



Polychlorinated biphenyls (PCBs)

CASRN 1336-36-3

(06/01/1997)

Contents

[I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE \(RfD\)](#)

[I.B. REFERENCE CONCENTRATION FOR CHRONIC
INHALATION EXPOSURE \(RfC\)](#)

[II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE](#)

[VI. BIBLIOGRAPHY](#)

[VII. REVISION HISTORY](#)

[VIII. SYNONYMS](#)

0294

Polychlorinated biphenyls (PCBs); CASRN 1336-36-3 (06/01/1997)

Health assessment information on a chemical substance is included in IRIS only after a comprehensive review of chronic toxicity data by U.S. EPA health scientists from several Program Offices and the Office of Research and Development. The summaries presented in Sections I and II represent a consensus reached in the review process. Background information and explanations of the methods used to derive the values given in IRIS are provided in the Background Documents.

STATUS OF DATA FOR PCBs

File On-Line 05/01/1989

Category (section)

Status

Last Revised

Oral RfD Assessment (I.A.)	message	06/01/1994
Inhalation RfC Assessment (I.B.)	no data	
Carcinogenicity Assessment (II.)	on-line	06/01/1997

I. CHRONIC HEALTH HAZARD ASSESSMENTS FOR NONCARCINOGENIC EFFECTS

I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name -- Polychlorinated biphenyls (PCBs)
CASRN -- 1336-36-3

I.A.1. ORAL RfD SUMMARY

Please check the following individual aroclor files for RfD assessments:
Aroclor 1016, Aroclor 1248, Aroclor 1254, Aroclor 1260.

I.B. REFERENCE CONCENTRATION FOR CHRONIC INHALATION EXPOSURE (RfC)

Substance Name -- Polychlorinated biphenyls (PCBs)
CASRN -- 1336-36-3

Not available at this time.

II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE

Substance Name -- Polychlorinated biphenyls (PCBs)

CASRN -- 1336-36-3

Last Revised -- 06/01/1997

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

II.A. EVIDENCE FOR CLASSIFICATION AS TO HUMAN CARCINOGENICITY

II.A.1. WEIGHT-OF-EVIDENCE CLASSIFICATION

Classification -- B2; probable human carcinogen

Basis -- A 1996 study found liver tumors in female rats exposed to Aroclors 1260, 1254, 1242, and 1016, and in male rats exposed to 1260. These mixtures contain overlapping groups of congeners that, together, span the range of congeners most often found in environmental mixtures. Earlier studies found high, statistically significant incidences of liver tumors in rats ingesting Aroclor 1260 or Clophen A 60 (Kimbrough et al., 1975; Norback and Weltman, 1985; Schaeffer et al., 1984). Mechanistic studies are beginning to identify several congeners that have dioxin-like activity and may promote tumors by

different modes of action. PCBs are absorbed through ingestion, inhalation, and dermal exposure, after which they are transported similarly through the circulation. This provides a reasonable basis for expecting similar internal effects from different routes of environmental exposure. Information on relative absorption rates suggests that differences in toxicity across exposure routes are small. The human studies are being updated; currently available evidence is inadequate, but suggestive.

II.A.2. HUMAN CARCINOGENICITY DATA

Inadequate. A cohort study by Bertazzi et al. (1987) analyzed cancer mortality among workers at a capacitor manufacturing plant in Italy. PCB mixtures with 54%, then 42% chlorine were used through 1980. The cohort included 2100 workers (544 males and 1556 females) employed at least 1 week. At the end of followup in 1982, there were 64 deaths reported, 26 from cancer. In males, a statistically significant increase in death from gastrointestinal tract cancer was reported, compared with national and local rates (6 observed, 1.7 expected using national rates, SMR=346, CI=141-721; 2.2 expected using local rates, SMR=274, CI=112-572). In females, a statistically significant excess risk of death from hematologic cancer was reported, compared with local, but not national, rates (4 observed, 1.1 expected, SMR=377, CI=115-877). Analyses by exposure duration, latency, and year of first exposure revealed no trend; however, the numbers are small.

A cohort study by Brown (1987) analyzed cancer mortality among workers at two capacitor manufacturing plants in New York and Massachusetts. At both plants the Aroclor mixture being used changed twice, from 1254 to 1242 to 1016. The cohort included 2588 workers (1270 males and 1318 females) employed at least 3 months in areas of the plants considered to have potential for heavy exposure to PCBs. At the end of followup in 1982, there were 295 deaths reported, 62 from cancer. Compared with national rates, a statistically significant increase in death from cancer of the liver, gall bladder, and biliary tract was reported (5 observed, 1.9 expected, SMR=263, $p < 0.05$). Four of these five occurred among females employed at the Massachusetts plant. Analyses by time since first employment or length of employment revealed no trend; however, the numbers are small.

A cohort study by Sinks et al. (1992) analyzed cancer mortality among workers at a capacitor manufacturing plant in Indiana. Aroclor 1242, then 1016, had been used. The cohort included 3588 workers (2742 white males and 846 white females) employed at least 1 day. At the end of followup in 1986, there were 192 deaths reported, 54 from cancer. Workers were classified into five exposure zones based on distance from the impregnation ovens. Compared with national rates, a statistically significant excess risk of death from skin cancer was reported (8 observed, 2.0 expected, SMR=410, CI=180-800); all were malignant melanomas. A proportional hazards analysis revealed no pattern of association with exposure zone; however, the numbers are small.

Other occupational studies by NIOSH (1977), Gustavsson et al. (1986) and Shalat et al. (1989) looked for an association between occupational PCB exposure and cancer mortality. Because of small sample sizes, brief followup

periods, and confounding exposures to other potential carcinogens, these studies are inconclusive.

Accidental ingestion: Serious adverse health effects, including liver cancer and skin disorders, have been observed in humans who consumed rice oil contaminated with PCBs in the "Yusho" incident in Japan or the "Yu-Cheng" incident in Taiwan. These effects have been attributed, at least in part, to heating of the PCBs and rice oil, causing formation of chlorinated dibenzofurans, which have the same mode of action as some PCB congeners (ATSDR, 1993; Safe, 1994).

II.A.3. ANIMAL CARCINOGENICITY DATA

Sufficient. Brunner et al. (1996) compared carcinogenicity across different Aroclors, dose levels, and sexes. Groups of 50 male or female Sprague-Dawley rats were fed diets with 25, 50, or 100 ppm Aroclor 1260 or 1254; 50 or 100 ppm Aroclor 1242; or 50, 100, or 200 ppm Aroclor 1016. There were 100 controls of each sex. The animals were killed at 104 weeks, after which a complete histopathologic evaluation was performed for control and high-dose groups; histopathologic evaluations of liver, brain, mammary gland, and male thyroid gland were also performed for low- and mid-dose groups.

Statistically significant increased incidences of liver adenomas or carcinomas were found in female rats for all Aroclors and in male rats for Aroclor 1260. Some of these tumors were hepatocholangiomas, a rare bile duct tumor seldom seen in control rats.

To investigate tumor progression after exposure has stopped, groups of 24 female rats were exposed for 52 weeks, then exposure was discontinued for an additional 52 weeks before the rats were killed. For Aroclors 1254 and 1242, tumor incidences from the stop study were approximately half those of the lifetime study; that is, nearly proportional to exposure duration. In contrast, stop-study tumor incidences were zero for Aroclor 1016, while for Aroclor 1260 they were generally greater than half those of the lifetime study. For 100 ppm Aroclor 1260, the stop study incidence was greater than that of the lifetime study, 71 vs. 48 percent.

Thyroid gland follicular cell adenomas or carcinomas were increased in males for all Aroclors; significant dose trends were noted for Aroclors 1254 and 1242. The increases did not continue proportionately above the lowest dose. No trends were apparent in females.

In female rats, the incidence of mammary tumors was decreased with lifetime exposure to Aroclor 1254 and, to a lesser extent, to 1260 or 1242; this result was not observed for Aroclor 1016. Decreases did not occur for any Aroclor in the stop study. The first mammary tumor was observed at a later age in the dosed groups.

Kimbrough et al. (1975) fed groups of 200 female Sherman rats diets with 0 or 100 ppm Aroclor 1260 for about 21 months. Six weeks later the rats were killed and their tissues were examined. Hepatocellular carcinomas and

neoplastic nodules were significantly increased in rats fed Aroclor 1260.

The National Cancer Institute (NCI, 1978) fed groups of 24 male or female Fischer 344 rats diets with 0, 25, 50, or 100 ppm Aroclor 1254 for 104-105 weeks (24 months). Then the rats were killed and their tissues were examined. The combined incidence of leukemia and lymphoma in males was significantly increased by the Cochran-Armitage trend test; however, since Fisher exact tests were not also significant, NCI did not consider this result clearly related to Aroclor 1254. Hepatocellular adenomas and carcinomas were increased. Morgan et al. (1981) and Ward (1985) reevaluated gastric lesions from this study and found 6 adenocarcinomas in 144 exposed rats. This result is statistically significant, as gastric adenocarcinomas had occurred in only 1 of 3548 control male and female Fischer 344 rats in the NCI testing program. Intestinal metaplasia in exposed rats differed morphologically from controls, suggesting Aroclor 1254 can act as a tumor initiator.

Schaeffer et al. (1984) fed male weanling Wistar rats a standard diet for 8 weeks, then divided them into three groups. One group was fed the basic diet; for the other groups 100 ppm Clophen A 30 or A 60 was added. Rats were killed at 801 832 days (26.3 27.3 months) and were examined for lesions in the liver and some other tissues. For both mixtures, preneoplastic liver lesions were observed after 500 days (16.4 months) and hepatocellular carcinomas after 700 days (23 months) in rats dying before the end of the study. The investigators concluded, "Clophen A 60 had a definite, and Clophen A 30 a weak, carcinogenic effect on rat liver."

Norback and Weltman (1985) fed groups of male and female Sprague-Dawley rats diets of 0 or 100 ppm Aroclor 1260 for 16 months; the latter dose was reduced to 50 ppm for 8 more months. After 5 additional months on the control diet, the rats were killed and their livers were examined. Partial hepatectomy was performed on some rats at 1, 3, 6, 9, 12, 15, 18, and 24 months to evaluate sequential morphologic changes. In males and females fed Aroclor 1260, liver foci appeared at 3 months, area lesions at 6 months, neoplastic nodules at 12 months, trabecular carcinomas at 15 months, and adenocarcinomas at 24 months, demonstrating progression of liver lesions to carcinomas. By 29 months, 91% of females had liver carcinomas and 95% had carcinomas or neoplastic nodules; incidences in males were smaller, 4% and 15%, respectively. Vater et al. (1995) obtained individual animal results to determine whether the partial hepatectomies, which exert a strong proliferative effect on the remaining tissue, affected the incidence of liver tumors. They reported that the hepatectomies did not increase the tumor incidence. Among females fed Aroclor 1260, liver tumors developed in 4 of 7 animals with hepatectomies and 37 of 39 without hepatectomies; no liver tumors developed in controls or males with hepatectomies.

Moore et al. (1994) reevaluated the preceding rat liver findings (Kimbrough et al., 1975; NCI, 1978; Schaeffer et al., 1984; Norback and Weltman, 1985) using criteria and nomenclature that had changed to reflect new understanding of mechanisms of toxicity and carcinogenesis. The reevaluation found somewhat fewer tumors than did the original investigators. The apparent increase for Clophen A 30 (Schaeffer et al., 1984) is no longer statistically significant.

II.A.4. SUPPORTING DATA FOR CARCINOGENICITY

Several studies of less-than-lifetime exposure are supportive of a carcinogenic response (Kimbrough et al., 1972; Kimbrough and Linder, 1974; Kimura and Baba, 1973; Ito et al., 1973, 1974; Rao and Banerji, 1988).

PCBs give generally negative results in tests of genetic activity (ATSDR, 1993), implying that PCBs induce tumors primarily through modes of action that do not involve gene mutation. Initiation-promotion studies for several commercial PCB mixtures and congeners show tumor promoting activity in liver and lung; these studies are beginning to identify a subset of mixture components that may be significant contributors to cancer induction (Silberhorn et al., 1990). Toxicity of some PCB congeners is correlated with induction of mixed-function oxidases; some congeners are phenobarbital-type inducers, others are 3-methylcholanthrene-type inducers, and some have mixed inducing properties (McFarland and Clarke, 1989). The latter two groups most resemble 2,3,7,8-tetrachlorodibenzo-p-dioxin in structure and toxicity.

Studies of structurally related agents: Studies of 2,3,7,8-tetrachlorodibenzo-p-dioxin and a polybrominated biphenyl (PBB) mixture are summarized here because the pattern of tumors found by Brunner et al. (1996) mimics the tumors induced in rats by these structurally related agents. The National Toxicology Program (NTP, 1982) exposed groups of 50 male or female Osborne-Mendel rats by gavage to 0, 1.4, 7.1, or 71 ng/kg-day 2,3,7,8-tetrachlorodibenzo-p-dioxin for 2 years. Similar to the Brunner et al. (1996) study, liver tumors were increased in female rats and thyroid gland follicular cell tumors were increased in male rats. Mammary tumors were not, however, decreased in dosed female rats. In another study, NTP (1983) exposed groups of 51 male or female Fischer 344/N rats by gavage to 0, 0.1, 0.3, 1, 3, or 10 mg/kg-day of a PBB mixture ("Firemaster FF 1") for 6 months, then exposure was discontinued for 23 months before the animals were killed. Statistically significant increased incidences of liver tumors were found in male and female rats. Dose-related increased incidences of cholangiocarcinomas were found in male and female rats.

II.B. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM ORAL EXPOSURE

II.B.1. SUMMARY OF RISK ESTIMATES

Oral Slope Factor -- See txt

Drinking Water Unit Risk -- See txt

Extrapolation Method -- Linear extrapolation below LED10s (U.S. EPA, 1996b)

Drinking Water Concentrations at Specified Risk Levels:

Risk Level	Concentration
-----	-----
E-4 (1 in 10,000)	See txt
E-5 (1 in 100,000)	See txt
E-6 (1 in 1,000,000)	See txt

II.B.2. DOSE-RESPONSE DATA (CARCINOGENICITY, ORAL EXPOSURE)

Tumor Type -- Liver hepatocellular adenomas, carcinomas, cholangiomas, or cholangiocarcinomas

Test Animals -- Female Sprague-Dawley rats

Route -- Diet

Reference -- Brunner et al., 1996; Norback and Weltman, 1985

	Administered Dose (ppm)	Human Equivalent Dose (mg/kg)/day	Tumor Incidence
	-----	-----	-----
Aroclor 1260	0	0	1/85
	25	0.35	10/49
	50	0.72	11/45
	100	1.52	24/50
Aroclor 1254	0	0	1/85
	25	0.36	19/45
	50	0.76	28/49
	100	1.59	28/49
Aroclor 1242	0	0	1/85
	50	0.75	11/49
	100	1.53	15/45
Aroclor 1016	0	0	1/85
	50	0.72	1/48
	100	1.43	7/45
	200	2.99	6/50
Aroclor 1260 (Norback and Weltman, 1985)	0	0.75	1/45

II.B.3. ADDITIONAL COMMENTS (CARCINOGENICITY, ORAL EXPOSURE)

The cancer potency of PCB mixtures is determined using a tiered approach that depends on the information available. The following tier descriptions discuss all environmental exposure routes:

TIERS OF HUMAN SLOPE FACTORS FOR ENVIRONMENTAL PCBs

HIGH RISK AND PERSISTENCE

Upper-bound slope factor: 2.0 per (mg/kg)/day
Central-estimate slope factor: 1.0 per (mg/kg)/day

Criteria for use:

- Food chain exposure
- Sediment or soil ingestion
- Dust or aerosol inhalation
- Dermal exposure, if an absorption factor has been applied
- Presence of dioxin-like, tumor-promoting, or persistent congeners
- Early-life exposure (all pathways and mixtures)

LOW RISK AND PERSISTENCE

Upper-bound slope factor: 0.4 per (mg/kg)/day
Central-estimate slope factor: 0.3 per (mg/kg)/day

Criteria for use:

- Ingestion of water-soluble congeners
- Inhalation of evaporated congeners
- Dermal exposure, if no absorption factor has been applied

LOWEST RISK AND PERSISTENCE

Upper-bound slope factor: 0.07 per (mg/kg)/day
Central-estimate slope factor: 0.04 per (mg/kg)/day

Criteria for use: Congener or isomer analyses verify that congeners with more than 4 chlorines comprise less than 1/2% of total PCBs.

Slope factors are multiplied by lifetime average daily doses to estimate the cancer risk. SAMPLE CALCULATIONS ARE GIVEN IN U.S. EPA (1996a). Although PCB exposures are often characterized in terms of Aroclors, this can be both imprecise and inappropriate. Total PCBs or congener or isomer analyses are recommended.

When congener concentrations are available, the slope-factor approach can

be supplemented by analysis of dioxin TEQs to evaluate dioxin-like toxicity. Risks from dioxin-like congeners (evaluated using dioxin TEQs) would be added to risks from the rest of the mixture (evaluated using slope factors applied to total PCBs reduced by the amount of dioxin-like congeners). SAMPLE CALCULATIONS ARE GIVEN IN U.S. EPA (1996a).

Depending on the specific application, either central estimates or upper bounds can be appropriate. Central estimates describe a typical individual's risk, while upper bounds provide assurance that this risk is not likely to be underestimated if the underlying model is correct. The upper bounds calculated in this assessment reflect study design and provide no information about sensitive individuals or groups. Central estimates are useful for estimating aggregate risk across a population. Central estimates are used for comparing or ranking environmental hazards, while upper bounds provide information about the precision of the comparison or ranking.

Some PCBs persist in the body and retain biological activity after exposure stops (Anderson et al., 1991a). Compared with the current default practice of assuming that less-than-lifetime effects are proportional to exposure duration, rats exposed to a persistent mixture (Aroclor 1260) had more tumors, while rats exposed to a less persistent mixture (Aroclor 1016) had fewer tumors (Brunner et al., 1996). Thus there may be greater-than-proportional effects from less-than-lifetime exposure, especially for persistent mixtures and for early-life exposures.

Highly exposed populations include some nursing infants and consumers of game fish, game animals, or products of animals contaminated through the food chain. Highly sensitive populations include people with decreased liver function and infants (Calabrese and Sorenson, 1977).

Because of the potential magnitude of early-life exposures (ATSDR, 1993; Dewailly et al., 1991, 1994), the possibility of greater perinatal sensitivity (Calabrese and Sorenson, 1977; Rao and Banerji, 1988), and the likelihood of interactions among thyroid and hormonal development, it is reasonable to conclude that early-life exposures may be associated with increased risks. Due to this potential for higher sensitivity early in life, the "high risk" tier is used for all early-life exposure.

It is crucial to recognize that commercial PCBs tested in laboratory animals were not subject to prior selective retention of persistent congeners through the food chain (that is, the rats were fed Aroclor mixtures, not environmental mixtures that had been bioaccumulated). Bioaccumulated PCBs appear to be more toxic than commercial PCBs (Aulerich et al., 1986; Hornshaw et al., 1983) and appear to be more persistent in the body (Hovinga et al., 1992). For exposure through the food chain, risks can be higher than those estimated in this assessment.

In calculating these estimates, administered doses were expressed as a lifetime daily average calculated from weekly body weight measurements and food consumption estimates (Keenan and Stickney, 1996). Doses were scaled from rats to humans using a factor based on the 3/4 power of relative body weight.

UNIT RISK ESTIMATE AND DRINKING WATER CONCENTRATIONS

For ingestion of water-soluble congeners, the middle-tier slope factor can be converted to a unit risk estimate and drinking water concentrations associated with specified risk levels.

Upper-bound slope factor: 0.4 per (mg/kg)/day
Upper-bound unit risk: 1 x 10⁻⁵ per ug/L

Drinking water concentration associated with a risk of:

1 in 10,000	10 ug/L
1 in 100,000	1 ug/L
1 in 1,000,000	0.1 ug/L

These estimates should not be used if drinking water concentrations exceed 1000 ug/L, since above this concentration the dose-response curve in the experimental range may provide better estimates.

For food chain exposure or ingestion that includes contaminated sediment or soil, the slope factor for "high risk and persistence" should be used instead.

II.B.4. DISCUSSION OF CONFIDENCE (CARCINOGENICITY, ORAL EXPOSURE)

Joint consideration of cancer studies and environmental processes leads to a conclusion that environmental PCB mixtures are highly likely to pose a risk of cancer to humans. Although environmental mixtures have not been tested in cancer assays, this conclusion is supported by several complementary sources of information. Statistically significant, dose-related, increased incidences of liver tumors were induced in female rats by Aroclors 1260, 1254, 1242, and 1016 (Brunner et al., 1996). These mixtures contain overlapping groups of congeners that, together, span the range of congeners most frequently found in environmental mixtures. Several congeners have dioxin-like activity (Safe, 1994) and may promote tumors by different modes of action (Silberhorn et al., 1990); these congeners are found in environmental samples and in a variety of organisms, including humans (McFarland and Clarke, 1989).

The range of potency observed for commercial mixtures is used to represent the potency of environmental mixtures. The range reflects experimental uncertainty and variability of commercial mixtures, but not human heterogeneity or differences between commercial and environmental mixtures. Environmental processes alter mixtures through partitioning, transformation, and bioaccumulation, thereby decreasing or increasing toxicity. The overall effect can be considerable, and the range observed for commercial mixtures may underestimate the true range for environmental mixtures (Hutzinger et al., 1974; Callahan et al., 1979). Limiting the potency of environmental mixtures to the range observed for commercial mixtures reflects a decision to base potency estimates on experimental results, however uncertain, rather than apply safety factors to compensate for lack of information.

A tiered approach allows use of different kinds of information in

estimating the potency of environmental mixtures. When congener information is limited, exposure pathway is used to indicate whether environmental processes have decreased or increased a mixture's potency. Partitioning, transformation, and bioaccumulation have been extensively studied (Hutzinger et al., 1974; Callahan et al., 1979) and can be associated with exposure pathway, thus the use of exposure pathway to represent environmental processes increases confidence in the risks inferred for environmental mixtures. For example, evaporated or dissolved congeners tend to be lower in chlorine content than the original mixture; they tend also to be more inclined to metabolism and elimination and lower in persistence and toxicity. On the other hand, congeners adsorbed to sediment or soil tend to be higher in chlorine content and persistence, and bioaccumulated congeners ingested through the food chain tend to be highest of all. Rates of these processes vary over several orders of magnitude (Hutzinger et al., 1974; Callahan et al., 1979). When available, congener information is an important tool for refining a potency estimate that was based on exposure pathway.

Extrapolation to environmental levels is based on models that are linear at low doses. Low-dose-linear models are appropriate when a carcinogen acts in concert with other exposures and processes that cause a background incidence of cancer (Crump et al., 1976; Lutz, 1990). Even when the mode of action indicates a nonlinear dose-response curve in homogeneous animal populations, the presence of genetic and lifestyle factors in a heterogeneous human population tends to make the dose-response curve more linear (Lutz, 1990). This is because genetic and lifestyle factors contribute to a wider spread of human sensitivity, which extends and straightens the dose-response curve over a wider range.

Uncertainty around these estimates extends in both directions. The slope factor ranges primarily reflect mixture variability, and so are not necessarily appropriate for probabilistic analyses that attempt to describe model uncertainty and parameter uncertainty. Estimates based on animal studies benefit from controlled exposures and absence of confounding factors; however, there is uncertainty in extrapolating dose and response rates across species. Information is lacking to evaluate high-to-low-dose differences. PCBs are absorbed through ingestion, inhalation, and dermal exposure, after which they are transported similarly through the circulation (ATSDR, 1993). This provides a reasonable basis for expecting similar internal effects from different routes of environmental exposure. Information on relative absorption rates suggests that differences in toxicity across exposure routes are small. The principal uncertainty, though, is using commercial mixtures to make inferences about environmental mixtures.

When exposure involves the food chain, uncertainty extends principally in one direction: through the food chain, living organisms selectively bioaccumulate persistent congeners, but commercial mixtures tested in laboratory animals were not subject to prior selective retention of persistent congeners. Bioaccumulated PCBs appear to be more toxic than commercial PCBs (Aulerich et al., 1986; Hornshaw et al., 1983) and appear to be more persistent in the body (Hovinga et al., 1992). For exposure through the food chain, risks can be higher than those estimated in this assessment. Two highly exposed populations, nursing infants and consumers of contaminated game animals, are exposed through the food chain.

The dioxin-like nature of some PCBs raises a concern for cumulative

exposure, as dioxin-like congeners add to background exposure of other dioxin-like compounds and augment processes associated with dioxin toxicity. This weighs against considering PCB exposure in isolation or as an increment to a background exposure of zero. Confidence in this assessment's use of low-dose-linear models is enhanced when there is additivity to background exposures and processes (Crump et al, 1976; Lutz, 1990).

II.C. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM INHALATION EXPOSURE

II.C.1. SUMMARY OF RISK ESTIMATES

Inhalation Unit Risk -- See txt

Extrapolation Method -- Linear extrapolation below LED10s (U.S. EPA, 1996b)

Air Concentrations at Specified Risk Levels:

Risk Level	Concentration
-----	-----
E-4 (1 in 10,000)	See txt
E-5 (1 in 100,000)	See txt
E-6 (1 in 1,000,000)	See txt

II.C.2. DOSE-RESPONSE DATA (CARCINOGENICITY, INHALATION EXPOSURE)

See Dose-Response Data for oral exposure.

II.C.3. ADDITIONAL COMMENTS (CARCINOGENICITY, INHALATION EXPOSURE)

See Additional Comments for oral exposure.

For inhalation of evaporated congeners, the middle-tier slope factor can be converted to a unit risk estimate and ambient air concentrations associated with specified risk levels.

Upper-bound slope factor: 0.4 per (mg/kg)/day
Upper-bound unit risk: 1 x 10⁻⁴ per ug/cu.m

Ambient air concentration associated with a risk of:

1 in 10,000	1 ug/cu.m
1 in 100,000	0.1 ug/cu.m
1 in 1,000,000	0.01 ug/cu.m

These estimates should not be used if ambient air concentrations exceed 100 ug/cu.m, since above this concentration the dose-response curve in the experimental range may provide better estimates.

For inhalation of an aerosol or dust contaminated with PCBs, the slope factor for "high risk and persistence" should be used instead.

II.C.4. DISCUSSION OF CONFIDENCE (CARCINOGENICITY, INHALATION EXPOSURE)

See Discussion of Confidence for oral exposure. Information on relative absorption rates suggests that differences in toxicity across exposure routes are small.

II.D. EPA DOCUMENTATION, REVIEW, AND CONTACTS

II.D.1. EPA DOCUMENTATION

Source Document -- U.S. EPA, 1996a [Available from the Risk Information Hotline, Cincinnati OH. Telephone: (513)569-7254; FAX (513)569-7159)].

The source document and IRIS summary were considered at a public, external peer review workshop in May 1996. A workshop report was written by the review panel (U.S. EPA, 1996c). All comments have been carefully evaluated and considered in this IRIS summary. A record of these comments is summarized in the IRIS documentation files.

Other EPA Documentation -- U.S. EPA, 1988

II.D.2. REVIEW (CARCINOGENICITY ASSESSMENT)

Agency Work Group Review -- 08/22/1996

Verification Date -- 08/22/1996

II.D.3. U.S. EPA CONTACTS (CARCINOGENICITY ASSESSMENT)

Please contact the Risk Information Hotline for all questions concerning this assessment or IRIS, in general, at (513)569-7254 (phone), (513)569-7159 (FAX) or RIH.IRIS@EPAMAIL.EPA.GOV (internet address).

VI. BIBLIOGRAPHY

Substance Name -- Polychlorinated biphenyls (PCBs)
CASRN -- 1336-36-3
Last Revised -- 11/01/1996

VI.A. ORAL RfD REFERENCES

None

VI.B. INHALATION RfD REFERENCES

None

VI.C. CARCINOGENICITY ASSESSMENT REFERENCES

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

Anderson, L.M., S.D. Fox, D. Dixon, L.E. Beebe and H.J. Issaq. 1991. Long-term persistence of polychlorinated biphenyl congeners in blood and liver and elevation of liver aminopyrine demethylase activity after a single high dose of Aroclor 1254 to mice. *Environ. Toxicol. Chem.* 10: 681-690.

ATSDR (Agency for Toxic Substances and Disease Registry). 1993. Toxicological profile for polychlorinated biphenyls. ATSDR, Atlanta, GA. TP 92/16, update.

Aulerich, R.J., R.K. Ringer and J. Safronoff. 1986. Assessment of primary vs. secondary toxicity of Aroclor 1254 to mink. *Arch. Environ. Contam. Toxicol.* 15: 393-399.

Bahn, A.K., I. Rosenwaike, N. Herrmann, P. Grover, J. Stellman and K. O'Leary. 1976. Melanoma after exposure to PCB's. *New Engl. J. Med.* 295: 450.

Bahn, A.K., P. Grover, I. Rosenwaike, K. O'Leary and J. Stellman. 1977. Reply to letter from C. Lawrence entitled, "PCB? and melanoma". *New Eng. J. Med.* 296: 108.

Bertazzi, P.A., L. Riboldi, A. Pesatori, L. Radice and C. Zocchetti. 1987. Cancer mortality of capacitor manufacturing workers. *Am. J. Ind. Med.* 11(2): 165-176.

Brown, D.P. 1987. Mortality of workers exposed to polychlorinated biphenyls - An update. *Arch. Environ. Health.* 42(6): 333-339.

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

Brunner, M.J., T.M. Sullivan, A.W. Singer, et. al. 1996. An assessment of the chronic toxicity and oncogenicity of Aroclor-1016, Aroclor-1242, Aroclor-1254, and Aroclor-1260 administered in diet to rats. Study No. SC920192. Chronic toxicity and oncogenicity report. Battelle, Columbus OH.

Calabrese, E.J. and A.J. Sorenson. 1977. The health effects of PCBs with particular emphasis on human high risk groups. *Rev. Environ. Health.* 2: 285-304.

Callahan, M.A., M.W. Slimak, N.W. Gabel, et al. 1979. Water-related environmental fate of 129 priority pollutants, Vol. I, Ch. 36. U.S. EPA, Washington, DC. EPA 440/4 79 029a.

Crump, K.S., D.G. Hoel, C.H. Langley and R. Peto. 1976. Fundamental carcinogenic processes and their implications for low dose risk assessment. *Cancer Res.* 36: 2973-2979.

Dewailly, E., J.-P. Weber, S. Gingras and C. Laliberte. 1991. Coplanar PCBs in human milk in the province of Quebec, Canada: Are they more toxic than dioxin for breast fed infants? *Bull. Environ. Contam. Toxicol.* 47: 491-498.

Dewailly, E., J.J. Ryan, C. Laliberte, et al. 1994. Exposure of remote maritime populations to coplanar PCBs. *Environ. Health Perspect.* 102(Suppl. 1): 205-209.

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

Hornshaw, T.C., R.J. Aulerich and H.E. Johnson. 1983. Feeding Great Lakes fish to mink: Effects on mink and accumulation and elimination of PCBs by mink. *J. Toxicol. Environ. Health.* 11: 933-946.

Hovinga, M.E., M. Sowers and H.E.B. Humphrey. 1992. Historical changes in serum PCB and DDT levels in an environmentally-exposed cohort. *Arch. Environ. Contam. Toxicol.* 22: 362-366.

Hutzinger, O., S. Safe and V. Zitko. 1974. *The chemistry of PCB's.* CRC Press, Boca Raton, FL.

Ito, N., H. Nagasaki, M. Arai, S. Makiura, S. Sugihara and K. Hirao. 1973. Histopathologic studies on liver tumorigenesis induced in mice by technical polychlorinated biphenyls and its promoting effect on liver tumors induced by benzene hexachloride. *J. Natl. Cancer Inst.* 51(5): 1637-1646.

Ito, N., H. Nagasaki, S. Makiura and M. Arai. 1974. Histopathological studies on liver tumorigenesis in rats treated with polychlorinated biphenyls. *Gann.* 65: 545-549.

Keenan, R.E. and J.A. Stickney. 1996. ChemRisk, Portland, ME. Letter to J. Cogliano, U.S. EPA, Washington, DC. June 24.

Kimbrough, R.D. and R.E. Linder. 1974. Induction of adenofibrosis and hepatomas in the liver of BALB/cJ mice by polychlorinated biphenyls (Aroclor 1254). *J. Natl. Cancer Inst.* 53(2): 547-552.

Kimbrough, R.D., R.E. Linder and T.B. Gaines. 1972. Morphological changes in livers of rats fed polychlorinated biphenyls: Light microscopy and ultrastructure. *Arch. Environ. Health.* 25: 354-364.

Kimbrough, R.D., R.A. Squire, R.E. Linder, J.D. Strandberg, R.J. Montali and V.W. Burse. 1975. Induction of liver tumors in Sherman strain female rats by polychlorinated biphenyl Aroclor 1260. *J. Natl. Cancer Inst.* 55(6): 1453-1459.

Kimura, N.T. and T. Baba. 1973. Neoplastic changes in the rat liver induced by polychlorinated biphenyl. *Gann.* 64: 105-108.

Lutz, W.K. 1990. Dose-response relationship and low dose extrapolation in chemical carcinogenesis. *Carcinogenesis.* 11(8): 1243-1247.

McFarland, V.A. and J.U. Clarke. 1989. Environmental occurrence, abundance, and potential toxicity of polychlorinated biphenyl congeners: Considerations for a congener-specific analysis. *Environ. Health Perspect.* 81: 225-239.

Moore, J.A., J.F. Hardisty, D.A. Banas and M.A. Smith. 1994. A comparison of liver tumor diagnoses from seven PCB studies in rats. *Reg. Toxicol. Pharmacol.* 20: 362-370.

Morgan, R.W., J.M. Ward and P.E. Hartman. 1981. Aroclor 1254-induced intestinal metaplasia and adenocarcinoma in the glandular stomach of F344 rats. *Cancer Res.* 41: 5052-5059.

NTP (National Toxicology Program). 1982. Carcinogenesis bioassay of 2,3,7,8-tetrachlorodibenzo-p-dioxin (CAS no. 1746 01 6) in Osborne-Mendel rats and B6C3F1 mice (gavage study). NTP Tech. Rep. Ser. No. 209. Research Triangle Park, NC.

NTP (National Toxicology Program). 1983. Carcinogenesis studies of polybrominated biphenyl mixture (Firemaster FF 1) (CAS no. 67774 32 7) in F344/N rats and B6C3F1 mice (gavage studies). NTP Tech. Rep. Ser. No. 244. Research Triangle Park, NC.

NCI (National Cancer Institute). 1978. Bioassay of Aroclor 1254 for possible carcinogenicity. *Carcinogenesis Tech. Rep. Ser. No. 38.*

NIOSH (National Institute for Occupational Safety and Health). 1977. Criteria for a Recommended Standard . . . Occupational Exposure to Polychlorinated Biphenyls (PCBs). U.S. DHEW, PHS, CDC, Rockville, Md. Publ. No. 77-225.

Norback, D.H. and R.H. Weltman. 1985. Polychlorinated biphenyl induction of hepatocellular carcinoma in the Sprague-Dawley rat. *Environ. Health Perspect.* 60: 97-105.

Rao, C.V. and A.S. Banerji. 1988. Induction of liver tumors in male Wistar rats by feeding polychlorinated biphenyls (Aroclor 1260). *Cancer Lett.* 39: 59-67.

Safe, S. 1994. Polychlorinated biphenyls (PCBs): Environmental impact, biochemical and toxic responses, and implications for risk assessment. *Crit. Rev. Toxicol.* 24(2): 87-149.

Schaeffer, E., H. Greim and W. Goessner. 1984. Pathology of chronic polychlorinated biphenyl (PCB) feeding in rats. *Toxicol. Appl. Pharmacol.* 75: 278-288.

Shalat, S.L., L.D. True, L.E. Fleming and P.E. Pace. 1989. Kidney cancer in utility workers exposed to polychlorinated biphenyls (PCBs). *Br. J. Ind. Med.*

46(11): 823-824.

Silberhorn, E.M., H.P. Glauert and L.W. Robertson. 1990. Carcinogenicity of polyhalogenated biphenyls: PCBs and PBBs. Crit. Rev. Toxicol. 20(6): 439-496.

Sinks, T., G. Steele, A.B. Smith, K. Watkins and R.A. Shults. 1992. Mortality among workers exposed to polychlorinated biphenyls. Am. J. Epidemiol. 136(4): 389-398.

U.S. EPA. 1988. Drinking Water Criteria Document for Polychlorinated Biphenyls (PCBs). Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Drinking Water, Washington, DC.

U.S. EPA, 1996a. PCBs: Cancer Dose-Response Assessment and Application to Environmental Mixtures. Prepared by the National Center for Environmental Assessment, Washington DC.

U.S. EPA. 1996b. Proposed Guidelines for Carcinogen Risk Assessment; notice. Fed. Reg. 61(79): 17960-18011.

U.S. EPA. 1996c. Report on peer review workshop on "PCBs: Cancer-dose response assessment and application to environmental mixtures." National Center for Environmental Assessment, Washington, DC.

Vater, S.T., S.F. Velazquez and V.J. Cogliano. 1995. A case study of cancer data set combinations for PCBs. Reg. Toxicol. Pharmacol. 22: 2-10.

Ward, J.M. 1985. Proliferative lesions of the glandular stomach and liver in F344 rats fed diets containing Aroclor 1254. Environ. Health Perspect. 60: 89-95.

VII. REVISION HISTORY

Substance Name -- Polychlorinated biphenyls (PCBs)
CASRN -- 1336-36-3

Date	Section	Description
05/01/1989	II.	Carcinogen summary on-line
01/01/1990	II.	Text edited
01/01/1990	VI.	Bibliography on-line
01/01/1992	IV.	Regulatory Action section on-line

06/01/1994	I.A.	Message only
01/01/1996	II.	Note added to assessment
10/01/1996	II.	File replaced; cancer potency of mixtures addressed
11/01/1996	VI.C.	References revised
04/01/1997	III.,IV., V.	Drinking Water Health Advisories, EPA Regulatory Actions, and Supplementary Data were removed from IRIS on or before April 1997. IRIS users were directed to the appropriate EPA Program Offices for this information.
06/01/1997	II.C.3.	Units corrected in Upper-bound Unit Risk

VIII. SYNONYMS

Substance Name -- Polychlorinated biphenyls (PCBs)
CASRN -- 1336-36-3
Last Revised -- 05/01/1989

1336-36-3

AROCLOR

AROCLOR 1221

AROCLOR 1232

AROCLOR 1242

AROCLOR 1248

AROCLOR 1254

AROCLOR 1260

AROCLOR 1262

AROCLOR 1268

AROCLOR 2565

AROCLOR 4465

AROCLOR 5442

BIPHENYL, POLYCHLORO-
CHLOPHEN

CHLOREXTOL

CHLORINATED BIPHENYL

CHLORINATED DIPHENYL

CHLORINATED DIPHENYLENE

CHLORO BIPHENYL

CHLORO 1,1-BIPHENYL

CLOPHEN

DYKANOL

FENCLOR

INERTEEN

KANECHLOR

KANECHLOR 300

KANECHLOR 400

MONTAR

NOFLAMOL

PCB

PCBs
PHENOCHLOR
PHENOCLOR
POLYCHLORINATED BIPHENYL
Polychlorinated Biphenyls
POLYCHLOROBIPHENYL
PYRALENE
PYRANOL
SANTOTHERM
SANTOTHERM FR
SOVOL
THERMINOL FR-1
UN 2315
.

[IRIS Home Page](#)

[Substance File List](#)



**Send
Comments**



Search



**NCEA
Home Page**



**ORD
Home Page**



**EPA
Home Page**

Last updated: **5 May 1998**

URL: <http://www.epa.gov/iris/subst/0294.htm>