table 7.1 that fish are the primary foodstuff containing environmental background levels of PCBs; additional fish monitoring data are cited below. The contamination of fish is a consequence of the contamination of the aquatic environment and resulting bioconcentration (EPA 1980a).

Since the early 1960s, the FDA has conducted the Total Diet Studies, which have also been known as the Market Basket surveys. These studies, conducted on an annual basis, analyze ready-to-eat foods collected in markets from a number of cities nationwide to determine the intake of selected contaminants in the American diet. Table 7.2 presents the recent results of the Total Diet Studies with respect to PCBs. Since the mid-1970s, individual diets for adult males (19 years old), infants, and toddlers have been analyzed. Assuming that the average adult male weighs 70 kg and that the estimated dietary intake of PCBs is approximately 0.008  $\mu\text{g}/\text{kg}/\text{day}$  (average of the three most recent figures reported in Table 7.2), the average daily intake via diet would be 0.56  $\mu\text{g}$  (560 ng). This estimate indicates that consumption of food may be a major source of PCB exposure in humans; however, the source of the PCBs in food may be significant. In the recent years of the Total Diet Study, the primary source of PCBs in the diet has been in the food category meat-fish-poultry (Gartrell et al. 1986a, 1985a,b). FDA chemists have found that the source of the PCBs in the meat-fish-poultry composite is almost always due to the fish component (Jelinek and Corneliussen 1976). This suggests that persons consuming less than the average amounts of fish will be exposed to lower quantities of PCBs.

#### 7.2.4.2 Fish and precipitation

The U.S. Fish and Wildlife Service has analyzed whole fish samples collected nationwide for PCB residues as part of the National Pesticide Monitoring Program (Schmitt et al. 1985). Between 1980 and 1981, 315 fish were collected from 107 stations nationwide. PCB residues were detected in 94% of all fish, with the geometric mean concentration of all Aroclors (wet weight) found to be 0.53  $\mu\text{g}/\text{g}$ . This concentration is lower than previous monitoring in 1976 to 1977 and 1978 to 1979, which found concentrations of 0.88 and 0.85  $\mu\text{g}/\text{g}$ , respectively. It should be noted that these fish analyses pertain to whole fish samples, which are composites of both the edible and nonedible portions of the fish. Therefore, the concentrations reported may not necessarily reflect the actual human exposure that will occur from oral consumption. Composite fish samples taken from major tributaries and embayments of Lake Superior and Lake Huron in 1983 contained PCB levels of 600 to 72,000 ng/g on a lipid basis (Jaffe et al. 1985). Analysis of 62 samples of commercial fish (primarily from Lake Ontario) collected in 1980 found levels of 0.11 to 4.90 ppm (Ryan et al. 1984).

Based on available monitoring data from the literature, the following PCB ranges (in ng/L) in rainwater appear to be typical at the various locations (Eisenreich et al. 1981): urban (10 to 250), rural (1 to 50), Great Lakes (10 to 150), marine (0.5 to 10), and remote (1 to 30). PCB levels of 0.160 to 1.0 ng/L have been detected in snow from the Antarctic (Tanabe et al. 1983). A review of PCB monitoring of precipitation is available (Mazurek and Simoneit 1985).

**Table 7.2. Estimated dietary intake of PCBs for adults, infants, and toddlers ( $\mu\text{g}/\text{kg}/\text{day}$ )**

Fiscal year	Adult	Infant	Toddler
1981-1982	0.003	ND <sup>a</sup>	ND
1980	0.008	ND	ND
1979	0.014	ND	ND
1978	0.027	0.011	0.099
1977	0.016	0.025	0.030
1976	T <sup>b</sup>	T	ND

<sup>a</sup>ND = not detected.

<sup>b</sup>T = trace.

Source: Gartrell et al. 1985a,b,c and 1986a,b.

### 7.3 OCCUPATIONAL EXPOSURES

It was estimated that approximately 12,000 U.S. workers were potentially exposed to PCBs annually from 1970 to 1976 (NIOSH 1977a). At present, however, PCBs are no longer manufactured or used industrially in the United States. Therefore, occupational exposure to those workers involved in producing PCBs or manufacturing products with PCBs should no longer occur. The potential for occupational exposure still exists, however, since PCB-containing transformers and capacitors remain in use. Exposure may occur during repair or accidents of electrical equipment containing PCBs (Wolff 1985). Occupational exposure may also occur during waste site cleanup of PCB-containing waste sites.

### 7.4 POPULATIONS AT HIGH RISK

Several groups are at high risk from PCBs because of unusually high exposures. Persons occupationally exposed to PCBs are at high risk. Nursing infants may be exposed to high PCB concentrations in the breast milk of lactating women (EPA 1985a), especially if the women consume large amounts of contaminated fish. Levels found in breast milk are discussed in Sect. 2.2.3.1.

Other subpopulations are at high risk from PCBs because they are more sensitive to toxic effects of exposure. Embryos, fetuses, and neonates are potentially susceptible because of physiological differences from adults. They generally lack the hepatic microsomal enzyme systems that facilitate detoxification and excretion of PCBs (Calabrese and Sorenson 1977, Gillette 1967, Nyhan 1961). Breast-fed infants have additional risk caused by a steroid excreted in human breast milk, but not cow's milk, that inhibits glucuronyl transferase activity and thus glucuronidation and excretion of PCBs (Calabrese and Sorenson 1977, Gartner and Arias 1966). Children exposed to the antibiotic novobiocin may also be at greater risk because novobiocin noncompetitively inhibits glucuronyl transferase activity in vitro (Lokietz et al. 1963, Calabrese and Sorenson 1977).

Other subpopulations that are potentially more sensitive to PCBs include those with incompletely developed glucuronide conjugation mechanisms, such as those with Gilbert's syndrome or Crigler and Najjar syndrome (Lester and Schmid 1964, Calabrese and Sorenson 1977). Persons with hepatic infections may have decreased glucuronide synthesis, making them more sensitive because of their decreased capacity to detoxify and excrete PCBs (Calabrese and Sorenson 1977).

The indoor air in seven public buildings (schools, offices) was monitored in Minnesota during 1984 for Aroclors 1242, 1254, and 1260 (Oatman and Roy 1986). The total mean Aroclor concentration in the indoor air of the three buildings using PCB transformers was found to be nearly twice as high as that in the air of the four buildings not using PCB transformers ( $457 \pm 223$  s.d. vs  $229 \pm 106$  s.d.  $\text{ng}/\text{m}^3$ ). It is also noteworthy that the levels found in all the indoor airs were significantly higher than in typical ambient outdoor air.

The indoor air in a number of laboratories, offices, and homes was monitored for various Aroclors. It was found that "normal" indoor air concentrations of PCBs were at least one order of magnitude higher than

those in the surrounding outdoor atmosphere (MacLeod 1981). For example, average PCB levels were  $0.10 \mu\text{g}/\text{m}^3$  inside an industrial research building and  $0.21 \mu\text{g}/\text{m}^3$  inside the laboratories compared with  $<0.02 \mu\text{g}/\text{m}^3$  outside the facility. The average PCB level inside one home was  $0.31 \mu\text{g}/\text{m}^3$ , while outside on the same day, the level was  $0.004 \mu\text{g}/\text{m}^3$ . It was suggested that certain electrical appliances and devices (such as fluorescent lighting ballast), which have PCB-containing components, can emit PCBs into the indoor air, thereby elevating indoor PCB levels significantly above outdoor background levels.

## 8. ANALYTICAL METHODS

### 8.1 ENVIRONMENTAL MEDIA

The method widely used in laboratories for the analysis of PCBs in complex environmental samples is capillary column gas chromatography with electron capture (EC) detection (Schneider et al. 1984, Alford-Stevens et al. 1986). The use of mass spectrometry (MS) detectors has increased significantly, but most laboratories rely on EC detectors. EC detectors are more sensitive than MS detectors operated in electron ionization mode; the sensitivity difference can be as much as 2 or 3 orders of magnitude (Alford-Stevens et al. 1986). Table 8.1 lists several analytical methods, which have been standardized by either the EPA or NIOSH, for PCB analysis. The methods for water and for soil and sediment that are required by the EPA Contract Laboratory Program (EPA 1987c) are designated as CLP on Table 8.1. Details of sample collection, storage, and analysis of PCBs are available (Erickson 1986).

The analytical methods referenced in Table 8.1 pertain to the detection of Aroclor formulations and not individual PCB isomers. With EPA Method 680, however, PCBs are identified and measured by the level of chlorination (EPA 1985c). This method has been used only since 1981, and most environmental data reported before that were probably underestimated.

The determination of Aroclor concentrations (rather than the level of chlorination) in environmental samples is complex and can produce significantly different results from different laboratories even though the analytical procedures have been standardized (Alford-Stevens et al. 1985). As a result of the difference in biodegradability, water solubility, and volatility of individual PCB isomers, the concentrations of these individual isomers in environmental samples can be strikingly different from the commercial PCB analytical reference standards.

### 8.2 BIOMEDICAL SAMPLES

Analytical methods used for biomedical samples are listed in Table 8.2. Gas chromatography-mass spectrometry procedures developed to determine milligram-per-kilogram levels of PCBs in breast milk and fat (Hutzinger et al. 1974) usually have lower sensitivity than EC detectors (Safe et al. 1985, Smrek and Needham 1982). No accepted quantitative procedure for the determination of the total PCB content in human tissue sample exists. The PCB standard mixture selected for quantification varies between investigators since no standard mixture exists with the same peak pattern as in human tissues because of differences in metabolism of the various PCB isomers. In recent years, high-resolution gas chromatography has made it possible to use single PCB congeners for quantitation. The selection of the congeners may be made on the basis of

Table 8.1. Analytical methods for environmental media<sup>a</sup>

Sample matrix	Sample preparation	Analytical method	Detection limit	Accuracy/precision	References
Air	Adsorption on glass filter and Florisil; hexane desorption	GC/EC	0.0006 mg/m <sup>3</sup> for 50-L sample	4.4% RSD (analytical) at concentrations <10 mg/m <sup>3</sup>	NIOSH 1984a (method 5503)
Air	Adsorption on Florisil; hexane desorption; perchlorination	GC/EC	0.01 mg/m <sup>3</sup> (32 pg/injection)	2.8% RSD (analytical and perchlorination) at concentrations <10 mg/m <sup>3</sup>	NIOSH 1977a (method P & CAM 253)
Water	Extraction with methylene chloride; dry extract; exchange to hexane	GC/EC	0.065 µg/L (PCB-1242)	Standard deviation 1.6–5.5% and accuracy 88–96% at 25–110 µg/L	EPA 1987c (method 680-CLP <sup>b</sup> )
Water	Extraction with methylene chloride	GC/MS	30–36 µg/L (PCB-1221, 1254)	Standard deviation 11–13% and accuracy 77–80% at 5–2,400 µg/L	EPA 1982a (method 625)
Air	Adsorption on water-deactivated Florisil, hexane desorption; perchlorination with antimony pentachloride at 288°C	GC/EC	NR	NR	Lin and Que Hee 1985, 1987
Soil, sediments, and other solid sample matrices	Extraction with hexane-acetone mixture, Florisil column chromatographic clean-up and desulfurization by copper or mercury, if necessary	GC/EC	<1 µg/g	NR	EPA 1982b (method 8080)
Soil/sediment (low level)	Sample mixed with anhydrous sodium sulfate extracted with 1:1 methylene chloride/acetone, concentrate and clean-up by gel permeation and micro alumina column	GC/EC	80 µg/kg (required quantitation limit)	NR	EPA 1987c (CLP <sup>b</sup> )

<sup>a</sup>GC = gas chromatography; EC = electron capture; MS = mass spectroscopy; RSD = relative standard deviation; NR = not reported.

<sup>b</sup>As required by Contract Laboratory Program.

Table 8.2. Analytical methods for biological samples

Sample matrix	Sample preparation	Analytical method <sup>a</sup>	Detection limit	Accuracy/precision	References
Blood serum	Extract serum with ethyl ether and <i>n</i> -hexane; treat with methanolic KOH; extract with hexane and column chromatographic cleanup by silica gel	HRGC/EC	1.0 ng/mL on 10-mL sample	>80% accuracy at 25–400 ng/mL	NIOSH 1984b (method 8004)
Tissue, eggs, fat	See Bush and Lo 1973	TLC	0.5 mg/kg	Precision $\pm 0.05$ mg/kg at 0.5 mg/kg	IARC 1978
Serum	Mixed solvent extraction, column chromatographic cleanup on silica gel	GC/EC	NR	Accuracy 92.6% at 50 $\mu\text{g/L}$ and 114.1% at 10 $\mu\text{g/L}$ ; accuracy 89.6–138.1% at 9.9–74.2 $\mu\text{g/L}$ for inter-laboratory determinations	Burse et al. 1983a,b
Serum	Solvent extraction, column chromatographic cleanup on 10% silver nitrate on silica gel	GC/EC	NR	Accuracy 93.7% at 41 $\mu\text{g/L}$	Needham et al. 1980
Serum	Mixed solvent extraction, column chromatographic cleanup with hydrated silica gel for separation of PCBs from PBBs	GC/EC	2.5 ng/mL	Accuracy 95.3% at 100 $\mu\text{g/L}$ and 105–127% at 10 $\mu\text{g/L}$	Needham et al. 1981
Adipose tissue	Solvent extraction, column chromatographic cleanup on sulfuric acid/silica gel and 10% silver nitrate/silica gel columns	GC/EC	NR	Accuracy 91–93% at 3 $\mu\text{g/g}$	Smrek and Needham 1982
Human milk	Mixed solvent extraction, cleanup on Florisil-silicic acid column	HRGC/EC	NR	NR	Mes et al. 1984
Serum	Solvent extraction with diethyl ether and hexane, sulfuric acid, and silica column cleanup	HRGC/EC	0.1 ng/mL	85% at 25–125 ng/mL	Luotamo et al. 1985
Blood	Solvent extraction with hexane, methanolic KOH hydrolysis, silica gel, and alumina column cleanup and perchlorination	GC/EC	NR	NR	Lin and Que Hee 1985, 1987

<sup>a</sup>HRGC = high-resolution gas chromatography; GC = gas chromatography; EC = electron capture; TLC = thin-layer chromatography; NR = not reported.

their abundance in the samples, their toxicity, or their availability in analytical standards. A congener-specific analysis of a commercial PCB preparation and the PCB composition of a human milk sample have been reported by Safe et al. (1985). Variables in sampling method may also greatly influence results. For example, PCB levels in milk fat may decrease during lactation and with maternal age, weight, and purity (Jensen 1987). It has been shown by Lawton et al. (1985) that random error, interlaboratory variations in procedure, and methods used for reporting data can all have considerable impact on the reported PCB levels in human tissues. Such effects, however, should not deter investigators from using serum PCB data for assessing environmental exposure to populations or for statistical correlations with clinical parameters in epidemiological studies. Caution should be exercised when comparing exposure estimates or health effect studies reported by different investigators or when considering "the use of a specific serum PCB tolerance limit as a basis for administration action" (Lawton et al. 1985).

## 9. REGULATORY AND ADVISORY STATUS

### 9.1 INTERNATIONAL

No data were located in the available literature.

### 9.2 NATIONAL

#### 9.2.1 Regulations

##### 9.2.1.1 Air

AGENCY	ADVISORY
OSHA	Chlorodiphenyl (42% chlorine)-Skin TWA--1.0 mg/m <sup>3</sup> (PEL) (OSHA 1985)
	Chlorodiphenyl (54% chlorine)-Skin TWA--0.5 mg/m <sup>3</sup> (PEL) (OSHA 1985)

##### 9.2.1.2 Food

FDA temporary tolerances			
Agency	Standard	Value (ppm)	References
FDA	Foods	0.2-3.0	EPA 1988a
FDA	Packaging	10.0	EPA 1988a

##### 9.2.1.3 Water

PCBs are prohibited in any discharge from any PCB manufacturer (EPA 1977).

PCBs are regulated under the Clean Water Act Effluent Guidelines for the following industrial point sources: electroplating, steam electric, asbestos manufacturing, timber products processing, metal finishing, paving and roofing, paint formulating, ink formulating, gum and wood, carbon black, and aluminum forming (EPA 1988c).

#### 9.2.2 Advisory Guidance

##### 9.2.2.1 Air

AGENCY	ADVISORY
	PCBs
NIOSH	REL-TWA--1.0 µg/m <sup>3</sup> , the minimum reliable detectable concentration (NIOSH 1977b)

**Aroclor 1254**

American Conference of Government Industrial Hygienists (ACGIH) TLV-TWA--0.5 mg/m<sup>3</sup> (ACGIH 1986)

**Aroclor 1242**

ACGIH TLV-TWA--1 mg/m<sup>3</sup> (ACGIH 1986)

**9.2.2.2 Water**

**AGENCY**

**ADVISORY**

EPA	Ambient water quality criteria (AWQC)--0.79 to 0.0079 ng/L for carcinogenicity at 10 <sup>-5</sup> to 10 <sup>-7</sup> risk levels (EPA 1980ba)
	Drinking water criteria (DWC)--0.5 to 0.005 µg/L for carcinogenicity at 10 <sup>-4</sup> to 10 <sup>-6</sup> risk levels (EPA 1988a)
National Academy of Sciences (NAS)	Suggested no adverse response level (SNARL)--350 µg/L (NAS 1980)

**Aroclor 1016**

EPA	Longer-term health advisory (HA) (adult)--0.0035 mg/L (EPA 1988a)
	Longer-term HA (child)--0.001 mg/L (EPA 1988a)

**9.2.2.3 Soil**

**AGENCY**

**ADVISORY**

EPA	Permissible PCB soil contamination levels corresponding to: Noncancer 10-day HA (adult)--700 µg/day Noncancer 10-day HA (child)--100 µg/day Cancer risk specific doses: 1.75 to 0.00175 µg/day at 10 <sup>-4</sup> to 10 <sup>-7</sup> risk levels (EPA 1986d)
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**9.2.2.4 Others**

**AGENCY**

**ADVISORY**

EPA	Reportable quantity (RQ) (statutory)--10 lb (EPA 1985d) RQ (proposed)--1 lb (EPA 1987d)
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**9.2.3 Data Analysis**

**Carcinogenic potency.** EPA (1988a,b) determined that the positive evidence for carcinogenicity of Aroclor 1254, Aroclor 1260, Kaneclor 500, and Clophen A-30 and A-60 in animals, along with inadequate evidence in humans, places these PCBs in category B2, probable human carcinogens. Because any PCB mixture that contains appreciable amounts of the components in Aroclors 1254 and 1260, Kaneclor 500, and Clophen A-30 and A-60 are likely to present a carcinogenic risk and because of

the variety and variability of PCB mixtures, EPA (1988a,b) recommended that all commercial PCB mixtures be considered to have a similar carcinogenic potential and classified all PCB mixtures in category B2. IARC (1982) has classified PCBs in Group 2B based on sufficient evidence in animals, inadequate evidence in humans, and inadequate evidence for mutagenicity. NIOSH (1986) recommended that PCBs be regarded as potential human carcinogens in the workplace.

EPA (1988a,b) used the Norback and Weltman (1985) study as the basis for a quantitative carcinogenicity risk assessment for PCBs. The dietary level of 100 ppm Aroclor 1260 was converted to an intake of 5 mg/kg/day by assuming that a rat consumes food equal to 5% of its body weight per day. This dosage was converted to a TWA dosage of 3.45 mg/kg/day to reflect the fact that rats received 100 ppm for 16 months, 50 ppm for 8 months, and 0 ppm for the last 5 months. The rat dosage was converted to an equivalent human dose of 0.59 mg/kg/day on the basis of relative body surface areas. Incidences of trabecular carcinomas, adenocarcinomas, and neoplastic nodules in the liver were combined to produce total incidences of 45/47 in treated females and 1/49 in controls. Using these data, EPA (1988a,b) calculated a human  $q_1^*$  of  $7.7 \text{ (mg/kg/day)}^{-1}$ . Because there is no information regarding which constituents of any PCB mixture might be carcinogenic, Aroclor 1260 is assumed to be representative of other mixtures, and this potency estimate applies to them as well (EPA 1988a,b). The  $q_1^*$  was verified by the EPA agency-wide CRAVE committee on April 22, 1987<sup>1</sup> (EPA 1988b).

### 9.3 STATE

Regulations and advisory guidance from the states were not available.

## 10. REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists). 1986. Threshold Limit Values and Biological Exposure Indices for 1986-1987. Cincinnati, Ohio.

Albro PW, Fishbein L. 1972. Intestinal absorption of polychlorinated biphenyls in rats. Bull Environ Contam Toxicol 8:26 (cited in EPA 1985a).

Alford-Stevens AL, Bellar TA, Eichelberger JW, Budde WL. 1986. Accuracy and precision of determinations of chlorinated pesticides and polychlorinated biphenyls with automated interpretation of mass spectrometric data. Anal Chem 58(9):2022-2029.

Alford-Stevens AL, Budde WL, Bellar TA. 1985. Interlaboratory study on determination of polychlorinated biphenyls in environmentally contaminated sediments. Anal Chem 57:2452-2457.

Allen JR. 1975. Response of the nonhuman primate to polychlorinated biphenyl exposure. Fed Proc 34:1675-1679.

Allen JR, Abrahamson LJ. 1973. Morphological and biochemical changes in the liver of rats fed polychlorinated biphenyls. Arch Environ Contam Toxicol 1:265-280 (cited in EPA 1988a).

\* Allen JR, Barsotti DA. 1976. The effects of transplacental and mammary movement of the PCBs on infant rhesus monkeys. Toxicology 6:331.

\* Allen JR, Barsotti DA, Carstens LA. 1980. Residual effects of polychlorinated biphenyls on adult nonhuman primates and their offspring. J Toxicol Environ Health 6(1):55-66 (cited in EPA 1988a).

\* Allen JR, Barsotti DA, Lambrecht LK, Van Miller JP. 1979. Reproductive effects of halogenated aromatic hydrocarbons on nonhuman primates. Ann NY Acad Sci 320:419.

Allen JR, Carstens LA, Abrahamson LJ, Marljar RJ. 1975. Responses of rats and nonhuman primates to 2,5,2',5'-tetrachlorobiphenyl. Environ Res 9:265-273 (cited in EPA 1988a).

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\* Key studies.

\*\* No other names provided.

Allen JR, Carstens LA, Barsotti DA. 1974a. Residual effects of short-term, low-level exposure of nonhuman primates to polychlorinated biphenyls. *Toxicol Appl Pharmacol* 30:440-451.

Allen JR, Norback DH. 1973. Polychlorinated biphenyl and triphenyl induced gastric mucosal hyperplasia in primates. *Science* 179:498.

Allen JR, Norback DH, Hsu IC. 1974b. Tissue modifications in monkeys as related to absorption distribution and excretion of polychlorinated biphenyls. *Arch Environ Contam Toxicol* 2(1):86-95.

Alvares AP, Fischbein A, Anderson KE, Kappas A. 1977. Alterations in drug metabolism in workers exposed to polychlorinated biphenyls. *Clin Pharmacol Ther* 22:140.

Alvares AP, Kappas A. 1979. Lead and polychlorinated biphenyls: Effects on heme and drug metabolism. *Drug Metab Rev* 10:91-106.

Amano M, Yagi K, Nakajima H, Takehara R, Sakai H, Umeda G. 1984. Statistical observations about the causes of death of patients with oil poisoning. *Japan Hygiene* 39:1-5 (cited in EPA 1988a).

Anderson HA. 1985. Utilization of adipose tissue biopsy in characterizing human halogenated hydrocarbon exposure. *Environ Health Perspect* 60:127-131.

Anderson LM, Van Havere K, Budinger JM. 1983. Effects of polychlorinated biphenyls on lung and liver tumors initiated in suckling mice by *N*-nitrosodimethylamine. *J Nat Cancer Inst* 71(1):157-163 (cited in EPA 1985a).

Ando M, Saito H, Wakisaka I. 1985. Transfer of polychlorinated biphenyls to newborn infants through the placenta and mothers' milk. *Arch Environ Contam Toxicol* 14(1):51-57.

\* Aulerich RJ, Ringer RK. 1977. Current status of PCB toxicity, including reproduction to mink. *Arch Environ Contam Toxicol* 6:279.

Bahn AK, Grover P, Rosenwaike I, O'Leary K, Stellman J. 1977. PCB and melanoma. *N Engl J Med* 296:108 (cited in EPA 1988a).

Bahn AK, Rosenwaike I, Herrmann N, Grover P, Stellman J, O'Leary K. 1976. Melanoma after exposure to PCBs. *N Engl J Med* 295:450.

Baker EL, Landrigan PJ, Glueck CJ, et al. 1980. Metabolic consequences of exposure to polychlorinated biphenyls (PCB) in sewage sludge. *Am J Epidemiol* 112:553-563.

Baker FD, Bush B, Tumasonis CF, Lo FC. 1977. Toxicity and persistence of low-level PCBs in adult Wistar rats, fetuses, and young. *Arch Environ Contam Toxicol* 5(2):143-156.

- Baker JE, Eisenreich SJ, Johnson TC, Halfman BM. 1985. Chlorinated hydrocarbon cycling in the benthic nepreloid layer of Lake Superior. *Environ Sci Technol* 19:854-861.
- Bannister R, Davis D, Zacharewski T, Tizard I, Safe S. 1987. Aroclor 1254 as a 2,3,7,8-tetrachlorodibenzo-*p*-dioxin antagonist: Effects on enzyme induction and immunotoxicity. *Toxicology* (in press).
- Barnes P, Bellin J, DeRosa C, et al. 1987. Reference dose (RfD): Description and use in health risk assessments. Appendix A of the Integrated Risk Information System. EPA 600/8-86-0321. Washington, D.C.: Office of Health and Environmental Assessment, Office of Research and Development.
- \* Barsotti DA, Allen JR. 1975. Effects of polychlorinated biphenyls on reproduction in the primate. *Fed Proc* 34:338.
- \* Barsotti DA, Van Miller JP. 1984. Accumulation of a commercial polychlorinated biphenyl mixture (Aroclor 1016) in adult rhesus monkeys and their nursing infants. *Toxicology* 30(1):31-44.
- \* Barsotti DA, Marlar RJ, Allen JR. 1976. Reproductive dysfunction in rhesus monkeys exposed to low levels of polychlorinated biphenyls (Aroclor 1248). *Food Cosmet Toxicol* 14:99-103.
- Becker GM, McNulty WP, Bell M. 1979. Polychlorinated biphenyls-induced morphologic changes in the gastric mucosa of the rhesus monkey. *Invest* 40:373.
- Bell M. 1983. Intrastructural features of the murine cutaneous microvasculature after exposure to polychlorinated biphenyls compounds (PCBs) and benzo(a)pyrene (BAP). *Virchows Arch B* 42(2):131-142 (cited in EPA 1988a).
- Benthe HF, Knop J, Schmoldt A. 1972. Absorption and distribution of polychlorinated biphenyls (PCB) after inhalatory application. *Arch Toxicol* 29:85.
- Berry DL, DiGiovanni J, Juchau MR, Bracken WM, Gleason GL, Slaga TJ. 1978. Lack of tumor-promoting ability of certain environmental chemicals in a two-stage mouse skin tumorigenesis assay. *Res Commun Chem Pathol Pharmacol* 20(1):101-108.
- Berry DL, Slaga TJ, DiGiovanni J, Juchau MR. 1979. Studies with chlorinated dibenzo-*p*-dioxins, polybrominated biphenyls, and polychlorinated biphenyls in a two-stage system of mouse skin tumorigenesis: Potent anticarcinogenic effects. *Ann NY Acad Sci* 320:405-414.
- Bertazzi PA, Riboldi L, Pesatori A, Radice L, Zocchetti C. 1987. Cancer mortality of capacitor manufacturing workers. *Am J Ind Med* 11:165-176.

Bidleman TF. 1981. Interlaboratory analysis of high molecular weight organochlorines in ambient air. *Atmos Environ* 15:619-624.

Billings RE, McMahon RE. 1978. Microsomal biphenyl hydroxylation: The formation of 3 hydroxybiphenyl and biphenyl catechol. *Mol Pharmacol* 14:145-154.

Biocca M, Gupta BNL, Chae K, McKinney JD, Moore JA. 1981. Toxicity of selected symmetrical hexachlorobiphenyl isomers in the mouse. *Toxicol Appl Pharmacol* 58:461-474 (cited in EPA 1988a).

Birnbaum LS, Weber H, Harris MW, Lamb JC, McKinney JD. 1985. Toxic interaction of specific polychlorinated biphenyls and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin: Increased incidence of cleft palate in mice. *Toxicol Appl Pharmacol* 77:292-302.

Blazak WF, Marcun JB. 1975. Attempt to introduce chromosomal breakage in chicken embryos with Aroclor 1242. *Poultry Sci* 54:310 (cited in Harbison 1986).

\* Bleavins MR, Aulerich RJ, Ringer RK. 1980. Polychlorinated biphenyls (Aroclors 1016 and 1242): Effects on survival and reproduction in mink and ferrets. *Arch Environ Contam Toxicol* 9(5):627-635.

Bleavins MR, Breslin WJ, Aulerich RJ, Ringer RK. 1984. Placental and mammary transfer of a polychlorinated biphenyl mixture (Aroclor 1254) in the European ferret (*Mustela putorius furo*). *Environ Toxicol Chem* 3(4):637-644.

Boon JP, Duinker JC. 1986. Monitoring of cyclic organochlorines in the marine environments. *Environ Monit Assess* 7:189-208.

Bopp RF, Simpson HJ, Olsen CR, Trier RM, Kostyk N. 1982. Chlorinated hydrocarbons and radionuclide chronologies in sediments of the Hudson River and Estuary, N.Y. *Environ Sci Technol* 16:666.

Brezner E, Terkel J, Perry AS. 1984. The effect of Aroclor 1254 (PCB) on the physiology of reproduction in the female rat--I. *Comp Biochem Physiol* 77(1):65-70.

Brown DP. 1986. Mortality of Workers Exposed to Polychlorinated Biphenyls -- An Update. Cincinnati, Ohio: Industry Wide Studies Branch, Div. of Surveillance, Hazard Evaluation and Field Studies, National Institute National Institute for Occupational Safety and Health, Centers for Disease Control, U.S. Public Health Service, Dept. of Health and Human Services. NTIS PB86-206000.

Brown DP, Jones M. 1981. Mortality and industrial hygiene study of workers exposed to polychlorinated biphenyls. *Arch Environ Health* 36(3):120-129.

- Brown JF, Jr., Bedard BL, Brennan MJ, Carnahan JC, Feng H, Wagner RE. 1987. Polychlorinated biphenyl dechlorination in aquatic sediments. *Science* 236:709-712.
- Brown JF, Jr., Lawton RW. 1984. Polychlorinated biphenyl (PCB) partitioning between adipose tissue and serum. *Bull Environ Contam Toxicol* 33:277-280.
- Brown WR, Heddle JA. 1979. The mutagenic activity of 61 agents as determined by the micronucleus, *Salmonella*, and sperm abnormality assays. *Can J Genet Cytol* 21:319-333.
- \* Bruckner JV, Khanna KL, Cornish HH. 1973. Biological responses of the rat to polychlorinated biphenyls. *Toxicol Appl Pharmacol* 24:434-448.
- \* Bruckner JV, Khanna KL, Cornish HH. 1974. Effect of prolonged ingestion of polychlorinated biphenyls on the rat. *Food Cosmet Toxicol* 12:323.
- Burkhard LP, Armstrong DE, Andren AW. 1985. Henry's law constants for the polychlorinated biphenyls. *Environ Sci Technol* 19:590-596.
- Burse VW, Needham LL, Korver MP et al. 1983a. Gas-liquid chromatographic determination of polychlorinated biphenyls and a selected number of chlorinated hydrocarbons in serum. *J Assoc Off Anal Chem* 66:32-39.
- Burse VW, Needham LL, Lapeza CR, Jr., et al. 1983b. Evaluation of potential analytical approach for determination of polychlorinated biphenyls in serum: Interlaboratory study. *J Assoc Off Anal Chem* 66:956-968.
- Bush B, Snow J, Koblantz. 1984. Polychlorobiphenyl (PCB) congeners, p,p'-DDE, and hexachlorobenzene in maternal and fetal cord blood from mothers in upstate New York. *Arch Environ Contam Toxicol* 13:517-527.
- Calabrese EJ, Sorenson AJ. 1977. The health effects of PCBs with particular emphasis on human high risk groups. *Rev Environ Health* 2(4):285-304 (cited in EPA 1988a).
- Calandra JC. 1976. Summary of toxicological studies on commercial PCBs. In: *Proceedings of the National Conference of Polychlorinated Biphenyls*. EPA Report 560/6-75-004 (cited in Harbison 1986).
- Callahan MA, Slimak MW, Gabel NW, et al. 1979. Water-related environmental fate of 129 Priority Pollutants Vol. I. Chap 36. EPA 440/4-79-029a. Washington, DC: Environmental Protection Agency.
- Carey AE, Gowen JA, Tai H, Mitchell WG, Wiersma GB. 1979a. Pesticide residue levels in soils and crops from 37 states, 1972 - National Soils Monitoring Program (IV). *Pestic Monit J* 12:209-229.

Carey AE, Douglas P, Tai H, Mitchell WG, Wiersma GB. 1979b. Pesticide residue concentrations in soils of five United States cities, 1971 - Urban Soils Monitoring Program. *Pestic Monitor J* 13:17-22.

\* Carter JW. 1985. Effects of dietary PCBs (Aroclor 1254) on serum levels of lipoprotein cholesterol in Fischer rats. *Bull Environ Contam Toxicol* 34(3):427-431.

Chakraborty D, Bhattacharyya A, Chatterjee J, et al. 1978. Biochemical studies on polychlorinated biphenyls toxicity in rats: Manipulation by Vitamin C. *Int J Vitam Nutr Res* 48:22 (cited in EPA 1985a).

Chase KH, Wong O, Thomas D, Berney BW, Simon RK. 1982. Clinical and metabolic exposure to polychlorinated biphenyls (PCBs). *J Occup Med* 24:109-114 (cited in Kreiss 1985).

Chemline. 1987. On-line computer data base. National Library of Medicine. June 4, 1987.

Chen PH, Luo ML, Wong CK, Chen CJ. 1982. Comparative rates of elimination of some individual polychlorinated biphenyls from the blood of PCB-poisoned patients in Taiwan. *Food Chem Toxicol* 20(4):417-425.

Chen PH, Wong CK, Rappe C, Nygren M. 1985. Polychlorinated biphenyls, dibenzofurans and quaterphenyls in toxic rice-bran oil and in the blood and tissues of patients with PCB poisoning (Yu-Cheng) in Taiwan. *Environ Health Perspect* 29:475-678 (cited in EPA 1988a).

Christensen ER, Lo CK. 1986. Polychlorinated biphenyls in dated sediments of Milwaukee Harbor, Wisconsin. *Environ Pollut* 12:217-232.

Chu CK, Stella VJ, Bruckner JV, Jiang WD. 1977. Effects of long-term exposure to environmental levels of polychlorinated biphenyls on pharmacokinetics of pentobarbital in rats. *J Pharm Sci* 66(2):238-241 (cited in EPA 1988a).

\* Collins WT, Capen CC. 1980a. Fine structural lesions and hormonal alterations in thyroid glands of perinatal rats exposed in utero and by milk to polychlorinated biphenyls. *Am J Pathol* 99:125-142.

Collins WT, Capen CC. 1980b. Biliary excretion of thyroxine-I-125 and fine structural alterations in the thyroid glands of Gunn-rats fed PCBs. *Lab Invest* 43:158.

Collins WT, Capen CC. 1980c. Ultrastructural and functional alterations of the rat thyroid gland produced by polychlorinated biphenyls compared with iodide excess and deficiency, and thyrotropin and thyroxine administration. *Virchows Arch B*: 33(3):213-231.

Collins WT, Capen CC, Kasza L, Carter C, Dailey RE. 1977. Effect of polychlorinated biphenyl (PCB) on the thyroid gland of rats. Ultrastructural and biochemical investigations. *Am J Pathol* 89:119.

- Colombi A, Maroni M, Ferioli A et al. 1982. Increase in urinary porphyrin excretion in workers exposed to polychlorinated biphenyls. *J Appl Toxicol* 2(3):117-121.
- Condon SK. 1983. (Commonwealth of Massachusetts Department of Public Health). Personal Communications, August 25 and 28, 1983 (cited in Kreiss 1985).
- Conolly RB, Szabo S, Jaeger RJ. 1979. Vinylidene fluoride. Acute hepatotoxicity in rats pretreated with PCB or phenobarbital. *Proc Exp Biol Med* 162:163 (cited in EPA 1985a).
- Creaser CS, Fernandes AR. 1986. Background levels of polychlorinated biphenyls in British soils. *Chemosphere* 15:499-508.
- Davidorf FH, Knupp JA. 1979. Epidemiology of ocular melanoma. Incidence and geographic relationship in Ohio (1967-1977). *Ohio State Med J* 75(9):561-564.
- DiGiovanni J, Viaje A, Berry DL, Slaga TJ, Juchau MR. 1977. Tumor-initiating ability of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and Aroclor 1254 in the two-stage system of mouse skin carcinogenesis. *Bull Environ Contam Toxicol* 18(5):552-557.
- Dikshith TSS, Rockwood W, Abraham R, Coulston F. 1975. Effects of polychlorinated biphenyls (Aroclor 1254) on rat testis. *Exp Mol Pathol* 22:376 (cited in EPA 1988a).
- Drill VA, Freiss SL, Hays HW, Loomis TA, Shaffer CB. 1981. Potential Health Effects in the Human from Exposure to Polychlorinated Biphenyls (PCBs) and Related Impurities. Unpublished report. Arlington, Va: Drill, Freiss, Hays, Loomis and Shaffer, Inc.
- Drotman DP, et al.\*\* 1981. Human Exposure to PCBs in Southern Idaho. Internal report. EPA-79-105-2, Atlanta: Centers for Disease Control, November 2, 1981 (cited in Kreiss 1985).
- Drotman DP, Baxter PJ, Liddle JA, Brokopp CD, Skinner MD. 1983. Contamination of the food chain by polychlorinated biphenyls from a broken transformer. *Am J Public Health* 73:290-292.
- Duggan RE, Corneliussen PE, Duggan MB, McMahon BM, Martin RJ. 1983. Pesticide Residue Levels in Foods in the United States from July 1, 1969, to June 30, 1976. Washington, D.C.: Food and Drug Administration, Division of Chemical Technology.
- Durfee RL. 1976. Production and usage of PCBs in the United States. In: Proceedings of the National Conference on Polychlorinated Biphenyls, Chicago, 1975. EPA-560/6-75-004. Washington, D.C.: Environmental Protection Agency, pp. 103-107.

Eduljee G, Badsha K, Price L. 1985. Environmental monitoring for PCB and heavy metals in the vicinity of a chemical waste disposal facility-I. *Chemosphere* 14:1371-1382.

Eduljee G, Badsha K, Scudamore N. 1986. Environmental monitoring for PCB and trace metals in the vicinity of a chemical waste disposal facility-II. *Chemosphere* 15:81-93.

Eisenreich SJ, Looney BB, Thornton JD. 1981. Airborne organic contaminants in the Great Lakes ecosystem. *Environ Sci Technol* 15:30-38.

Emmett EA. 1985. Polychlorinated biphenyl exposure and effects in transformer repair workers. *Environ Health Perspect* 60:185-192.

EPA (Environmental Protection Agency). 1976. PCBs in the United States. Industrial Use and Environmental Distribution. PB-252 012. Springfield, Va: National Technical Information Service, pp. 4-5, 34-35, 54-57, 198-210, 322-334 (cited in IARC 1978).

EPA (Environmental Protection Agency). 1977. Polychlorinated biphenyls (PCBs): Toxic pollutant effluent standards, final rule. *Fed Regist* 42(22):6531-6555.

EPA (Environmental Protection Agency). 1979. Polychlorinated biphenyls (PCBs): Proposed rulemaking for PCB manufacturing exemptions. *Fed Regist* 44(106):31564-31567.

EPA (Environmental Protection Agency). 1980a. Hazard Waste Generation and Commercial Hazardous Waste Management Capacity: An Assessment. SW-894. Washington, D.C.: EPA, p. D-4.

EPA (Environmental Protection Agency). 1980b. Ambient Water Quality Criteria for Polychlorinated Biphenyls. EPA 440/5-80-068. Washington, D.C.: EPA. NTIS PB81-117798.

EPA (Environmental Protection Agency). 1982a. Test Methods. Methods for Organic Chemical Analysis of Municipal and Industrial Wastewater. EPA 600/4-82-057. Cincinnati, Ohio: EPA, pp. 608-1 - 608-11; 625-1 - 625-12.

EPA (Environmental Protection Agency). 1982b. Test Methods for Evaluating Solid Waste. SW-846. Washington, D.C.: Office of Solid Waste and Emergency Response, EPA, pp. 8080-1 - 8080-17.

EPA (Environmental Protection Agency). 1985a. Drinking Water Criteria Document for Polychlorinated Biphenyls (PCBs). Draft. Washington, DC: Office of Drinking Water. NTIS PB 86-118312/AS.

EPA (Environmental Protection Agency). 1985b. Health Assessment Document for Polychlorinated Dibenzo-*p*-Dioxins. EPA/600/8-84/014F, pp. II-1 - II-29; IV-1 - IV-37.

- EPA (Environmental Protection Agency). 1985c. Method 680, Determination of Pesticides and PCBs in Water and Soil/Sediment by Gas Chromatography/Mass Spectrometry. Cincinnati, Ohio: Environmental Monitoring and Support Laboratory, Office of Research and Development, Environmental Protection Agency (cited in Alford-Stevens 1986).
- EPA (Environmental Protection Agency). 1985d. Notification requirements, reportable quantity adjustments, final rule and proposed rule. Fed Regist 50(65):13456-13523.
- EPA (Environmental Protection Agency). 1985e. Baseline Estimates and Time Trends for Beta-Benzene Hexachloride, Hexachlorobenzene, and Polychlorinated Biphenyls in Human Adipose Tissue 1970-1983. EPA 560/5-85-025. Washington, D.C.: Office of Toxic Substances, Exposure Evaluation Division. Doc. No. NHATS-SS-01.
- EPA (Environmental Protection Agency). 1986a. Reference Values for Risk Assessment. Prepared by the Office of Health and Environmental Assessment for the Office of Solid Waste, Washington, D.C. Cincinnati, Ohio: Environmental Criteria and Assessment Office.
- EPA (Environmental Protection Agency). 1986b. Broad scan analysis of the FY 82 national human adipose tissue survey specimens. Volume III - Semi-Volatile Organic Compounds. EPA-560/5-86-037. Washington, D.C.: Office of Toxic Substances.
- EPA (Environmental Protection Agency). 1986c. Guidelines for carcinogen risk assessment. Fed Regist 51(185):33992-34003.
- EPA (Environmental Protection Agency). 1986d. Development of Advisory Levels for Polychlorinated Biphenyls (PCBs) Cleanup. EPA/600/6-86-02. Washington, D.C.
- EPA (Environmental Protection Agency). 1987a. Polychlorinated biphenyl spills cleanup policy; final rule. Fed Regist 52(63):10688-10710.
- EPA (Environmental Protection Agency). 1987b. Graphical Exposure Modeling System (GEMS). Personal computer version April 1987. Research Triangle Park, N.C.: EPA.
- EPA (Environmental Protection Agency). 1987c. U.S. Contract Laboratory Program. Statement of Work for Organics Analyses, Multi-Media, Multi-Concentration. Revised 8/87.
- EPA (Environmental Protection Agency). 1987d. Reportable quantity adjustments. Proposed rule. Fed Regist 52(50):8140.
- EPA (Environmental Protection Agency). 1988a. Drinking Water Criteria Document for Polychlorinated Biphenyls (PCBs). ECAO-CIN-414. Final. April 1988.

EPA (Environmental Protection Agency). 1988b. IRIS (Integrated Risk Information System), CRAVE (Carcinogen Risk Assessment Validation Endeavor) for polychlorinated biphenyls. (Verification date: 4/22/87). On-line: input pending. Cincinnati, Ohio: Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

EPA (Environmental Protection Agency). 1988c. Analysis of Clean Water Act Effluent Guidelines Pollutants. Summary of the Chemicals Regulated by Industrial Point Source Category, 40 CFR Parts 400-475. Draft. Prepared by Industrial Technology Division (WH 552). Washington, D.C.: Office of Water Regulations and Standards, Office of Water, Environmental Protection Agency.

EPA-NIH (Environmental Protection Agency-National Institutes of Health). 1987. OHM-TADS (Oil and Hazardous Materials Technical Assistance Data System). On-line: 1987. Washington, DC. EPA-NIH.

Erickson, MD. 1986. Analytical chemistry of PCBs. Stoneham, Mass.: Butterworth Publishers, pp. 55-338.

Fein GG. 1984. Intrauterine exposure of humans to PCBs: Newborn effects. EPA-600/53-84-060. Duluth, Minn: EPA. PB-84-188-887.

Fein GG, Jacobson JL, Jacobson SW, Schwartz PM, Dowler JK. 1984. Prenatal exposure to polychlorinated biphenyls - effects on birth size and gestational age. *J Pediatrics* 105:315-320.

Felt GR, Mueller WF, Iatropoulos MJ, Coulston F, Korte F. 1977. Chronic toxicity of 2,5,4'-trichlorobiphenyl in young rhesus monkeys. I. Body distribution elimination and metabolism. *Toxicol Appl Pharmacol* 41(3):619-627 (cited in EPA 1988a).

Feltz HR. 1980. Significance of bottom material data in evaluation water quality. In: *Contam Sed Fate Transport Case Studies Model Tox*. Ann Arbor, Mich: Ann Arbor Science 1:271-287.

Finklea J, Priester LE, Creason JP, Hauser T, Hinners T, Hammer D. 1972. I. Polychlorinated biphenyl residues in human plasma expose a major urban pollution problem. *Am J Public Health* 62:645-651 (cited in Kreiss 1985).

Fischbein A. 1985. Liver function tests in workers with occupational exposure to polychlorinated biphenyls (PCBs): Comparison with Yusho and Yu-Cheng. *Environ Health Perspect* 60:145-150.

Fischbein A, Rizzo JN, Solomon SJ, Wolff MS. 1985. Oculodermatological findings in workers with occupational exposure to polychlorinated biphenyls. *Br J Ind Med* 42(6):426-430.

Fischbein A, Wolff MS, Bernstein, Selikoff IJ. 1982. Dermatological findings in capacitor manufacturing workers exposed to dielectric fluids containing polychlorinated biphenyls. *Arch Environ Health* 37:69-74.

- \* Fischbein A, Wolff MS, Lilis R, Thornton J, Selikoff IJ. 1979. Clinical findings among PCB-exposed capacitor manufacturing workers. *Ann NY Acad Sci* 320:703-715.
- \* Fishbein L. 1974. Toxicity of chlorinated biphenyls. *Ann Rev Pharmacol* 14:139-156.
- Frank R, Braun HE, Van Hoveholdrinet M, Sirons GJ, Ripley BD. 1982. Agriculture and water quality in the Canadian Great Lakes Basin: V. Pesticide use in 11 agricultural watersheds and presence in steam water, 1975-77. *J Environ Qual* 11:497.
- Gage JC, Holm S. 1976. The influence of molecular structure on the retention and excretion of polychlorinated biphenyls by the mouse. *Toxicol Appl Pharmacol* 36:555-560.
- \* Garthoff LH, Cerra FE, Marks EM. 1981. Blood chemistry alteration in rats after single and multiple gavage administration of polychlorinated biphenyls. *Toxicol Appl Pharmacol* 60(1):33-44.
- Garthoff LH, Friedman L, Farber TM, et al. 1977. Biochemical and cytogenetic effects in rats caused by short-term ingestion of Aroclor 1254 or Firemaster BP6. *J Toxicol Environ Health* 3:769 (cited in EPA 1988a).
- Gartner LM, Arias IM. 1966. Studies of prolonged neonatal jaundice in the breast-fed infant. *J Pediat* 68(1):54 (cited in EPA 1988a).
- Gartrell MJ, Craun JC, Podrebarac DS, Gunderson EL. 1985a. Pesticides, selected elements, and other chemicals in adult total diet samples October 1979 - September 1980. *J Assoc Off Anal Chem* 68:1184-1197.
- Gartrell MJ, Craun JC, Podrebarac DS, Gunderson EL. 1985b. Pesticides, selected elements, and other chemicals in adult total diet samples October 1979 - September 1980. *J Assoc Off Anal Chem* 68:862-873.
- Gartrell MJ, Craun JC, Podrebarac DS, Gunderson EL. 1985c. Pesticides, selected elements, and other chemicals in infant and toddler diet samples, October 1979 - September 1980. *J Assoc Off Anal Chem* 68:1163-1183.
- Gartrell MJ, Craun JC, Podrebarac DS, Gunderson EL. 1986a. Pesticides, selected elements, and other chemicals in adult total diet samples October 1980 - March 1982. *J Assoc Off Anal Chem* 69:146-161.
- Gartrell MJ, Craun JC, Podrebarac DS, Gunderson EL. 1986b. Pesticides, selected elements, and other chemicals in infant and toddler total diet samples October 1980 - March 1982. *J Assoc Off Anal Chem* 69:123-145.
- Giam CS, Chan HS, Neff GS, Atlas EL. 1978. Phthalate ester plasticizers: A new class of marine pollutant. *Science* 199:419-421.

Gillette JR. 1967. Individually different responses to drugs according to age, sex and functional or pathological state. In: Wolstenhome G, Proter R, eds. Drug Responses in Man. London: Churchill, p. 28 (cited in EPA 1988a).

Goldstein JA, Hickman P, Jue DL. 1974. Experimental hepatic porphyria induced by polychlorinated biphenyls. Toxicol Appl Pharmacol 27:437-448.

Goto M, Sugiura K, Hattori M, Miyagawa T, Okamura M. 1974. Metabolism of 2,3-dichlorobiphenyl-<sup>14</sup>C and 2,4,6-trichlorobiphenyl-<sup>14</sup>C in the rat. Chemosphere 5:227-232 (cited in EPA 1988a).

Grant DL, Phillips WEJ. 1974. The effect of age and sex on the toxicity of Aroclor 1254, a polychlorinated biphenyl, in the rat. Bull Contam Toxicol 12:145-152 (cited in EPA 1988a).

Green S, Carr JV, Palmer KA, Oswald EJ. 1975a. Lack of cytogenetic effects in bone marrow and spermatogonial cells in rats treated with polychlorinated biphenyls (Aroclors 1242 and 1254). Bull Environ Contam Toxicol 13:14-22.

Green S, Sauro FM, Friedman L. 1975b. Lack of dominant lethality in rats treated with polychlorinated biphenyls (Aroclor 1242 and 1254). Food Cosmet Toxicol 13:507-510.

Griffin RA, Chou SFJ. 1981. Movement of PCBs and other persistent compounds through soil. Water Sci Technol 13:1153-1163.

Gustavsson P, Hogstedt C, Rappe C. 1986. Short-term mortality and cancer incidence in capacitor manufacturing workers exposed to polychlorinated biphenyls. Am J Ind Med 10:341-344.

Guzelian PS. 1985. Clinical evaluation of liver structure and function in humans exposed to halogenated hydrocarbons. Environ Health Perspect 60:159-164.

\* Haake JM, Safe S, Mayura K, Phillips TD. 1987. Aroclor 1254 as an antagonist of the teratogenicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. Toxicol Lett (in press).

Hansch C, Leo AJ. 1985. Medchem Project. Issue No. 26. Claremont, Calif: Pomona College.

Harbison RD. 1986. Genotoxic effects of PCBs. Draft report sent to Dr. John Craddock. St. Louis, Mo: Monsanto Chem.

Hashimoto K, Akasaka S, Takagi Y, et al. 1976. Distribution and excretion of [<sup>14</sup>C]polychlorinated biphenyls after their prolonged administration to male rats. Toxicol Appl Pharmacol 37:415-423.

Hatton RE. 1979. Chlorinated biphenyls and related compounds. In: Grayson M, Eckroth D, eds. Kirk-Othmer Encyclopedia of Chemical Technology, Vol. 5, New York: John Wiley and Sons, pp. 844-848.

- Hattula ML. 1985. Mutagenicity of PCBs and their pyrosynthetic derivatives in cell-mediated assay. *Environ Health Perspect* 60:255-257.
- Hawley JK. 1985. Assessment of health risk for exposure to contaminated soil. *Risk Anal* 5(4):289-302.
- Heddle JA, Bruce WR. 1977. Comparison of tests for mutagenicity or carcinogenicity using assays for sperm abnormalities, formation of micronuclei and mutations in *Salmonella*. In: Hiatt HH, et al., ed. *Origins of Human Cancer*. Cold Spring Harbor Conference on Cell Proliferation. Cold Spring Harbor, N.Y.: Cold Spring Harbor Lab 4:1549 (cited in EPA 1988a).
- Heit M, Klusek C, Baron J. 1984. Evidence of deposition of anthropogenic pollutants in remote Rocky Mountain lakes. *Water Air Soil Pollut* 22:403-416.
- Hill RH, Jr. 1985. Effects of polyhalogenated aromatic compounds on porphyrin metabolism. *Environ Health Perspect* 60:139-143.
- Hollifield HC. 1979. Rapid nephelometric estimate of water solubility of highly insoluble organic chemicals of environmental interest. *Bull Environ Contam Toxicol* 23:579-586.
- Hoopingarner R, et al.\*\* 1972. Polychlorinated biphenyl interactions with tissue culture cells. *Environ Health Perspect* 1:155 (cited in Harbison 1986).
- \* Hornshaw TC, Safronoff J, Ringer RK, Aulerich RJ. 1986. LC50 test results in polychlorinated biphenyl-fed mink: Age, season and diet comparisons. *Arch Environ Contam Toxicol* 15(6):717-723.
- HSDB (Hazardous Substances Data Bank). 1987. On-line computer data base. National Library of Medicine. June 4, 1987.
- Hubbard HL. 1964. Chlorinated biphenyl and related products. In: Standen A, ed. *Kirk-Othmer Encyclopedia of Chemical Technology*, 2nd ed., Vol. 5, New York: John Wiley and Sons, p. 291.
- Humphrey HEB. 1976. Evaluation of changes of the level of polychlorinated biphenyls (PCB) in human tissue. Final Report on FDA Contract 223-73-2209. Lansing, Michigan: Michigan Department of Public Health.
- Humphrey HEB. 1983a. Population studies of PCBs in Michigan residents. In: D'Itri FM, Kamrin MA, eds. *PCBs: Human and Environmental Hazards*. Ann Arbor, Mich: Ann Arbor Science Publications, pp. 299-310 (cited in Kreiss 1985).
- Humphrey HEB. 1983b. Evaluation of humans exposed to waterborne chemicals of the Great Lakes. Final report for EPA Co-operative Agreement (CR807192) (cited in Kreiss 1985).

Hutton JJ, Meier J, Hackney C. 1979. Comparison of the in vitro mutagenicity and metabolism of dimethylnitrosamine and benzo[a]pyrene in tissues from inbred mice treated with phenobarbital, 3-methylcholanthrene or polychlorinated biphenyls. *Mutat Res* 66:75 (cited in EPA 1985a).

Hutzinger S, Safe S, Zitko V. 1974. The chemistry of PCBs. Cleveland, Ohio: Chemical Rubber Publishing Co (cited in Callahan et al. 1979, IARC 1978).

Iatropoulos MJ, Bailey J, Adams HP, Coulston, Hobson W. 1978. Response of nursing infant rhesus to Clophen A-30 or hexachlorobenzene given to their lactating mothers. *Environ Res* 16(1-3):38-47 (cited in EPA 1988a).

IARC (International Agency for Research on Cancer). 1978. IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans. Polychlorinated Biphenyls and Polybrominated Biphenyls. IARC, Vol. 18. Lyon, France: World Health Organization.

IARC (International Agency for Research on Cancer). 1982. IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans. Suppl 4. Lyon, France: World Health Organization.

Ito N, Nagasaki H, Makiura S, Arai M. 1974. Histopathological studies on liver tumorigenesis in rats treated with polychlorinated biphenyls. *Gann* 66:545-549 (cited in EPA 1985a).

Jacobson JL, Fein GG, Jacobson SW, et al. 1984a. The transfer of polychlorinated biphenyls (PCBs) and polybrominated biphenyls (PBBs) across the human placenta and into maternal milk. *Am J Public Health* 74(4):378-379.

Jacobson JL, Jacobson SW, Schwartz PM, Fein GG, Dowler JK. 1984b. Prenatal exposure to an environmental toxic: A test of the multiple effects model. *Dev Psych* 20:523-532.

Jacobson SW, Fein GG, Jacobson JL, Schwartz PM, Dowler JK. 1985. The effect of intrauterine PCB exposure on visual recognition memory. *Child Dev* 56:856-860.

Jaffe R, Stemmler EA, Eitzer BD, Hites RA. 1985. Anthropogenic, polyhalogenated, organic compounds in sedentary fish from Lake Huron and Lake Superior tributaries and embayments. *J Great Lakes Res* 11:156-162.

Jelinek CF, Corneliussen PE. 1976. Levels of PCBs in the U.S. food supply. In: *Proceedings of the National Conference on Polychlorinated Biphenyls*, Chicago, 1975. EPA-560/6-75-004. Washington, D.C.: Environmental Protection Agency, pp. 147-154.

Jensen AA. 1983. Chemical contaminants in human milk. *Res Rev* 89:1, 75, 82-94.

- Jensen AA. 1987. Polychlorobiphenyls (PCBs), polychlorodibenzo-*p*-dioxins (PCDDs) and polychlorodibenzofurans (PCDFs) in human milk, blood, and adipose tissue. *Sci Total Environ* 64:259-293.
- Jensen RG, Clark RM, Ferris AM. 1980. Composition of the lipids in human milk: A review. *Lipids* 15:345-355 (cited in Kimbrough 1987a)
- Jensen S, Sundstrom G. 1974. Structures and levels of most chlorobiphenyls in the technical PCB products and in human adipose tissue. *Ambio* 3:70-76 (cited in EPA 1988a).
- Kasza L, Collins WT, Capen CC, Garthoff LH, Friedman L. 1978. Comparative toxicity of polychlorinated biphenyls and polybrominated biphenyl in the rat thyroid gland: Light and electron microscopic alterations after subacute dietary exposure. *J Environ Pathol Toxicol*, May-June (5):587-599.
- Kato N, Kawai K, Yoshida A. 1981. Effect of dietary level of ascorbic acid on the growth, hepatic lipid peroxidation, and serum lipids in guinea pigs fed polychlorinated biphenyls, Aroclor 1254. *Bull Environ Contam Toxicol* 18:243 (cited in EPA 1985a).
- Keplinger ML, et al.\*\* 1971. Toxicological studies with polychlorinated biphenyls. *Toxicol Appl Pharmacol* 53:389 (cited in Harbison 1986).
- Kim NK, Stone DW. n.d. Organic chemicals and drinking water. NYS Dept Health, p. 101.
- Kimbrough RD. 1987a. Human health effect of polychlorinated biphenyls (PCBs) and polybrominated biphenyls (PBBs). *Ann Rev Pharmacol Toxicol* 27:87.
- Kimbrough RD. 1987b. Toxicology of halogenated biphenyls, dibenzodioxins, and dibenzofurans. *ISI Atlas of Sciences: Pharmacology* 1:139-142.
- Kimbrough RD, Linder RE. 1974. Induction of adenofibrosis and hepatomas in the liver of Balb/CJ mice by polychlorinated biphenyls (Aroclor 1254). *J Nat Cancer Inst* 53:547 (cited in EPA 1988a).
- Kimbrough RD, Linder RE, Gaines TB. 1972. Morphological changes in livers of rats fed polychlorinated biphenyls. *Arch Environ Health* 25:354.
- Kimbrough RD, Squire TA, Linder RE, Strandberg JD, Montali RJ, Burse VW. 1975. Induction of liver tumors in Sherman strain female rats by polychlorinated biphenyl Aroclor 1260. *J Nat Cancer Inst* 55:1453-1459.
- Kleinert JJ. 1976. Sources of polychlorinated biphenyls in Wisconsin. In: *Proceedings of the National Conference on Polychlorinated Biphenyls*, Chicago, 1975. EPA-560/6-75-004. Washington, D.C.: Environmental Protection Agency, pp. 124-126.

- Kokoszka L, Flood J. 1985. A guide to EPA-approved PCB disposal methods. *Chem Eng* 92(14):41-43.
- Koller LD. 1977. Enhanced polychlorinated biphenyls lesions in Moloney leukemia virus-infected mice. *Clin Toxicol* 11(1):107-116.
- Kraul I, Karlog O. 1976. Persistent organochlorinated compounds in human organs collected in Denmark 1972-73. *Acta Pharmacol Toxicol (Kbh)* 38(2):38-73 (cited in EPA 1985a).
- Kreiss K. 1985. Studies on populations exposed to polychlorinated biphenyls. *Environ Health Perspect* 60:193-199.
- Kreiss K, Roberts C, Humphrey HEB. 1982. Serial PBB levels, PCB levels, and clinical chemistries in Michigan's PBB cohort. *Arch Environ Health* 37:141-147 (cited in Kreiss 1985).
- Kreiss K, Zack MM, Kimbrough RD, Needham LL, Smrek AL, Jones BT. 1981. Association of blood pressure and polychlorinated biphenyl levels. *J Am Med Assoc* 245(24):2505-2509.
- Kurachi M. 1983. A new sulfur-containing derivative and possibility of conjugate formation of PCBs in mice or rats. *Agric Biol Chem* 47(6):1183-1191.
- Kurachi M, Mio T. 1983a. On fluctuation of PCBs under various unnatural conditions in mice. *Agric Biol Chem* 47(6):1173-1181.
- Kurachi M, Mio T. 1983b. Studies on excretion and accumulation of PCBs in connection with their partial metabolism in the animal body. Part III. On the formation of a conjugate of PCBs with glutathione and its further metabolism in mice or rats. *Agric Biol Chem* 47(6):1193-1199.
- Kuratsune M. 1986. Letter to A Chiu and D Bayliss. Carcinogen Assessment Group, Washington, D.C.: Environmental Protection Agency. June 30 (cited in EPA 1988a).
- Kuratsune M, Shapiro R. 1984. PCB poisoning in Japan and Taiwan. *Am J Ind Med* 5:1-153.
- Larsson P. 1985. Contaminated sediments of lakes and oceans act as sources of chlorinated hydrocarbons for release to water and atmosphere. *Nature* 317:347-349.
- Lawrence C. 1977. PCB? and melanoma. *New Engl J Med* 296:108.
- Lawton RW, Brown JF, Ross MR, Feingold J. 1982. Comparability and precision of serum PCB measurements. *Arch Environ Health* 40:29-37.
- Lawton RW, Ross MR, Feingold J, Brown JF, Jr. 1985. Effects of PCB exposure on biochemical and hematological finding in capacitor workers. *Environ Health Perspect* 60:165-184.

- Leifer A, Brink RH, Thom GC, Partymiller KG. 1983. Environmental transport and transformation of polychlorinated biphenyls. EPA-560/5-83-025. Washington, D.C.: Office of Pesticides and Toxic Substances. NTIS No. PB84-142579.
- Lester R, Schmid R. 1964. Bilirubin metabolism. *New Engl J Med* 270(15):779 (cited in EPA 1985a).
- Letz G. 1983. The toxicology of PCB's - an overview for clinicians. *The Western J Med* 138:534-540.
- Lewis RG, Martin BE, Sgontz DL, Howes JE, Jr. 1985. Measurements of fugitive atmospheric emissions of polychlorinated biphenyls from hazardous waste landfills. *Environ Sci Technol* 19:986-991.
- Lin JM, Que Hee SS. 1985. Optimization of perchlorination conditions for some representative polychlorinated biphenyls. *Anal Chem* 57:2130-2134.
- Lin JM, Que Hee SS. 1987. Change in chromatogram patterns after volatilization of some Aroclors, and the associated quantitation problems. *Am Ind Hyg Assoc J* 48:599-607.
- \* Linder RE, Gaines TB, Kimbrough RD. 1974. The effect of PCB on rat reproduction. *Food Cosmet Toxicol* 12:63.
- \* Litterst CL, Farber TM, Baker AM, van Loon EJ. 1972. Effect of polychlorinated biphenyls on hepatic microsomal enzymes in the rat. *Toxicol Appl Pharmacol* 23:112-122.
- Lokietz H, Dowben RM, Hsia DY. 1963. Studies on the effect of Novobiocin and glucuronyl transferase. *Pediatrics* 32:47 (cited in EPA 1985a).
- Loose LD, Pittman KA, Benitz KF, Silkworth JB, Mueller W, Coulston F. 1978a. Environmental chemical-induced immune dysfunction. *Ecotoxicol Environ Safety* 2:173.
- Loose LD, Silkworth JB, Pittman KA, Benitz KF, Mueller W, . 1978b. Impaired host resistance to endotoxic and malaria in polychlorinated biphenyl and hexachlorobenzene-treated mice. *Inf Immun* 20(1):30.
- Lucas RM, Iannacchione VG, Melroy DK. 1982. Polychlorinated Biphenyls in Human Adipose Tissue and Mother's Milk. Report. Research Triangle Institute, Research Triangle Park, N.C. RTI/1864/50-03F. NTIS PB83-253179.
- Luotamo M, Jrvisalo, Aitio A. 1985. Analysis of polychlorinated biphenyls (PCBs) in human serum. *Environ Health Perspect* 60:327-332.
- Lyman WJ, Reehl WF, Rosenblatt DH. 1982. Handbook of Chemical Property Estimation Methods. New York: McGraw-Hill, pp. 15-16.

Massachusetts Department of Public Health. 1987. Final Report of Greater New Bedford PCB Health Effects Study 1984-1987. Boston, Mass: Mass. Dept. of Public Health.

Mabey WR, Smith JH, Podoll RT, et al. 1981. Aquatic Fate Process Data for Organic Priority Pollutants. EPA 440/4-81-014. Washington D.C.: Environmental Protection Agency, Monitoring and Data Support Division, Office of Water Regulations and Standards, pp. 115-128.

MacLeod KE. 1981. Polychlorinated biphenyls in indoor air. Environ Sci Technol 15:926-8.

Makiura S, Aoe H, Sugihara S, Hirao K, Arai M, Ito N. 1974. Inhibitory effect of polychlorinated biphenyls on liver tumorigenesis in rats treated with 3'-methyl-4-dimethylaminoazobenzene, N-2-fluorenylacetamide, and diethylnitrosamine. J Nat Cancer Inst 53:1253-1257 (cited in IARC 1978).

Maroni N, Columbi A, Arbosti G, Cantoni S, Foa V. 1981a. Occupational exposure to polychlorinated biphenyls in electrical workers. II. Health effects. Br J Ind Med 38:55-60.

Maroni N, Columbi A, Cantoni S, Ferioli E, Foa V. 1981b. Occupational exposure to polychlorinated biphenyls in electrical workers. I. Environmental and blood polychlorinated biphenyls concentrations. Br J Ind Med 38:49-54.

Masuda Y, Kagawa R, Kuroki H, Tokudom S, Kuratsune M. 1979. Transfer of various polychlorinated biphenyls to the fetuses and offspring of mice. Food Cosmet Toxicol 17(6):623-627.

Mazurek MA, Simoneit BRT. 1985. Organic components in bulk and wet-only precipitation. CRC Crit Rev Environ Control 16:41-47 (cited in EPA 1988a).

McConnell EE, McKinney JD. 1978. Exquisite toxicity in the guinea pig to structurally-similar halogenated dioxins, furans, biphenyls and naphthalenes. Toxicol Appl Pharmacol 45:298 (cited in EPA 1988a).

McNulty WP, Becker GM, Cory HT. 1980. Chronic toxicity of 3,3',4,4'- and 2,2',5,5'-tetrachlorobiphenyls in rhesus macques. Toxicol Appl Pharmacol 56(2):182-190 (cited in EPA 1985a).

Meigs JW, Albom JJ, Kartin Bl. 1954. Chloracne from an unusual exposure to Arochlor. J Am Med Assoc 154:1417-1418.

Mes J, Doyle JA, Adam BR, Davies DJ, Turton D. 1984. Polychlorinated biphenyls and organochlorine pesticides in milk and blood of Canadian women during lactation. Arch Environ Contam Toxicol 13:217-223.

- Mieure JP, Hicks O, Kaley RG, Saeger VW. 1976. Characterization of polychlorinated biphenyls. In: National Conference on Polychlorinated Biphenyls, Chicago, 1975. EPA-560/6-75-004. Washington, D.C.: Environmental Protection Agency, pp. 84-93.
- Miller JW. 1985. Congenital PCB poisoning: A reevaluation. *Environ Health Perspect* 60:211-214.
- Mizutani T, Hidaka K, Matsumoto M. 1977. A comparative study on accumulation and elimination of tetrachlorobiphenyl isomers in mice. *Bull Environ Contam Toxicol* 18:454 (cited in EPA 1988a).
- Monsanto. 1974. PCBs-Aroclors Tech Bull. O/PL 306A. St. Louis, Mo (cited in Callahan et al. 1979)
- Morgan RW, Ward JM, Hartman PE. 1981. Aroclor 1254-induced intestinal metaplasia and adenocarcinoma in the glandular stomach of F344 rats. *Cancer Res* 41:5052-5059.
- Morselli L, Brocco D, Pirni A. 1985. The presence of polychlorodibenzo-p-dioxins (PCDDs), polychlorodibenzofurans (PCDFs), and polychlorobiphenyls (PCBs) in fly ashes from various municipal incinerators under different technological and working conditions. *Ann Chim* 75:59-64.
- Mosley CL, Emmett E. 1984. NIOSH Health Hazard Evaluation Report. GSA. Switchgear Shop. HETA80-007-1520. NTIS PB86-133741.
- Muehlebach S, Bickel MH. 1981. Pharmacokinetics in rats of 2,4,5,2',4',5'-hexachlorobiphenyl, an unmetabolizable lipophilic model compound. *Xenobiotica* 11(4):249-257 (cited in EPA 1988a).
- Murphy TJ, Formanski LJ, Brownawell B, Meyer JA. 1985. Polychlorinated biphenyl emissions to the atmosphere in the Great Lakes region. Municipal land fills and incinerators. *Environ Sci Technol* 19(10):924-946.
- Murray HE, Ray LE, Giam CS. 1981. Phthalic acid esters, total DDT and polychlorinated biphenyls in marine samples from Galveston Bay, Texas. *Bull Environ Contam Toxicol* 26:769-774.
- Nagasaki H, Tomii S, Mega T. 1975. Factors affecting induction of liver cancer by BHC and PCBs in mice. Abstract No. 235. *Jpn J Hyg* 30:134 (cited in IARC 1978).
- NAS (National Academy of Sciences). 1980. Drinking Water and Health. Vol. 3, Washington, D.C.: National Academy Press, pp. 25-67 (cited in EPA 1988a).
- NCI (National Cancer Institute). 1978. Bioassay of Aroclor 1254 for possible carcinogenicity. NCI-GC-TR-38. Bethesda, Md: National Cancer Institute. NTIS PB279624.

Needham LL, Amrek AL, Head SL, Burse VW and Liddle JA. 1980. Column chromatography separation of polychlorinated biphenyls from dichlorodiphenyltrichloroethane and metabolites. *Anal Chem* 52:2227-2229.

Needham LL, Burse VW, Price HA. 1981. Temperature-programmed gas chromatographic determination of polychlorinated and polybrominated biphenyls in serum. *J Assoc Off Anal Chem* 64:1131-1137.

Nelson NN, Hammon PB, Nisbet ICT, Sarofim AF, Drury WH. 1972. Polychlorinated biphenyls - environmental impact. *Environ Res* 5:249-362 (cited in EPA 1988a).

Nilsson B, Ramel C. 1974. Genetic tests on *Drosophila melanogaster* with polychlorinated biphenyls (PCB). *Hereditas* 77:319-322 (cited in EPA 1988a).

NIOSH (National Institute for Occupational Safety and Health). 1977a. NIOSH Manual of Analytical Methods. 2nd ed. Taylor DG, ed. Vol. 1. Cincinnati, Ohio: U.S. Department of Health and Human Services, NIOSH, pp. 244-1 - 253-7.

NIOSH (National Institute for Occupational Safety and Health). 1977b. Criteria for a recommended standard. Occupational Exposure to Polychlorinated Biphenyls (PCBs). Rockville, Md: U.S. Department of Health, Education and Welfare, Public Health Service, Centers for Disease Control. NIOSH Publ 77-225.

NIOSH (National Institute for Occupational Safety and Health). 1984a. NIOSH Manual of Analytical Methods. 3rd ed. Eller PM, ed. Vol. 2. Cincinnati, Ohio: U.S. Department of Health and Human Services, NIOSH, pp. 5503-1 - 5503-5.

NIOSH (National Institute for Occupational Safety and Health). 1984b. NIOSH Manual of Analytical Methods. 3rd ed. Eller PM, ed. Vol. 1. Cincinnati, Ohio: U.S. Department of Health and Human Services, NIOSH, pp. 8004-1 - 8004-4.

NIOSH (National Institute for Occupational Safety and Health). 1986. Polychlorinated Biphenyls (PCBS): Potential Health Hazards from Electrical Equipment Fires or Failures. Department of Health and Human Services. NIOSH Publ 86-111.

Nishizumi M. 1976. Radioautographic evidence for adsorption of polychlorinated biphenyls through the skin. *Ind Health* 14:41-44.

Norback DH, Mack E, Blomquist KA, Allen JR. 1978. Metabolic study of 2,4,5,2',4',5'-hexachlorobiphenyl in rhesus monkeys. *Toxicol Appl Pharmacol* 45:331 (cited in EPA 1985a).

\* Norback DH, Weltman RH. 1985. Polychlorinated biphenyl induction of hepatocellular carcinoma in the Sprague-Dawley rat. *Environ Health Perspect* 60:97-105.

NTIS (National Technical Information Service). 1987. Federal research in progress: On-line database.

Nyhan WL. 1961. Toxicity of drugs in the neonatal period. *J Pediatr* 59(1):1 (cited in EPA 1988a).

Oatman L, Roy R. 1986. Surface and indoor air levels of polychlorinated biphenyls in public buildings. *Bull Environ Contam Toxicol* 37:461-466.

Oesterle D, Deml E. 1983. Promoting effect of polychlorinated biphenyls on development of enzyme-altered islands in livers of weanling and adult rats. *J Cancer Res Clin Oncol* 105(2):141-146 (cited in EPA 1985a).

Orris P, Kominsky JR, Hryhorczyk D, Melius J. 1986. Exposure to polychlorinated biphenyls from an overheated transformer. *Chemosphere* 15:1305-1311.

OSHA (Occupational Safety and Health Administration). 1985. Code of Federal Regulations. OSHA Occupational Standards. Permissible Limits. 29 CFR 1910.1000.

Ouw HK, Simpson GR, Siyali DS. 1976. Use and health effects of Aroclor 1242, a polychlorinated biphenyl in an electrical industry. *Arch Environ Health* 31:189.

Paris DF, Steen WC, Baughman GL. 1978. Role of the physicochemical properties of Aroclor 1016 and 1242 in determining their fate and transport in aquatic environments. *Chemosphere* 7(4):319-325 (cited in Callahan et al. 1979)

Parkinson A, Thomas PE, Ryan DE, et al. 1983. Differential time course of induction of rat liver microsomal cytochrom P-450 isozymes and epoxide hydrolase by Aroclor 1254. *Arch Biochem Biophys* 225:203-215 (cited in EPA 1988a).

Peakall DB, Lincer JL, Bloom SE. 1972. Embryonic mortality and chromosomal alterations caused by Aroclor 1254 in ring doves. *Environ Health Perspect* 1:103-104 (cited in EPA 1988a).

Pereira MA, Herren SL, Britt AL, Khoury MM. 1982. Promotion by polychlorinated biphenyls of enzyme-altered foci in rat liver. *Cancer Lett* 15(2):185-190 (cited in EPA 1985a).

Ray LE, Murray HE, Giam CS. 1983. Organic pollutants in marine samples from Portland, Maine. *Chemosphere* 12:1031-1038.

Reid D, Fox JM. 1982. Polychlorinated biphenyl report, Old Forge, Lackawanna County, Pennsylvania Department of Health, Division of Environmental Health, April 1982 (cited in Kreiss 1985).

Requejo AG, West RH, Hatcher PG, McGillivray PA. 1979. Polychlorinated biphenyls and chlorinated pesticides in soils of the Everglades national park and adjacent agricultural areas. *Environ Sci Technol* 13:931-936.

\* Ringer RK, Aulerich RJ, Bleavins MR. 1981. Biological effects of PCBs and PBBs on mink and ferrets: A review. In: Khan MAQ, ed. Halogenated Hydrocarbons: Health and Ecological Effects. Elmsford N.Y.: Pergamon Press, pp. 329-343 (cited in Hornshaw et al. 1986).

Rodgers PW, Swain WR. 1983. Analysis of polychlorinated biphenyl (PCB) loading trends in Lake Michigan. *J Great Lakes Res* 9:548-58.

Rogan WJ, Gladen BC, McKinney JD, et al. 1986. Neonatal effects of transplacental exposure to PCBs and DDE. *J Pediatr* 109:335-341.

Rogan WJ, Gladen BC, McKinney JD et al. 1987. Polychlorinated biphenyls (PCBs) and dichlorodiphenyl dichloroethane (DDE) in human milk: Effects on growth, morbidity and duration of lactation. *Am J Public Health* 77:1294-1297.

Rožanova LF. 1943. [Toxicity of some chlorinated aromatic hydrocarbons]. *Farmakol Toksikol* 6:48. (In Russian) (cited in NIOSH 1977b).

Ryan JJ, Lau PY, Pilon JC, Lewis D, McLeod HA, Gervais A. 1984. Incidence and levels of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in Lake Ontario commercial fish. *Environ Sci Technol* 18:719-721.

Safe S. 1976. Overview of analytical identification and spectroscopic properties. In: National Conference on Polychlorinated Biphenyls, Chicago, 1975. EPA-560/6-75-004. Washington, D.C.: Environmental Protection Agency, pp. 94-102 (cited in IARC 1978).

Safe S. 1980. Affidavit dated April 23, 1980. University of Guelph, Guelph, Ontario, Canada.

Safe S. 1980. Halogenated biphenyls, terphenyls, naphthalenes, dibenzodioxins and related products. Metabolism uptake, storage and bioaccumulation. *Toxicol Environ Health* 4:81-107.

Safe S, Bandiera S, Sawyer T, et al. 1985a. PCBs: Structure-function relationships and mechanism of action. *Environ Health Perspect* 60:47-56.

Safe S, Hutzinger O, Jones D. 1975. The mechanism of chlorobiphenyl metabolism. *J Agric Food Chem* 23:851-853.

Safe S, Safe L, Mullin M. 1985b. Polychlorinated biphenyls: Congener-specific analysis of a commercial mixture and a human milk extract. *J Agric Food Chem* 33:24-29.

Sager DB. 1983. Effect of postnatal exposure to polychlorinated biphenyls on adult male reproductive function. *Environ Res* 31(1):76-94.

Sahl JD, Crocker TT, Gordon RJ, Faeder EJ. 1985a. Polychlorinated biphenyl concentrations in the blood plasma of a selected sample of nonoccupationally exposed Southern California working adults. *Sci Total Environ* 46:9-18.

- Sahl JD, Crocker T, Gordon RJ, Faeder EJ. 1985b. Polychlorinated biphenyls in the blood of personnel from an electric utility. *J Occup Med* 27:639-643.
- \* Sanders OT, Zepp RL, Kirkpatrick RL. 1974. Effect of PCB ingestion on sleeping times, organ weights, food consumption, serum corticosterone and survival of albino mice. *Bull Environ Contam Toxicol* 12(4):394-399.
- SANSS (Structure and Nomenclature Search System). 1987. Chemical Information System (CIS) computer data base.
- Schaeffer E, Greim H, Goessner W. 1984. Pathology of chronic polychlorinated biphenyl (PCB) feeding in rats. *Toxicol Appl Pharmacol* 75:278-288.
- Schechter A, Tiernan T. 1985. Occupational exposure to polychlorinated dioxins, polychlorinated furans, polychlorinated biphenyls, and biphenylenes after an electrical panel and transformer accident in an office building in Binghamton, N.Y. *Environ Health Perspect* 60:305-313.
- Schmitt CJ, Zajicek JL, Ribick MA. 1985. National pesticide monitoring program. Residues of organochlorine chemicals in freshwater fish, 1980-1981. *Arch Environ Contam Toxicol* 14:225-260.
- Schneider JF, Bourne S, Boparai S. 1984. Parallel capillary column gas chromatography in the determination of chlorinated pesticides and PCBs. *J Chromatogr* 22(5):203-206.
- Schnellmann RG, Putnam CW, Sipes IG. 1983. Metabolism of 2,2',3,3',6,6'-hexachlorobiphenyl and 2,2',4,4',5,5'-hexachlorobiphenyl by human hepatic microsomes. *Biochem Pharmacol* 32:3233-3239 (cited in EPA 1988a).
- Schnellmann RG, Volp RF, Putnam CW, Sipes IG. 1984. The hydroxylation, dechlorination and glucuronidation of 4,4'-dichlorobiphenyl by human hepatic microsomes. *Biochem Pharmacol* 33:3503-3509 (cited in EPA 1988a).
- Schoeny R. 1982. Mutagenicity testing of chlorinated biphenyls and chlorinated dibenzofurans. *Mutat Res* 101:45-56 (cited in EPA 1988a).
- Schoeny RS, Smith CC, Loper JC. 1979. Non-mutagenicity for *Salmonella* of the chlorinated hydrocarbons Aroclor 1254, 1,2,4-trichlorobenzene, mirex and kepone. *Mutat Res* 68:125.
- Schwartz PM, Jacobson SW, Fein G, Jacobson JL, Price HA. 1983. Lake Michigan fish consumption as a source of polychlorinated biphenyls in human cord serum, maternal serum and milk. *Pub Amer J Public Health* 73(3):293-296.
- Sipes IG, McLain GE, Jr, Podolsky TL, Brown BR, Jr. 1978. Bioactivation of halothane: Correlation with hepatotoxicity. *Int Congr Serx-Excerpta Med* 440:238 (cited in EPA 1985a).

Sklarew DS, Girvin DC. 1987. Attenuation of polychlorinated biphenyls in soils. *Rev Environ Contam Toxicol* 98:1-41.

Smith AB, Schloemer J, Lowry LK, et al. 1981a. Cross-Sectional Medical Survey of a Group of Workers Occupationally Exposed to Polychlorinated Biphenyls (PCBs) at an Electrical Equipment Manufacturing Plant. Cincinnati, Ohio: National Institute for Occupational Safety and Health, Division of Surveillance, Hazard Evaluations and Field Studies, and Lipid Research Center, University of Cincinnati Medical Center (cited in Drill et al. 1981).

Smith AB, Schloemer J, Lowry LK, et al. 1981b. Cross-Sectional Medical Survey of Two Groups of Workers Occupationally Exposed to Polychlorinated Biphenyls (PCBs) in the Maintenance, Repair, and Overhaul of Electrical Transformers. Cincinnati, Ohio: National Institute for Occupational Safety and Health, Division of Surveillance, Hazard Evaluations and Field Studies, and Lipid Research Center, University of Cincinnati Medical Center (cited in Drill et al. 1981).

Smith AB, Schloemer J, Lowry LK, et al. 1981c. Metabolic and Health Consequences of Occupational Exposure to Polychlorinated Biphenyls (PCBs). Cincinnati, Ohio: National Institute for Occupational Safety and Health, Division of Surveillance, Hazard Evaluations and Field Studies, and Lipid Research Center, University of Cincinnati Medical Center (cited in Drill et al. 1981).

Smith AB, Schloemer J, Lowry LK, et al. 1982. Metabolic and health consequences of occupational exposure to polychlorinated biphenyls. *Br J Ind Med* 39:361-369 (cited in Wolff 1985, Kreiss 1985).

Smrek AL, Needham LL. 1982. Simplified cleanup procedures for adipose tissue containing polychlorinated biphenyls, DDT, and DDT metabolites. *Bull Environ Contam Toxicol* 28:718-722.

Sparling J, Fung D, Safe S. 1980. Bromo- and chlorobiphenyl metabolism: GC/MS identification of urinary metabolites and the effects of structure on their rates of excretion. *Biomed Mass Spectrom* 7:13-20 (cited in EPA 1988a).

Spencer F. 1982. An assessment of the reproductive toxic potential of Aroclor 1254 in female Sprague-Dawley rats. *Bull Environ Contam Toxicol* 28(3):290-297.

Steinberg KK, Freni-Titulaer LWJ, Rogers TN, et al. 1986. Effects of polychlorinated biphenyls and lipemia on serum analytes. *J Toxicol Environ Health* 19:369-381.

Stone PJ Ed. 1981. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, D.C.: Bureau of Explosives, Association of American Railroads, p. 418.

Sundstrom G, Hutzinger D, Safe S. 1976a. The metabolism of chlorobiphenyls - A review. *Chemosphere* 5:267.

- Sundstrom G, Hutzinger D, Safe S. 1976b. The metabolism of 2,2',4,4',5,5'-hexachlorobiphenyl by rabbits, rats and mice. *Chemosphere* 4:249 (cited in EPA 1988a).
- Swackhamer DL, Armstrong DE. 1986. Estimation of the atmospheric and nonatmospheric contributions and losses of polychlorinated biphenyls for Lake Michigan on the basis of sediment records of remote lakes. *Environ Sci Technol* 20(9):879-883.
- Tanabe S, Nakagawa Y, Tatsukawa R. 1981. Absorption efficiency and biological half-life of individual chlorobiphenyls in rats treated chlorobiphenyl products. *Agric Biol Chem* 45:717-726 (cited in EPA 1988a).
- Tanabe S, Hidaka H, Tatsukawa R. 1983. PCBs and chlorinated hydrocarbon pesticides in Antarctic atmosphere and hydrosphere. *Chemosphere* 12:277-288.
- Tanabe S, Tanaka H, Tatsukawa R. 1984. Polychlorobiphenyls, DDTs and hexachlorocyclohexane isomers in the western North Pacific ecosystem. *Arch Environ Contam Toxicol* 13:731-738.
- Tatematsu M, Nakanishi K, Murasaki G, Miyata Y, Hirose M, Ito N. 1979. Enhancing effect of inducers of liver microsomal enzymes on induction of hyperplastic liver nodules by *N*-2-fluorenylacetylamide in rats. *J Nat Cancer Inst* 63(6):1411-1416 (cited in EPA 1985a).
- Taylor PR, Lawrence CE, Hwang HL, Paulson AS. 1984. Polychlorinated biphenyls: Influence on birthweight and gestation. *Am J Public Health* 74(10):1153-1154.
- \* Thomas PT, Hinsdill RD. 1978. Effect of polychlorinated biphenyls on the immune responses of rhesus monkeys and mice. *Toxicol Appl Pharmacol* 44:41-51.
- Thomas RL, Frank R. 1981. PCBs in sediment and fluvial suspended solids in the Great Lakes. In: Mackay D, et al., eds. *Phys Behav PCDs Great Lakes*. Ann Arbor, Mich: Ann Arbor Science, pp. 245-267.
- Tiernan TO, Taylor ML, Garret JH, et al. 1983. PCDDs, PCDFs and related compounds in the effluents from combustion processes. *Chemosphere* 12:595-606.
- Tiernan TO, Taylor ML, Garret JH, et al. 1985. Sources and fate of polychlorinated dibenzodioxins, dibenzofurans and related compounds in human environments. *Environ Health Perspect* 59:145-58.
- \* Treon JF, Cleveland FP, Cappel JW, Atchley RW. 1956. The toxicity of the vapours of Aroclor 1242 and Aroclor 1254. *Am Ind Hyg Assoc Q* 17:204-213.

USITC (U.S. International Trade Commission). 1978. Imports of benzenoid chemicals and products 1977. USITC Publ 900. Washington, D.C.: USITC, p. 26.

USITC (U.S. International Trade Commission). 1979. Imports of benzenoid chemicals and products 1978. USITC Publ 990. Washington, D.C.: USITC, p. 26.

USITC (U.S. International Trade Commission). 1980. Imports of benzenoid chemicals and products 1979. USITC Publ 1083. Washington, D.C.: USITC, p. 28.

USITC (U.S. International Trade Commission). 1982. Imports of benzenoid chemicals and products 1981. USITC Publ 1272. Washington, D.C.: USITC, p. 25.

Van Duuran BL. 1981. Cocarcinogens and tumor promoters and their environmental importance. *J Environ Pathol Toxicol* 4:959-960.

Vernon AA, et al.\*\* 1981. High levels of polychlorinated biphenyls in serum specimens, Kansas. Internal report ELI-80-23-2, Centers for Disease Control, Atlanta, November 16, 1981 (cited in Kreiss 1985).

View data base. 1989. Agency for Toxic Substances and Disease Registry (ATSDR), Atlanta, Georgia: Office of External Affairs, Exposure and Disease Registry Branch, February 1989.

\* Villeneuve DC, Grant DL, Khera K, Clegg DJ, Baer H, Phillips WEJ. 1971. The fetotoxicity of a polychlorinated biphenyl mixture (Aroclor 1254) in the rabbit and in the rat. *Environ Physiol* 1:67-71.

Villeneuve DC, Grant DL, Phillips WEJ. 1972. Modification of pentobarbital sleeping times in rats following chronic PCB ingestion. *Bull Environ Contam Toxicol* 7:264 (cited in EPA 1985a).

\* Vos JG, Beems RB. 1971. Dermal toxicity studies of technical polychlorinated biphenyls and fractions thereof in rabbits. *Toxicol Appl Pharmacol* 19:317-633.

Vos JG, Notenboom-Ram E. 1972. Comparative toxicity study of 2,4,5, 2',4',5'-hexachlorobiphenyl and a polychlorinated biphenyl mixture in rabbits. *Toxicol Appl Pharmacol* 23:563-578.

Vos JG, deRoij T. 1972. Immunosuppressive activity of a polychlorinated biphenyl preparation on the humoral immune response in guinea pigs. *Toxicol Appl Pharmacol* 21:549-555.

Vos JG, van Genderen H. 1973. Toxicological aspects of immunosuppression. In: Deichman WB, ed. *Pesticides in the Environment, A Continuing Controversy*. Miami, Fla.: Eighth International Conference on Toxicology and Occupational Medicine. New York: Intercontinental Medical Book Co. (cited in EPA 1988a).

- Ward JM. 1985. Proliferative lesions of the glandular stomach and liver in F344 rats fed diets containing Arclor 1254. *Environ Health Perspect* 60:89-95.
- Watanabe M, Sugahara T. 1981. Experimental formation of cleft palate in mice with polychlorinated biphenyls (PCB). *Toxicology* 19(1):49-53 (cited in EPA 1988a).
- Weant GE, McCormick GS. 1984. Nonindustrial sources of potential toxic substances and their applicability to source apportionment methods. EPA 450/4-84-003; NTIS PB84-231232. Research Triangle Park, N.C.: Environmental Protection Agency, pp. 36, 86.
- Welsch F. 1985. Effects of acute or chronic polychlorinated biphenyl ingestion on maternal metabolic homeostasis and on the manifestations of embryotoxicity caused by cyclophosphamide in mice. *Arch Toxicol* 27(2):104-113.
- Welty ER. 1983. Personal communication, August 8, 1983 (cited in Kreiss 1985).
- Wester RC, Bucks DAW, Maibach HI, Anderson J. 1983. Polychlorinated biphenyls (PCBs): Dermal absorption, systemic elimination and dermal wash efficiency. *J Toxicol Environ Health* 12:511-519.
- Wickizer TM, Brilliant LB, Copeland R, Tilden R. 1981. Polychlorinated biphenyl contamination of nursing mothers' milk in Michigan. *Am J Public Health* 71:132-137.
- Wolff MS. 1983. Occupational derived chemicals in breast milk. *Am J Ind Med* 4:259-281 (cited in EPA 1985a).
- Wolff MS. 1985. Occupational exposure to polychlorinated biphenyls (PCBs). *Environ Health Perspect* 60:133-138.
- Wolff MS, Fischbein A, Thornton J, Rice C, Lillis R, Selikoff IJ. 1982a. Body burden of polychlorinated biphenyls among persons employed in capacitor manufacturing. *Int Arch Occup Environ Health* 49:199-208 (cited in Kreiss 1985).
- Wolff MS, Thornton J, Fischbein A, Lillis R, Selikoff IJ. 1982b. Disposition of polychlorinated biphenyl congeners in occupationally exposed person. *Toxicol Appl Pharmacol* 62(2):294-306.
- Wyndham C, Devenish J, Safe S. 1976. The in vitro metabolism, macromolecular binding and bacterial mutagenicity of 4-chlorobiphenyl, a model PCB substrate. *Res Commun Chem Pathol Pharmacol* 15:563 (cited in EPA 1985a)
- Wyss PA, Muhleback S, Bickel MH. 1986. Long-term pharmacokinetics of 2,2',4,4',5,5'-hexachlorobiphenyl (6-CB) in rats with constant adipose tissue mass. *Drug Metab Dispos* 14:361-365 (cited in EPA 1988a).

Yakushiji T, Watanabe I, Kuwabara et al. 1978. Long-term studies of the excretion of polychlorinated bipheyls (PCBs) through the mother's milk of an occupationally-exposed worker. Arch Environ Toxicol 7:493-504 (cited in EPA 1988a).

Yoshimura H, Yamamoto HA. 1975. A novel route of excretion of 2,4,3',4'-tetrachlorobiphenyl in rats. Bull Environ Contam Toxicol 13:681-688 (Cited in EPA 1985a).

Yoshimura H, Yoshihara S. 1976. Toxicological aspects. II. The metabolic fate of PCBs and their toxicological evaluation. In: Higuchi K, ed. PCB Poisoning and Pollution. Tokyo: Kondansha Ltd, pp. 41-67 (cited in EPA 1985a)

Young SS. 1985. Letter to the editor. Toxicol Appl Pharmacol 78:321-322.

## 11. GLOSSARY

**Acute Exposure**--Exposure to a chemical for a duration of 14 days or less, as specified in the Toxicological Profiles.

**Bioconcentration Factor (BCF)**--The quotient of the concentration of a chemical in aquatic organisms at a specific time or during a discrete time period of exposure divided by the concentration in the surrounding water at the same time or during the same time period.

**Carcinogen**--A chemical capable of inducing cancer.

**Ceiling value (CL)**--A concentration of a substance that should not be exceeded, even instantaneously.

**Chronic Exposure**--Exposure to a chemical for 365 days or more, as specified in the Toxicological Profiles.

**Developmental Toxicity**--The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism.

**Embryotoxicity and Fetotoxicity**--Any toxic effect on the conceptus as a result of prenatal exposure to a chemical; the distinguishing feature between the two terms is the stage of development during which the insult occurred. The terms, as used here, include malformations and variations, altered growth, and in utero death.

**Frank Effect Level (FEL)**--That level of exposure which produces a statistically or biologically significant increase in frequency or severity of unmistakable adverse effects, such as irreversible functional impairment or mortality, in an exposed population when compared with its appropriate control.

**EPA Health Advisory**--An estimate of acceptable drinking water levels for a chemical substance based on health effects information. A health advisory is not a legally enforceable federal standard, but serves as technical guidance to assist federal, state, and local officials.

**Immediately Dangerous to Life or Health (IDLH)**--The maximum environmental concentration of a contaminant from which one could escape within 30 min without any escape-impairing symptoms or irreversible health effects.

**Intermediate Exposure**--Exposure to a chemical for a duration of 15-364 days, as specified in the Toxicological Profiles.

**Immunologic Toxicity**--The occurrence of adverse effects on the immune system that may result from exposure to environmental agents such as chemicals.

**In vitro**--Isolated from the living organism and artificially maintained, as in a test tube.

**In vivo**--Occurring within the living organism.

**Key Study**--An animal or human toxicological study that best illustrates the nature of the adverse effects produced and the doses associated with those effects.

**Lethal Concentration(L0) (LCLO)**--The lowest concentration of a chemical in air which has been reported to have caused death in humans or animals.

**Lethal Concentration(50) (LC50)**--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

**Lethal Dose(L0) (LDLO)**--The lowest dose of a chemical introduced by a route other than inhalation that is expected to have caused death in humans or animals.

**Lethal Dose(50) (LD50)**--The dose of a chemical which has been calculated to cause death in 50% of a defined experimental animal population.

**Lowest-Observed-Adverse-Effect Level (LOAEL)**--The lowest dose of chemical in a study or group of studies which produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

**Lowest-Observed-Effect Level (LOEL)**--The lowest dose of chemical in a study or group of studies which produces statistically or biologically significant increases in frequency or severity of effects between the exposed population and its appropriate control.

**Malformations**--Permanent structural changes that may adversely affect survival, development, or function.

**Minimal Risk Level**--An estimate of daily human exposure to a chemical that is likely to be without an appreciable risk of deleterious effects (noncancerous) over a specified duration of exposure.

**Mutagen**--A substance that causes mutations. A mutation is a change in the genetic material in a body cell. Mutations can lead to birth defects, miscarriages, or cancer.

**Neurotoxicity**--The occurrence of adverse effects on the nervous system following exposure to a chemical.

**No-Observed-Adverse-Effect Level (NOAEL)**--That dose of chemical at which there are no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

**No-Observed-Effect Level (NOEL)**--That dose of chemical at which there are no statistically or biologically significant increases in frequency or severity of effects seen between the exposed population and its appropriate control.

**Permissible Exposure Limit (PEL)**--An allowable exposure level in workplace air averaged over an 8-h shift.

$q_1^*$ --The upper-bound estimate of the low-dose slope of the dose-response curve as determined by the multistage procedure. The  $q_1^*$  can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually  $\mu\text{g}/\text{L}$  for water,  $\text{mg}/\text{kg}/\text{day}$  for food, and  $\mu\text{g}/\text{m}^3$  for air).

**Reference Dose (RfD)**--An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure of the human population to a potential hazard that is likely to be without risk of deleterious effects during a lifetime. The RfD is operationally derived from the NOAEL (from animal and human studies) by a consistent application of uncertainty factors that reflect various types of data used to estimate RfDs and an additional modifying factor, which is based on a professional judgment of the entire database on the chemical. The RfDs are not applicable to nonthreshold effects such as cancer.

**Reportable Quantity (RQ)**--The quantity of a hazardous substance that is considered reportable under CERCLA. Reportable quantities are: (1) 1 lb or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Sect. 311 of the Clean Water Act. Quantities are measured over a 24-h period.

**Reproductive Toxicity**--The occurrence of adverse effects on the reproductive system that may result from exposure to a chemical. The toxicity may be directed to the reproductive organs and/or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of this system.

**Short-Term Exposure Limit (STEL)**--The maximum concentration to which workers can be exposed for up to 15 min continually. No more than four excursions are allowed per day, and there must be at least 60 min between exposure periods. The daily TLV-TWA may not be exceeded.

**Target Organ Toxicity**--This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

**Teratogen**--A chemical that causes structural defects that affect the development of an organism.

**Threshold Limit Value (TLV)**--A concentration of a substance to which most workers can be exposed without adverse effect. The TLV may be expressed as a TWA, as a STEL, or as a CL.

**Time-weighted Average (TWA)**--An allowable exposure concentration averaged over a normal 8-h workday or 40-h workweek.

**Uncertainty Factor (UF)**--A factor used in operationally deriving the RfD from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population, (2) the uncertainty in extrapolating animal data to the case of humans, (3) the uncertainty in extrapolating from data obtained in a study that is of less than lifetime exposure, and (4) the uncertainty in using LOAEL data rather than NOAEL data. Usually each of these factors is set equal to 10.

**APPENDIX: PEER REVIEW**

A peer review panel was assembled for PCBs. The panel consisted of the following members: Dr. Rolf Hartung, Chairman, Toxicology Program, University of Michigan; Dr. James Olson, Associate Professor of Pharmacology and Therapeutics, SUNY Buffalo; Dr. Shane Que Hee, Associate Professor of Environmental Health, University of Cincinnati Medical Center. These experts collectively have knowledge of PCB's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in the Superfund Amendments and Reauthorization Act of 1986, Section 110.

A joint panel of scientists from ATSDR and EPA has reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply their approval of the profile's final content. The responsibility for the content of this profile lies with the Agency for Toxic Substances and Disease Registry.

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