



61681

TOXICOLOGICAL PROFILES:

SELECTED PCBs

**Revised Responses to Public Comments on
Scientific and Technical Issues**

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**Contract No. 68-C8-0004
Task 6**

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May 17, 1988



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SELECTED PCBs

Revised Responses to Public Comments on Scientific and Technical Issues

A. COMMENTS PERTAINING TO THE WHOLE PROFILE

- * a) Submitter #45, comment 15, recognizes that ATSDR has been tasked by Congress to develop toxicological profiles, but questions "the purpose and poor quality of the PCB document in light of the fact that USEPA just released a new summary of the toxicological properties of PCBs in late 1987 (1987 draft drinking water quality document)".

RESPONSE: During the preparation of the Toxicological Profile on PCBs, SRC consulted the most recent draft of the Drinking Water Criteria Document (May 1987) available at the time. SRC has obtained the latest draft (April, 1988), which will be consulted during the revision of the profile.

- b) Submitter #3b, comment 97, concludes "Overall, this document represents a reasonably comprehensive compendium of information relevant to considerations of the public health risks attributable to exposure to PCBs although, in some instances, the literature review is incomplete. In particular, some of the most recent published reports (some of which included CDC collaboration) on biological monitoring and human health effects from chronic, low-level exposures have not been cited or discussed in the profile." Reports were not specified by the submitter in this comment.

RESPONSE: Relevant uncited reports, specified by this and other submitters in subsequent comments, will be added to the profile.

- c) Submitter #13(C), comment 17, and Submitter #45, comment 6, observe that there are situations in which negative data have been omitted from the profile. Specific omissions identified by the submitters are indicated in subsequent specific comments.

RESPONSE: The issue of omitted negative data is addressed in the subsequent comments.

- d) Submitter #13(C), comment 18, indicates that it should be stated in all appropriate sections of the report that different commercial PCB mixtures (including Aroclors) possess different toxic potency.

RESPONSE: The variation in toxicity of PCB congeners and mixtures will be stated more clearly in the opening paragraph to Section 4.3. A statement regarding the variation in toxicity of PCBs will also be added to Section 2.2.

- * e) Submitter #66, comment 1, concurs with the general conclusion of the profile that insufficient evidence is available to characterize PCBs as human carcinogens, but expresses concern that heavy reliance on extrapolated animal data can "...prompt estimated human health risk levels which are extremely conservative and yet precipitate legislative and regulatory mandates unjustified by the nature of the risk involved and data used to derive the risk."

RESPONSE: SRC merely reported the EPA risk estimates as specified in the Guidance to Contractors.

- f) Submitter #49, comment 1, agrees and endorses the comments of Submitter #45.

RESPONSE: None required.

- g) Submitter #61, comment 1, adopts the "Specific Comments" of Submitter #45 except for a critique contained therein regarding Safe et al. (1985). Submitter #61 does not adopt the "General Comments" or "Executive Summary" of Submitter #45.

RESPONSE: None required.

- h) Submitter #62, comment 1, adopts the "Specific Comments" and Appendices of Submitter #45, with the exception of specific comment No. 36 regarding Safe et al. (1985).

RESPONSE: None required.

- i) Submitter #13(C), comment 40 observes that Kanechlor is misspelled at various locations throughout the document.

RESPONSE: Misspelled Kanechlor will be corrected.

1. PUBLIC HEALTH STATEMENT

- a) Submitter #13(C), comment 2, noting that the Public Health Statement appears targeted for the general public, states that it contains passages that are seriously flawed and

misleading with respect to known human health effects of PCB exposure. The submitter identifies these passages in subsequent specific comments.

RESPONSE: This issue is addressed in the subsequent comments.

- b) Submitter #13(C), comment 4, states that three references are made in the Public Health statement that clearly imply that human exposure to PCBs is known to result in a risk of cancer. This implication was considered to be inconsistent with the conclusion in Section 4.3.6.4 that "The available epidemiological data do not indicate a consistent tumorigenic effect among people exposed to PCBs". It is recommended by submitter #13(C), comment 7, that if reference to cancer is to be made in this section, it should be a simple statement of fact such as "Although studies are continuing, current epidemiological evidence among individuals exposed to the highest levels of PCB mixtures (i.e., those who worked directly with PCBs) do not indicate an increased risk of cancer".

RESPONSE: The references to cancer referred to by the submitter appear in Sections 1.4, 1.6 and 1.7. In section 1.4, it is stated "Effects of PCBs in experimentally exposed animals include liver damage, skin irritations, death, low birth weights and other reproductive effects, and cancer". In Section 1.6, it is stated "Based on information 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 770 additional cases of cancer in a population of 10,000 people and 770,000 additional cases of cancer in a population of 10,000,000 people." In Section 1.7 it is stated, in reference to the EPA drinking water criteria, that "With respect to cancer, however, it is assumed that 'any exposure involves some risk' in the absence of information to the contrary."

SRC feels that the statement in Section 1.4 is appropriate because (1) it is specified that cancer and the other effects occur in experimentally exposed animals, and (2) it is indicated in previous statements that adverse health effects in humans do not include cancer. The statement in Section 1.6 is appropriate because it is consistent with the June 2, 1987 Guidance To Contractors and indicates that the risk estimates are based on information that PCBs cause cancer in animals. Inclusion of the statement in Section 1.7 is specified for carcinogens by the Guidance to Contractors.

- c) Submitter #13(C), comment 9, indicates that results of unspecified recent EPA studies showing steadily declining

levels of PCBs in fish and adipose tissue should be discussed in the profile; it is implied that these results should be reflected in the Public Health Statement.

RESPONSE: Monitoring data for PCBs in human adipose and fish are discussed in Sections 2.2.2.1 and 7.2.4.1, respectively. A statement indicating that exposure to PCBs is declining will be added to Section 1.2 of the Public Health Statement.

1.1 WHAT ARE PCBs?

- a) Submitter #13(C), comment 3, states that there are only 206 (not 209) compounds within the category of PCBs. It is indicated that the number 209 used in the profile includes monochlorobiphenyls, which from a scientific standpoint are not polychlorinated biphenyls.

RESPONSE: Submitter #13(C) is technically correct. However, various EPA documents (e.g., Drinking Water Criteria Document, 1988) and publications by CDC personnel (e.g., Renate D. Kimbrough, Ann. Rev. Pharmacol. Toxicol. 27: 87-111, 1987) include the monochlorobiphenyls in the PCB family of compounds.

- b) Submitter #23(B), comment 1, apparently disagrees with the statement "The industrial manufacture of PCBs was stopped in the United States in October 1977 because it had been discovered that PCBs would accumulate and persist in the environment and could cause toxic effects," indicating that PCBs have produced adverse health effects in humans only as a result of acute high level industrial exposures.

RESPONSE: This statement in the profile was taken from Hatton (1979) and is referred to in the profile on p. 75, paragraph 2. The Hatton (1979) article indicates that the author (R.E. Hatton) is a spokesman for Monsanto, the former manufacturer of PCBs; therefore, the statement is believed to be accurate.

1.2 HOW MIGHT I BE EXPOSED TO PCBs?

- a) Submitter #45, comments 1, 16, 21 and 22, indicates that statements made in this section, Section 1.3 and elsewhere in the document, indicating that consumption of fish is the major source of PCB exposure for the general public, are incorrect and should be deleted. Calculations, other supporting evidence and discussion are provided to document that indoor air is the major

route of exposure for the general population.

RESPONSE: SRC generally disagrees with the comments made by Submitter #45 concerning exposure from fish. On page 1, paragraph 3, line 5 of the profile, consumption of fish is referred to as "a" major source and not "the" major source of PCB exposure to humans. However, the best data currently available suggests that consumption of fish may be "the" major source of PCB exposure to most Americans. The average dietary intake of 560 ng/day estimated in the profile (p. 85, line 8) was derived from data from the U.S. FDA. The U.S. FDA data resulted from monitoring of "ready-to-eat" foods throughout the U.S., and represents the diet of the average American adult. The average inhalation intake of 100 ng/day estimated in the profile (p. 82, line 4) was derived from extensive outdoor air monitoring. Submitter #45 contends that exposure from inhalation of indoor air is significantly higher than exposure from food, and has outlined a calculation which results in an exposure of 5000-6000 ng/day (Specific Comment 1). While Submitter #45 may be correct that indoor air contains higher levels of PCBs than outdoor air, the current available indoor air monitoring data are insufficient to make a general population exposure calculation similar to the one made by Submitter #45. The U.S. EPA's Drinking Water Criteria Document for Polychlorinated Biphenyls (1988) states (p. IV-29) "because there are few data on PCB levels in indoor air, the total exposure and fractional contribution from indoor air to exposure for humans remains difficult to assess." Submitter #45's indoor air calculation is based primarily on indoor air monitoring data of Oatman and Roy (1986) and MacLeod (1981). Both sources contain significant monitoring in buildings previously exposed to PCBs or containing PCB-containing appliances or electrical devices. In addition, Submitter #45's calculation assumes that the average American stays inside 24 hours a day, which is not realistic. Although SRC generally disagrees with these comments from Submitter #45, SRC believes that this section of the profile should be amended to reflect that a significant exposure potential may result from the inhalation of indoor air. Also, page 1, paragraph 3, lines 9-11 of the profile should be amended to specify outdoor air and change the word negligible to minor.

- b) Submitter #49, comment 6, indicates that the statement "Fish become contaminated with PCBs in water, which results in very high accumulation of PCBs in the fish tissue." is "...overly simplistic and not correct in general." The submitter suggests revising the wording of

the statement as follows: "Fish bioaccumulate PCBs from water, sediment, PCB laden particulates, and via the ingestion of PCB-contaminated prey. The PCB accumulation varies with, inter alia, fish species (lipid content, dietary and other habits, etc.), frequency of exposure, and the concentration of individual PCB congeners. Accumulated PCBs are not evenly distributed in all fish tissue, but rather are generally concentrated in the liver, gall bladder, and other nonedible portions of the fish." Rationale for the rewording is provided.

RESPONSE: SRC believes that the rewording suggested by Submitter #49 would improve the quality of the section. Therefore, it is suggested that some form of the rewording be incorporated into the profile.

- c) Submitter #45, comment 23, states that the profile is somewhat misleading in its presentation of ways that PCBs can be released into the environment; it is noted that disposal of the listed consumer products is very likely to release PCBs into the environment.

RESPONSE: Submitter #45 states that disposal of the listed consumer products are likely to result in the appearance of PCBs in sanitary landfills rather than secured landfills, which may result in release to the environment. SRC believes that Submitter #45 may be correct in this assumption. A statement can be added to the sources of release.

1.4 HOW DO PCBs AFFECT MY HEALTH?

- a) Submitter #13(C), comment 8, states that the part of the first sentence stating that "...liver effects are the only significant adverse health effects that have been observed in PCB-exposed workers." is untrue. Discussion supporting the inaccuracy of this statement is provided, including inconsistency with subsequent sections of the profile and reference to the Kimbrough (1987) review of human PCB effects.

RESPONSE: SRC agrees that liver effects should not be indicated to be adverse effects in the Public Health Statement and will delete the reference to liver effects.

- b) Submitter #49, comment 4, indicates that the profile in general and introduction in particular fails to note that prominent PCB researchers have concluded in recent

reviews (e.g., Kimbrough 1987) that observed acute health effects in humans have generally been minor, and that significant chronic health effects in humans have not been causally associated with PCB exposure.

RESPONSE: Sections 1.4 and 4.1 will be modified to reflect this conclusion.

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

- a) Submitter #13(C), comment 10 indicates that the entire section is misleading in that it implies that PCB exposure is a special or unique event; it should be made clear, due to the nature of PCBs, that some level of daily exposure is inevitable and that a range of PCB background levels in blood and adipose tissue will be found. Submitter #45, comment 24, recommends stating that nearly everyone has been exposed to PCBs, and that worldwide nearly all persons are likely to have detectable levels of PCBs in their body fat and blood.

RESPONSE: SRC agrees with these comments and will add an appropriate statement.

- b) Submitters #13(C) and #45 refer to the statement "Blood PCB levels are the best indicator of recent exposure to PCBs, and levels in the fat are the best indicators of long-term exposure." Submitter #13 (c), comment 10, indicates that the term "recent" is inadequately defined. Submitter #13(C), comment 11, indicates that distinction between blood and adipose PCB levels, in the context of a typical environmental exposure, is irrelevant because blood PCBs are in equilibrium with adipose PCBs and each may reflect body burden; discussion is provided. Submitter #45, comments 16 and 24, disagrees with the statement and provides discussion supporting the inaccuracy of the statement.

RESPONSE: The submitters indicate that there is no advantage for sampling blood versus fat for PCBs because (1) the redistribution phase is complete within approximately 24-48 hours and (2) typical environmental exposure involves small continuous amounts rather than occasional large amounts. However, as noted by Submitter #45, a relatively large and recent exposure to PCBs (i.e., an exposure occurring less than 24 hours before the measurement) might best be reflected by serum PCB levels. SRC suggests deleting the statement and adding the following sentence to the end of the paragraph:

"Blood tests are the easiest and safest and may detect large exposures that occurred within the previous one or two days." This statement would also address comment 1.5c.

- c) Submitter #3(B), comment 98, states "...the reader is left with the impression that the method of choice for measuring in vivo concentrations is by using adipose biopsy specimens, despite the generally accepted use of serum levels."

RESPONSE: It will be more clearly indicated that blood tests are the method of choice.

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

- * a) Submitter #13(C), comment 4, feels that the description of the EPA numerical risk assessment for cancer implies that PCB exposure is known to result in x cases of cancer per y population. Submitter #13(C), comment 6, indicates that while it may be relevant to include the EPA risk assessment in the profile with appropriate supporting discussion, the risk estimate should be deleted from the Public Health Statement because it is inappropriate and misleading. Submitter #13(C), comment 7, indicates that the doses in Figure 1.2 indicating "Minimal risk for effects other than cancer" imply that the doses possess a risk of cancer.

RESPONSE: This section was prepared in accordance with the Guidance to Contractors; therefore, no action by SRC is required.

- * b) Submitter #45, comment 25, states that a discussion of PCB carcinogenicity has no place under this heading because the heading implies that carcinogenic effects in humans are clearly known to result from PCB exposure.

RESPONSE: See response to Issue 1.6a above.

- * c) Submitter #45, comment 2 concludes that users of the profile may be misled into thinking that the cancer risk levels represent actual human risk, and that it is necessary to provide the basis, use of and limitations of the estimates in the profile. This comment also pertains to Sections 2.2.1.2 and 9.2.3.

RESPONSE: See response to Issue 1.6a above.

- * d) Submitter #45, comment 5, objects to providing risk numbers for the general public without any discussion of relative risks or the risks associated with current regulatory standards for carcinogenic substances. Discussion is provided. This comment also applies to Sections 2.2.1.2 and 9.2.3. Submitter #45, comment 27 concludes that the risk estimates and related discussion should be moved to a section in the document where it can be placed in a more accurate perspective, or deleted.

RESPONSE: See response to Issue 1.6a above.

- e) Submitter #49, comment 4, concludes that the discussion of cancer risk levels is overly simplified because the fact that Aroclors are mixtures of congeners of varying biological activity is not mentioned.

RESPONSE: SRC feels that inclusion of information regarding the varying biological activity of PCB congeners is inappropriate because the Public Health Statement is intended to communicate essential information to a lay audience.

- f) Submitter #49, comment 4, concludes that the discussion of cancer risk levels is misleading because it does not mention plausible alternative less conservative risk estimates. Submitter #66, comment 2, expresses concern that the range of estimated cancer risk levels "...may be far more conservative than necessary to protect human health and the environment considering the lack of data correlating PCB carcinogenicity to humans."

RESPONSE: The Guidance To Contractors specifies inclusion of the EPA cancer risk estimates.

- * g) Submitter #45, comments 4, 27 and 101, indicates that epidemiologic evidence can be used to demonstrate that the EPA potency factor is excessive. Supporting calculations and discussion are included in Comment 27. Comments 4 and 101 indicate that this issue also pertains to Sections 2.2.1.2 and 9.2.3.

RESPONSE: SRC merely reported the EPA risk estimates, in accordance with Guidance to Contractors.

- h) Submitter #13(C), comment 4, Submitter #45, comments 3 and 26, and Submitter #49, comment 2, observe that the risks associated with 1 $\mu\text{g}/\text{kg}/\text{day}$ exposure are incorrectly calculated from the 7.7 $(\text{mg}/\text{kg}/\text{day})^{-1}$ potency factor; the numbers of cases are too high by a factor of 10.

RESPONSE: The submitters are correct. The errors will be corrected.

- i) Submitter #45, comments 3 and 26, states that the 7.7 $(\text{mg}/\text{kg}/\text{day})^{-1}$ potency factor was mistakenly used in the profile and should be replaced by the proper q_1^* of 5.7 $(\text{mg}/\text{kg}/\text{day})^{-1}$, as SRC stated it would do in its response to peer review comments. This issue also pertains to Sections 2.2.1.2 and 9.2.3.

RESPONSE: SRC's statement of the q_1^* in the Peer Review Report was in error. The q_1^* of 7.7 $(\text{mg}/\text{kg}/\text{day})^{-1}$ is the appropriate potency factor as it is verified by the EPA agency-wide CRAVE committee.

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

- a) Submitter #13(C), comment 7, indicates that the statement "With respect to cancer, however, it is assumed that 'any exposure involves some risk' in the absence of information to the contrary" is inaccurate, and serves no apparent function other than to imply that any amount of PCBs in drinking water presents a risk of cancer.

RESPONSE: The Guidance To Contractors specifies inclusion of this statement for carcinogens.

- b) Submitter #13(C), comment 12, recognizes that the OSHA standards for PCBs are not presented in this section.

RESPONSE: The OSHA standards will be added.

- c) Submitter #49, comment 5, notes that ACGIH is incorrectly classified as a federal agency.

RESPONSE: Reference to the ACGIH recommendation will be deleted from Section 1.7 because ACGIH is not a federal agency.

- d) Submitter #49, comment 5, indicates that it is not indicated in this section, unlike Section 9, that some of the standards/recommendations specifically distinguish among Aroclors.

RESPONSE: It will be indicated that the OSHA standards are for specific PCBs (see comment 1.7b).

- * e) Submitter #45, comments 28 and 29, indicates that the basis for the disparity in the "acceptable dose" allowed by each standard or guideline should be explained. This reportedly would clearly demonstrate to readers unfamiliar with risk assessment that a considerable difference in opinion exists among scientific and regulatory groups as to what level of PCB exposure represents an acceptable risk. Approaches for comparing the standards and guidelines are discussed.

RESPONSE: This section was prepared in accordance with the Guidance to Contractors.

2. HEALTH EFFECTS SUMMARY

2.2 LEVELS OF SIGNIFICANT EXPOSURE

- a) Submitter #45, comment 30, objects to grouping results of inhalation studies of varying exposure duration together, particularly in the case of PCBs and other persistent chemicals.

RESPONSE: Exposures are classified by duration and type (i.e., intermittent or continuous) in Figures 2.1-2.3, and by exposure period (i.e., acute, intermediate or chronic) in Figures 2.4-2.6. Specific information regarding exposures is presented in the text. The figures are not intended to be interpreted without referral to the text.

2.2.1 Key Studies and Graphical Presentation

- a) Submitter #13(C), comment 18, states that Figures 2.1-2.3 should be consistent with Figures 2.4-2.6 with respect to indicating specific Aroclor mixtures.

RESPONSE: The ATSDR/EPA Science Review Panel suggested indicating specific PCB mixtures in

Figures 2.4-2.6 but not in Figures 2.1-2.3.

- b) Submitter #45, comment 18, indicates that effects are included in Figures 2.1-2.6 without the context of other studies that are negative. The submitter also indicates that the non-specific designation of effects in Figures 2.1-2.6 can be misleading (e.g., liver effects in Figure 4.5 refer to enzyme induction rather than toxicity).

RESPONSE: The lowest LOAELs and highest NOAELs for various toxicological endpoints are depicted in Figures 2.1-2.6; this approach is discussed and will be expanded in the introduction to Section 4.3. The Guidance To Contractors indicates that systemic/target organ effects should be generalized in Figures 2.1-2.6.

2.2.1.1 Inhalation exposure

- a) Submitter #45, comment 31, refers to the following statement in the Target organ/systemic toxicity subsection: "Since the FEL for Aroclor 1254 is lower than the NOAEL for Aroclor 1242, a minimal risk level cannot be derived." The submitter concludes that the statement differentiates the toxicity of the two Aroclor mixtures, supports the argument that separate toxicological consideration be given to the two mixtures, and is false because the potency of each mixture varies.

RESPONSE: This statement is appropriate if equivalent toxicity of PCBs is assumed for the purpose of risk assessment. The statement will be modified as follows to more clearly reflect this assumption: "...a minimal risk level for Aroclors as a class cannot be derived."

- b) Submitter #49, comments 19 and 20, concludes that the Fischbein et al. (1979) study does not provide sufficient data for estimating an inhalation LOAEL of 0.07 mg/m^3 for humans. Limitations of the study are discussed; these include lack of information regarding distributions of exposures and symptoms, lack of a control group, reliance on self-reported questionnaires and inconsistency with a subsequent study (Fischbein et al. 1982). These comments also pertain to Section 4.3.2.1.

RESPONSE: It is appropriate to conclude that there is an indication of a relationship between plasma levels of PCBs and abnormal SGOT levels/dermatologic findings in the Fischbein et al. (1982) study. Due to limitations of the study, the effects could be regarded as inconclusive and cannot be associated with specific exposure concentrations. Since other epidemiologic studies are consistent with this study in indicating altered liver enzymes and/or dermatologic effects in PCB-exposed workers, and since the effects in this study cannot be associated with specific exposure concentrations, it was deemed appropriate by the Science Review Panel to plot the range of reported exposure concentrations as LOAELs in Figures 2.1 and 2.4. SRC will indicate limitations of the Fischbein et al. (1979) data in the text and provide a brief explanation of the rationale for plotting the range.

- c) Submitter #49, comment 19, notes that the Ouw et al. (1976) study does not provide sufficient data for estimation of symptom prevalence, because a control group was not used and symptoms did not correlate with PCB blood levels.

RESPONSE: Reference to the Ouw et al. (1976) study is made in the following statement: "Occupational exposure to PCBs has been associated with alterations in serum levels of liver enzymes and dermatological effects such as chloracne (Meigs et al. 1954; Ouw et al. 1976; Fischbein et al. 1979, 1982; Baker et al. 1980; Smith et al. 1981a,b,c)". Inclusion of the Ouw et al. (1976) citation is appropriate because the intent of the statement is to indicate to the reader that data are available suggesting that the primary target organs in animals and humans data are the same. Since the Guidance To Contractors indicates that generalization is appropriate for studies that are not key, limitations of the Ouw et al. (1976) will not be discussed. A qualifying statement indicating that the results of some of the studies are equivocal will be added.

- d) Submitter #45, comment 32, states that the Developmental toxicity subsection implies that the Taylor et al. (1984) study provides evidence that PCBs cause developmental deficits in humans, and that limitations of this study are not indicated.

This submitter and submitter #49, comment 16, discuss limitations of this study and conclude that evidence for any association between PCB exposure and low birth weight is inconclusive. Submitter #49, comment 16, indicates that Taylor's expanded data of the same population, currently in draft form, needs to be obtained and added to the profile; results reportedly show no significant difference between the high and low exposure groups.

RESPONSE: Limitations of the Taylor et al. (1984) study will be indicated in Section 4.3.3.1. It will be indicated in Sections 2.2.1.1 and 4.3.3.1 that the results of this study are inconclusive. SRC contacted Dr. Taylor regarding the availability of the updated report. Dr. Taylor said that the report has been accepted for publication, but it is not available for outside use.

- e) Submitter #13(C), comment 28, indicates that the limited relevance of the Bahn et al. (1976, 1977) human carcinogenicity data should be mentioned. Submitter #45, comment 33, concludes that Bahn et al. (1976) should not be used as a key study and deleted; this conclusion is based on consideration of negative epidemiologic studies that were not cited in this Section and limitations of the Bahn et al. (1976) study.

RESPONSE: The results of the Bahn et al. (1976) study will be deleted. The statement regarding the overall weight of evidence of carcinogenicity in humans will be expanded.

2.2.1.2 Oral exposure

- a) Submitter #13(C), comment 17, and Submitter #45, comments 12 and 36, cite negative data for PCB mixtures other than Aroclor 1254 that were omitted from the profile: NOELs for reproductive effects in mink (Auerlich and Ringer, 1977) and decreased survival in rats (Schaeffer et al., 1984). Submitter #13(C), comment 17, indicates that omission of these data from the text and/or Figures 2.2 and 2.5, and inclusion of the data for Aroclor 1254 in Figure 2.2 without designation that it is specific for Aroclor 1254, gives the false impression that the FELS for Aroclor 1254 are for all Aroclors. The selective presentation of these data was discussed and deemed to be misleading.

Submitter #45, comment 36 notes that the obvious disparity between Aroclors in the Auerlich and Ringer (1977) study underscores the need to recognize that a study with a single PCB mixture will not necessarily be representative of the responses produced by other PCB mixtures.

RESPONSE: The omission of negative data is a consequence of the assumption of equivalent toxicity of Aroclors (i.e., the selection of the lowest LOAELs and highest NOAELs for the most toxic Aroclor). This approach was approved by the Science Review Panel.

- b) Submitter #13(C), comment 17, observed that the 25 ppm (1.25 mg/kg/day) dose from the NCI (1978) chronic rat bioassay of Aroclor 1254 is represented as a FEL for decreased survival in the text and Figures 2.2/2.5. As the summaries of this bioassay on pp. 16 and 52 indicate that the decreased survival (8%) at 25 ppm does not appear to be significant, the submitter concluded that 25 ppm actually represents a NOAEL.

RESPONSE: SRC feels that the 8% decrease in survival is significant since the effect is clearly dose-related.

- c) Submitter #45, comment 34, notes that chronic studies using Aroclor 1260 (Kimbrough et al. 1975) and Clophen A60 and Clophen A30 (Schaeffer et al. 1984) indicated that PCB exposure decreased mortality. Because these findings "contradict" the finding of increased mortality in the NCI (1978) study with Aroclor 1254, it was concluded that "...it is not appropriate that the ATSDR document states that chronic PCB levels greater than 25 ppm reduce survival. This statement is not true and therefore should be deleted from the document."

RESPONSE: The profile states "Reduced survival occurred in rats fed diets containing >25 ppm Aroclor 1254 for 104 weeks (NCI 1978)." This statement will be corrected to show that reduced survival occurred at \geq 25 ppm and will be retained because it is not erroneous. The 25 ppm (1.25 mg/kg/day) diet level represents a FEL for Aroclor 1254. NOAELs for other Aroclors and Clophens for reduced survival in the Kimbrough et al. (1975) and Schaeffer et al. (1984) are higher than the FEL for

Aroclor 1254, and NOAELs for reduced survival in other studies that are lower than the FEL from other studies are not available. Since equivalent toxicity of Aroclors is assumed for the purpose of risk assessment, it is appropriate to conclude that 1.25 mg/kg/day represents the lowest FEL for chronic oral exposure to Aroclors and that relevant NOAELs are not available.

- d) Submitter #45, comment 35, requests that the paragraph pertaining to developmental toxicity in humans be deleted completely or moved to a section of the document where limitations of the studies (Fein 1984; Fein et al. 1984; Rogan et al. 1986; Jacobson et al. 1985) can be addressed, because it cannot be concluded that the effects are definitely attributed to PCBs. The submitter indicates that if the studies are cited a brief summary of their weaknesses should be included; detailed discussion of the limitations of the studies is provided.

RESPONSE: This paragraph will be revised to more adequately express inconclusive results and limitations of the studies.

- e) Submitter #13(C), comment 5, disagrees with use of EPA's risk assessment for cancer based on the q_1^* of $7.7 \text{ (mg/kg/day)}^{-1}$, which was calculated with the incidence of carcinomas combined with neoplastic nodules and other non-cancerous lesions from the Norback and Weltman (1985) study. It was recommended that the q_1^* of $5.7 \text{ (mg/kg/day)}^{-1}$ based solely on the incidence of cancerous lesions, be used as the basis for the risk levels.

RESPONSE: SRC reported the EPA verified q_1^* [$7.7 \text{ (mg/kg/day)}^{-1}$] in accordance with the Guidance To Contractors.

- * f) Submitter #49, comment 7, states that the profile "...places undue emphasis on EPA estimates of carcinogenic potency." The submitter indicates that the profile should include a discussion of the conservative nature of EPA's assumptions employed in calculation of carcinogenic potency together with a presentation of alternative potency estimates. These comments also pertain to Sections 4.3.6.2 and 9.2.3. General remarks on EPA's conservatism, including reference to a recent OMB

evaluation of cancer risk estimation methodologies employed by federal agencies, are provided.

RESPONSE: In accordance with the Guidance To Contractors SRC (1) reported the verified EPA carcinogenic potency factor and (2) will include potency estimates derived by federal agencies other than EPA in Section 9.2.3.

- g) Submitter #13(C), comment 13, feels that the human cancer risk estimates in Figure 2.5 should be removed because it is indicated elsewhere in the profile that there is inadequate evidence of carcinogenicity in humans, and because inclusion of the estimates in Fig. 2.5 is inappropriate and misleading, especially to the lay reader, because Fig. 2.5 plots actual toxicity data.

RESPONSE: Inclusion of cancer risk estimates in Figure 2.5 is specified in the Guidance To Contractors.

- * h) Submitter #45, comment 37, concludes that the cancer risk estimate "...should be qualified and placed in the context of the caveats that are associated with its use before it is provided to the unknowledgeable general public as if it were a statement of fact." Shortcomings associated with the risk estimate are discussed.

RESPONSE: SRC reported the cancer risk estimates in accordance with the Guidance To Contractors. The general public is not the intended audience for Chapter 2.

- i) Submitter #45, comment 18 indicates that an FDA estimate of the daily intake of PCBs from food (Kolbye, 1972) can be graphed for human data in Figure 2.2.

RESPONSE: It is inappropriate to graph an estimate of the daily dietary intake of PCBs in Figure 2.2 because Figure 2.2 includes levels of significant exposure for specific toxic endpoints.

2.2.1.3 Dermal exposure

- a) Submitter #45, comment 38, observes that the

introductory paragraph fails to reflect quantitative information regarding dermal absorption of PCBs in animals. It is stated that the study by Webster et al. (1983; J. Toxicol. Environ. Health, 12:511), which is not cited in the profile, should be discussed in this paragraph. The results of this study are summarized by the submitter.

RESPONSE: The introductory paragraph is intended to qualitatively indicate that dermal exposure may be a significant route of PCB exposure. Results of the Webster et al. (1983) study will be summarized in Section 4.2.1.3.

- b) Submitter #45, comment 18, indicates that the study of Maroni et al. (1981a) can be used to calculate dermal doses in capacitor workers for inclusion in Figure 2.3. Submitter #45, comment 39, compares the 43.7 mg/kg/day dermal dose that caused liver and kidney degeneration in rabbits (Vos and Beems 1971) with doses that workers in the Maroni et al. (1981a, 1981b) study may have experienced from handling PCB-contaminated tools. The range of PCB concentrations on the workers' hands (2-28 ug/cm²) and assumed hand surface area (910 cm²) and body weight (70 kg) values were used by the submitter to calculate dermal doses of 0.026-0.364 mg/kg/day. Since none of the workers in this study had any clear evidence of liver disease and dermal exposure to PCBs in the general environment is several orders of magnitude lower than experienced by capacitor workers, it was concluded that dermal exposure to PCBs in the general environment is not likely to result in any risk of acute or subchronic effects.

RESPONSE: The Maroni et al. (1981a, 1981b) study, unlike other available occupational exposure studies, reports quantitative dermal exposure information. Results from this study therefore will be added to Section 2.2.1.3 and the dermal subsection of Section 4.3.2.1, and the introduction to Section 2.2.1.3 will be modified. A conservative dermal dose will be calculated from the exposure data and included in Figures 2.3 and 2.6. For purposes of calculating the dose, the submitter assumed a value for hand surface area of 910 cm², but did not provide a reference. SRC contacted the submitter, who gave the following reference: Hawley JK. 1985. Assessment of health risk from

exposure to contaminated soil. Risk Analysis; 5: 289-302. A different dermal dose can be calculated using a surface area for both hands of 720 cm² from Snyder WS et al. 1975. International Commission on Radiological Protection. No. 23: Report of the Task Group on Reference Man. Pergamon Press, NT, pp 17-20. SRC will obtain the Hawley (1985) reference and will determine which reference is a better source. A statement regarding the relative risks of occupational and environmental dermal exposure is inappropriate in Section 2.2.1.3 but can be added to the discussion in Section 4.3.2.1.

- c) Submitter #13(C) and Submitter #45 refer to the statement "Aroclor 1254 has shown weak tumor initiator but not promoter activity in two-stage carcinogenesis studies with mouse skin". Submitter #13(C), comment 14, concludes that the statement is misleading and misplaced, indicating that it belongs in the discussion of genotoxicity and mistakenly implies that PCBs are genotoxic. Citations for subsequent reports of essentially the same study (Berry et al. 1978, 1979) are provided that characterize Aroclor 1254 as "possessing little or no tumor initiating properties". Submitter #45, comment 40, observes that citation to DiGiovanni et al. (1977) is missing, and indicates that the weak tumor initiating activity occurred in the presence of TPA-induced promotion. Since a TPA-only control was not included in the study and Van Duuren (1982) found that TPA alone also produces a low incidence of skin cancer, it was concluded that the statement is inaccurate and should be deleted.

RESPONSE: SRC feels that it is most appropriate to evaluate two-stage carcinogenesis studies with carcinogenicity data because tumors are the endpoint and these studies traditionally have been included in reviews of carcinogenicity. The statement referring to the weak tumor initiating activity of Aroclors will be reevaluated following review of the reports identified by the submitters.

2.2.2 Biological Monitoring as a Measure of Exposure and Effects

2.2.2.1 Exposure

- a) Submitter #45, comment 41, states that the

literature should be searched "...for other informative studies of human adipose levels in the United States and other studies rather than relying upon the statistical analysis from a single data source for illustrating the important trends of PCB levels in human adipose tissue." The submitter provides nine citations and presents some of the results of these studies.

RESPONSE: The citations provided by the submitter will be reviewed and appropriate data will be incorporated into the profile.

- b) Submitter #45, comment 42, suggests that "...the text and tables be labeled in a consistent fashion such that the untrained reader can easily realize the frequent 1 to 2 order-of-magnitude difference observed between blood and adipose tissue PCB levels in relative terms (i.e. ppm in adipose and ppb in blood, or a reference to what conversion factor one might use to put these two tissue levels in directly comparable terms)."

RESPONSE: It is assumed that the intended audience for this section (health professionals) will be able to interpret the biological monitoring data as reported. The units used in the tables are those reported by the sources.

- c) Submitter #45, comment 43, indicates that the limitations and assumptions involved in the determination of tissue levels of PCBs need to be identified before the utilization of blood/adipose PCB levels can be considered accurate estimators of PCB exposure or body burden. Discussion is provided.

RESPONSE: The first paragraph will be expanded to discuss limitations and assumptions involved in monitoring for PCBs in serum and adipose.

- d) Submitter #45, comment 44, indicates that PCB blood level data from Sahl et al. (1985) should be added to Table 2.3 because it represents a timely and large "nonexposed" population.

RESPONSE: Data from this study will be added to Table 2.3.

- e) Submitter #45, comment 48, indicates that it should be noted that the data in Table 2.3 suggest that fish consumption may have no significant impact on a person's PCB body burden. Discussion is provided.

RESPONSE: The appropriateness of this suggestion will be considered following review of the New Bedford study. Results from this study will be added to Table 2.3.

- f) Submitter #45, comment 45, indicates that it would be more appropriate to present the information in the last paragraph following the introductory first paragraph. The submitter also indicates that the statement in the last paragraph that adipose and milk fat PCB levels are 100-200 times higher than serum levels is misleading, because there is no mention of the percentage of fat in breastmilk or PCB levels in whole breastmilk; inclusion of this information is suggested.

RESPONSE: SRC concurs with both issues and will make appropriate revisions.

- g) Submitter #45, comment 46, indicates that the statement from the last paragraph, "These levels are relatively high and apparently due to consumption of contaminated fish", implies that PCBs in breastmilk result primarily from the consumption of contaminated fish and should be deleted. Three references containing additional breastmilk PCB monitoring data are provided for comparison and more objective presentation of breastmilk PCB levels.

RESPONSE: The appropriateness of the statement will be considered following review of the references cited by the submitter.

2.2.2.2 Effects

- a) Submitter #45, comments 47 and 73, indicates that it is appropriate to add additional information regarding the Triana, Alabama study (Kreiss et al. 1981). This includes the finding that the association between log PCB concentrations and diastolic blood pressure were small and of borderline significance, and the finding that the

strongest correlation was between log DDT and log PCB serum levels. The submitter concurs with Kreiss (1985) that the latter finding eliminates the possibility of attributing effects solely to PCBs.

RESPONSE: The summary of the Kreiss et al. (1981) study will be revised to more clearly indicate that the effects cannot be attributed solely to PCBs due to DDT exposure.

- b) Submitter #45, comment 73, identifies uncited studies that investigated associations between PCB exposure and blood pressure (Bumgarner et al. 1973 and the New Bedford study). Submitter #3(B), comment 100, indicates that studies of populations in which elevated blood pressure and PCB exposure/body burden have been associated, other than the Triana, Alabama population in which other exposures were involved, were not considered in the profile.

RESPONSE: The Bumgarner et al. (1973) and New Bedford studies will be reviewed and summarized if appropriate.

- c) Submitter #45, comment 13, indicates that the review of PCB hepatic effects is biased and exaggerated, in part due to exclusion of results indicating no evidence for clinically significant effects (Fischbein et al. 1979; Smith et al. 1982; Lawton 1985) and limited usefulness of GGPT assays in epidemiologic studies (Guzelian, 1985). Submitter #13(C), comment 15, indicates that the abnormal liver indices are not placed in proper perspective; discussion regarding clinical significance and interpretation of PCB hepatic effects is provided.

RESPONSE: This section correlates information on biological monitoring with measurable biological alterations; these alterations may have inconsequential and/or unknown effects on health. Statements will be added to the first paragraph on hepatic effects indicating (1) factors that complicate interpretation of the data, (2) the uncertain clinical significance of some of the altered hepatic indices, and (3) the lack of evidence for liver toxicity.

- d) Submitter #45, comment 49, provides discussion indicating that the serum enzyme data of Ouw et al. (1976), Fischbein et al. (1979) and Chase et al. (1982) are inaccurately reported.

RESPONSE: These data were misinterpreted and will be deleted

- e) Submitter #45, comment 13, states that the sentence "...possible hepatocellular damage has been demonstrated only in occupationally exposed groups with higher PCB levels (Kreiss, 1985)" exaggerates and distorts Kreiss's actual conclusion, because a qualifying statement indicating that indices of obstructive liver disorders have not been demonstrated even in occupationally exposed groups was omitted.

RESPONSE: A qualifying statement will be added.

- f) Submitter #13(C), comment 16, states that the reference to Maroni et al. (1981a) reporting cases of liver failure is inaccurate, as asymptomatic hepatomegaly and elevated liver enzyme measurements could not be correlated with PCB exposure. Submitter #45, comments 13 and 50, observes that liver failure was not reported in the Maroni et al. (1981a) study. Hepatic data from this study are evaluated in comment 50; it is concluded that the findings were not remarkable and do not appear to be related to PCB exposure.

RESPONSE: The reference to liver failure will be deleted. Limitations of the study, which suggest that the alterations may not be related to PCB exposure, will be indicated.

2.2.3.2 Human exposure potential

- a) Submitter #49, comment 31, states that the sentence "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.", is a gross oversimplification of the true situation. Discussion is provided leading to the conclusion that "...the PCB concentration in the sediments (dry weight basis) is about the same as the PCB concentration in the

water column (dry weight basis) of particulates."

RESPONSE: SRC stands by the statement in the profile. Monitoring data have repeatedly shown that the concentration of PCBs in sediment and suspended material is higher than in the associated water.

- b) Submitter #49, comment 32, states that the conclusion "Thus, lower chlorinated PCBs should have a greater tendency to partition to the water than higher chlorinated PCBs." comprises an inversion of the actual situation. Discussion is provided indicating that all PCB congeners partition to particulate matter.

RESPONSE: SRC stands by the statement as presented in the profile. It appears that Submitter #49 has misread the sentence and therefore, misinterpreted the meaning. In comment 32, Submitter #49 states that PCBs partition to particulate matter rather than to water, which SRC agrees is correct. The statement in the profile simply notes that the lower chlorinated congeners are more likely to partition from particulates to water than are the higher chlorinated congeners.

- c) Submitter #45, comment 51, and Submitter #49, comment 33, refer to the sentence: "The exposure of lower chlorinated PCBs from drinking water from contaminated sources should remain about the same whether the water is filtered or not." Submitter #45 initially suggests that it may be more appropriate to change "The exposure of..." to "The exposure to...". Submitter #45 then states that the reference to filtration indicates that water treatment will be discussed; since it is not, the submitter concludes that the sentence should be deleted. Submitter #49 concludes that the statement is inaccurate because it is based on the concept that the lower chlorinated PCBs have a high solubility and ignores the fact that PCBs have substantial vapor pressure; discussion is provided.

RESPONSE: SRC agrees with Submitters #45 and #49 that the sentence should be deleted. It is not necessary and may be inaccurate.

- d) Submitter #45, comment 52, indicates that information regarding the risk associated with

exposure to airborne PCBs from a limited access site should be added to the second paragraph. Sentences from EPA (1987b) are cited and recommended for inclusion.

RESPONSE: SRC agrees with the comment made by Submitter #45. Inclusion of the data cited by Submitter #45 will improve the quality of the section.

2.3 ADEQUACY OF DATABASE

2.3.2 Adequacy of Database for Health Effect End Points

- a) Submitter #13(C), comment 20, expresses concern that studies of questionable relevance (e.g., developmental toxicity studies in humans) are included to achieve "some data" in specific categories. The use of such studies should be qualified because if these studies provide the only data in a particular category, a "some data" designation implies that more is known regarding the effects than actually is known. Submitter #45, comments 19 and 53, indicates that studies that are inconclusive, such as the human developmental toxicity studies, should not be considered as representing some data. Submitter #45, comment 53, suggests that the profile should clearly indicate if studies were available that could be relied upon to arrive at conclusions concerning the toxicities of PCBs.

RESPONSE: As indicated in Section 2.3.2.1, data which do not meet any of the criteria for "adequate" data are categorized as "some" data. "Some" data is a broad category that includes data ranging from marginal and equivocal to almost adequate. Equivocal toxicological data that are not already so indicated will be.

- b) Submitter #13(C), comment 22, and Submitter #45, comment 19, note that the significance of the asterisks in Figure 2.7 is not defined.

RESPONSE: The asterisks indicate that exposures were occupational (i.e., mixed exposure via the inhalation and dermal routes). These data are categorized with inhalation exposure because health effects data for exposed workers are discussed in inhalation subsections of Section 4.3. The

original figure submitted to ORNL explained the asterisks in a footnote on the figure. ORNL deleted the footnote in preparing the Draft for Public Comments. SRC will notify ORNL to reproduce the figure as it was originally supplied to them during the publication of the Final Toxicological Profile.

2.3.2.2 Description of highlights of graphs

- a) Submitter #45, comment 54, refers to the statement: "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." The submitter indicates that the acute data are described as being inadequately studied, notes that there is a considerable body of literature concerning the effects of orally administered PCBs, and asks what constitutes an "extensively investigated" route of PCB exposure.

RESPONSE: The Science Review Panel concluded that "some" data are available for acute oral toxicity. The general conditions used to categorize data adequacy are described in Section 2.3.2.1.

2.3.2.3 Summary of relevant ongoing research

- a) Submitter #45, comment 55, indicates that the description of the ongoing Rogan study implies that the comparison will yield information relevant to high-exposure (Taiwanese children) versus low-exposure (North Carolina children). The submitter states that the results from this study will have to be interpreted with extreme caution because the obvious failure to control for concomitant exposure to PCDFs will invalidate the results. Discussion and references pertaining to the role of PCDFs as casual agents in the Yusho and Yu-Cheng incidents is provided.

RESPONSE: No action is required. The role of PCDFs as casual agents in the Yusho and Yu-Cheng incidents is discussed in Section 4.1.

2.3.3.2 Monitoring of biological samples

- a) Submitter #45, comment 56, indicates that the New Bedford study has been completed.

RESPONSE: Appropriate data from the New Bedford study will be added.

2.3.3.3 Environmental considerations

- a) Submitter #49, comment 34, indicates that the statement "Methodology of sufficient sensitivity and specificity to measure PCBs in the environment exists" is misleading, because the method routinely used for PCB analysis in federal, state and local government laboratories (packed column gas chromatographic analysis) is not sufficiently sensitive or specific.

RESPONSE: The statement in the profile is correct and should not be changed. However, inclusion of a statement that various laboratories may not have the appropriate equipment may be informative.

- b) Submitter #13(C), comment 21, states that the sentence "The bioavailability of PCBs from environmental media appears to be fairly well understood." is inaccurate and should be revised. Submitter #13(C) considers the statement "There are no data on the effect of the environmental matrix or vehicle on the bioavailability of specific PCBs and PCB mixtures." (p.44, paragraph 1) to be more correct. Submitter #49, comment 35, indicates that the sentence is misleading because bioaccumulation and bioavailability of PCBs other than Aroclor mixtures (i.e., PCB congeners) is not well understood.

RESPONSE: SRC agrees with Submitters #13(C) and #49 that the sentence is misleading and will revise it.

- c) Submitter #45, comments 57 and 58, indicates that the statements indicating that bioavailability of PCBs from environmental media and environmental fate and transport of PCBs are fairly well understood require additional clarification. Reasons for clarification are discussed.

RESPONSE: The environmental fate of the PCBs has been studied more extensively than practically any other environmental pollutant. The results of all

the PCB studies indicate that general environmental fate of the PCBs is fairly well understood. SRC agrees with Submitter #45 that specific environmental fate processes require additional study and that site-specific (eg. New Bedford) understanding of PCB fate may not be well understood. Making this clarification in the profile may be a useful inclusion.

- d) Submitter #45, comment 59, concludes that the treatment of environmental behavior and fate is limited in scope and consists of broad and sweeping generalizations. The comments of Submitter #45 are focused primarily on toxicological sections of the profile due to time limitations during preparation; the submitter indicated that the failure to provide detailed comments on environmental behavior and fate should not be taken as concurrence with the broad and sweeping generalizations. This comment also applies to other sections of the profile pertaining to environmental chemistry.

RESPONSE: The environmental chemistry sections of the profile are somewhat general in scope, but this is due to the requirements of the profile. The ATSDR profiles are primarily intended to be toxicological profiles. Apparently, Submitter #45 would like a greater in-depth discussion of site-specific chemistry (e.g., New Bedford). Unfortunately, this is beyond the scope of the document.

- e) Submitter #49, comment 36, apparently disagrees with the statement "No studies were found that involve the environmental interaction of PCBs with other pollutants." The submitter states "The interaction of PCBs with other pollutants has been studied fairly thoroughly, including 1) studies of the adsorption of PCBs simultaneously with other organic pollutants, 2) bioaccumulation of PCBs in parallel with PAHs and organochlorine pesticides, 3) the interaction of PCBs with other pollutants in carcinogenesis, and 4) the relationships that exist between PCB metabolism and the metabolism of pollutants such as PAHs, aflatoxin and other compounds.", and recommends additional literature searching.

RESPONSE: No studies involving the environmental interactions of PCBs with other pollutants were

located during the preparation of the draft profile. Unfortunately, Submitter #49 does not cite any such study in their comment. In part, Submitter #49 also appears to be confusing biological interactions with environmental interactions. However, additional literature searching may be useful.

- f) Submitter #49, comment 37, disagrees with the statement "There are no known ongoing experimental studies pertaining to the environmental fate of PCBs,...". The submitter suggests additional literature searching, indicating that the environmental fate of PCBs is the object of many ongoing studies throughout the nation and world.

RESPONSE: Submitter #49 may be correct that many environmental studies concerning PCB are on-going. However, Submitter #49 does not reveal on-going studies of which they are aware. Most of the available literature concerns the results of studies which have been completed, as opposed to discussion of on-going studies. Submitter #45 has mentioned on-going studies in the New Bedford area; this should be included in the profile. Additional searching may be helpful.

3. CHEMICAL AND PHYSICAL PROPERTIES

3.1 CHEMICAL IDENTITY

- a) Submitter #13(C), comment 41 states that footnote b in Table 3.1 should be changed from "...used by Monsanto" to "... made by Monsanto."

RESPONSE: Submitter #13(C) is correct. This change should be made in the revised profile.

4. TOXICOLOGICAL DATA

- * a) Submitter #49, comments 12, 13 and 14, recommends addition of three sections to the profile. These would contain a comparison of health effects in animals and humans (comment 12), a review of qualitative and quantitative differences among Aroclors for various toxic parameters (including carcinogenesis) (comment 13), and a summary of effects with an indication of the strength of evidence for each effect (comment 14). Discussions and examples are provided.

RESPONSE: The addition of new sections is not the responsibility of SRC. The General Discussion sections for the various endpoints and the Overview to Chapter 4 include some the recommended discussions. Further discussion will be considered and incorporated into these subsections if appropriate.

4.1 OVERVIEW

- a) Submitter #13(C), comment 31, and Submitter #45, comment 14, agree with the intention not to review reports of the Yusho and Yu Cheng incidents because the health effects are generally attributed to PCDF contamination. There are occasional references to these incidents in subsequent sections; the submitters indicate that these references should be deleted because inclusion is inconsistent with the intention, inappropriate and misleading. Submitter #13(C), comment 32 believes that evidence used to conclude that the effects experienced in the rice oil poisoning incidents were not caused by PCBs should be included in the profile; this evidence is discussed and references are provided.

RESPONSE: References to the Yusho and Yu Cheng incidents in Section 4.3 are occasional, occurring in most instances in the general discussion sections. These references are appropriate because they are general statements that provide perspective and are consistent with the intent of the peer and Science Panel reviews. The reference to the Yusho incident in the carcinogenicity section (4.3.6.2) will be moved to the discussion (4.3.6.4). It is unnecessary to review the evidence used to conclude that the effects in the incidents were not caused by PCBs because the evidence is considered to be unequivocal and the profile is for Aroclor PCBs.

- b) Submitter #45, comment 60, indicates that the overview should not give the impression that PCB contaminated fish are the only important source of dietary PCB intake, and that all relevant sources of exposure for the general population should be indicated (e.g., indoor air of homes and public buildings).

RESPONSE: Available data indicate that PCB-contaminated fish are the primary source of dietary PCBs (see Section 7.2.4.1). A statement will be added indicating that it is possible that indoor air may be a significant source of PCB exposure.

- c) Submitter #45, comment 61, states that the sentence "Higher PCB levels may reach the offspring through nursing than through placental transfer." should be qualified. Reasons are discussed, including lack of evidence suggesting that breastmilk levels of PCBs are harmful and variables that influence the concentrations of PCBs in breastmilk. Related comments appear in Section 4.3.3.4.

RESPONSE: The statement addresses the potential for exposure, not toxicity, via breastmilk. Factors that can influence the concentrations of PCBs in breastmilk will be indicated in Section 4.2.2.2.

- d) Submitter #45, comment 62, indicates that changes are needed to provide a more complete overview of metabolism. These include qualifying the generalization that PCB metabolites tend to be produced via an arene oxide intermediate by indicating that 3-hydroxybiphenyl formation appears to result from a direct insertion reaction (Billings and McMahon, 1978), and clarifying the suggestion that vicinal unsubstituted carbon atoms may be helpful but not essential to PCB metabolism. Discussion regarding the latter issue is provided.

RESPONSE: The generalization states: "PCB metabolites tend to be 3- or 4-hydroxy compounds produced via an arene oxide intermediate." This statement will be revised as follows: "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 latter pathway will be indicated in Section 4.2.3.2. The statement pertaining to the vicinal unsubstituted carbon atoms will be replaced with the following sentences: "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."

- e) Submitter #45, comment 63, observes that the hexachlorobiphenyl compound for which a biological half-life is given includes only four position designations, and that a citation for the half-life data is not provided.

RESPONSE: The error will be corrected. The overview

should not contain references. Citations for the half-life data are provided in Section 4.2.4.2.

- f) Submitter #45, comment 64, indicates that there is no evidence to support the statement indicating that biochemical effects have been associated with Aroclor exposure in the general population (p. 42, fourth paragraph, last sentence). Results of studies examining these effects are reviewed by the submitter. The submitter concludes that the term "equivocal association" would be more appropriate in the overview to describe the relationship between both occupational and environmental Aroclor exposures and increased enzyme levels.

RESPONSE: The statement will be reworded as follows: Inconsistent subclinical alterations in serum enzyme indicators of possible hepatocellular damage have been associated with occupational and environmental exposure to Aroclors.

- g) Submitter #45, comment 67, objects to the statement concluding that various "fetotoxic" effects have been associated with PCB exposure in humans. The submitter indicates that the evidence is largely equivocal and that the reader should be made aware that it cannot be relied upon.

RESPONSE: The statement will be revised to indicate that the evidence for developmental toxicity in humans is equivocal.

4.2 TOXICOKINETICS

4.2.2 Distribution

4.2.2.2 Oral

- a) Submitter #45, comment 68, strongly disagrees with the inclusion of the unsupported speculation of Jacobson et al. (1985) that placental transfer of PCB could be more harmful than breastmilk transfer. Results of studies providing evidence to the contrary are summarized.

RESPONSE: SRC agrees with the evidence provided by the submitter and will delete the speculative statement.

4.3 TOXICITY

- a) Submitter #49, comment 38, agrees with the introductory discussion of factors that complicate evaluating the toxicity of PCBs.

RESPONSE: No response is required.

- b) Submitter #49, comment 39, and Submitter #45, comments 11 and 69, refer to the statement "...it is assumed that effects resulting from exposure to a specific Aroclor are representative of effects which may be produced by other Aroclors." Submitter #49 states that the statement is patently untrue, and that any attempt to derive toxic endpoints for all PCBs based on data from a single Aroclor is misleading and probably untrue. Submitter #45 concludes that the statement is indefensible; the basis for the conclusion is presented, including evidence from the profile documenting that the toxicity of Aroclors is not equivalent. Submitter #45, comment 11, suggests that EPA methodology for the evaluation of toxicological data for chemical mixtures (51FR34014) should be considered when evaluating PCBs; an outline of the EPA procedure is provided. Submitter #45, comment 69, concludes that the approach of assuming that all PCBs represent equivalent hazards and produce equivalent toxicities should be abandoned. Submitter #45, comment 74, indicates that the results of the Biocca et al. (1981) study (p. 55, paragraph 2) should be considered in reevaluating the opinion that all Aroclor mixtures should be considered as being equally toxic.

RESPONSE: The approach taken is consistent with EPA policy and was approved by the Science Review Panel.

4.3.1 Lethality and Decreased Longevity

4.3.1.2 Oral

- a) Submitter #13(C), comments 25 and 37, Submitter #45, comments 7 and 70, and Submitter #49, comment 29, indicate that survival data from chronic studies in addition to the NCI (1978) bioassay should be included in the profile. These comments indicate that survival data from the Kimbrough et al. (1975), Schaffer et al. (1984), Young (1985) and Norback and Weltman (1985) studies should be included and discussed, as they indicate that

decreased survival is not a universal finding in chronic PCB studies and suggest that carcinomas associated with exposure to 60% chlorine PCB mixtures are not life-shortening.

RESPONSE: The Guidance To Contractors specifies that (1) only the key study for each effect, route and species is to be described in detail (in three or four sentences), and (2) results of studies which are not key are to be grouped together and generalized. The NCI (1978) bioassay is the key study for chronic survival since equivalent toxicity of Aroclors is assumed for the purpose of risk assessment. A general statement regarding unchanged or increased survival in the Kimbrough et al. (1975), Schaffer et al. (1984), Norback and Weltman (1985) and Young (1985) studies therefore will be added to this section of the profile.

- b) Submitter #45, comments 16 and 70, indicates that the that the statement "The cause of death was unspecified but may have been related to development of nodular hyperplasia in the liver.", referring to death in the NCI (1978) bioassay, is speculative and should be deleted.

RESPONSE: SRC will delete the statement and indicate that the cause of death was not specified.

4.3.2 Systemic/Target Organ Toxicity

4.3.2.1 Liver

- a) Submitter #13(C), comment 30 states that the general discussion statement "Hepatotoxicity is suggested in occupationally exposed humans (EPA, 1987a; Drill et al., 1981)." is not true for the reasons discussed in comments 15 and 16 (Section 2.2.2.2).

RESPONSE: The statement will be revised to indicate that studies of Aroclor-exposed workers provide suggestive evidence for subclinical alterations in liver enzyme levels but no evidence of hepatotoxicity. It will be indicated that elevated liver enzymes are not necessarily indicative of an adverse effect and may be an adaptation response.

- b) Submitter #45, comment 10, indicates that the

literature cited in the first paragraph summarizing clinical measurements of capacitor workers should be reevaluated, since there is no evidence that chronic PCB exposure results in liver injury, elevated serum lipid levels or other indications of overt clinical dysfunction in these workers. Supporting text from Smith et al. (1982) is cited.

RESPONSE: The first sentence of this paragraph will be reworded to more clearly indicate that occupational exposure to Aroclors is associated equivocally with liver enzyme alterations and that there is no evidence for impaired liver function.

- c) Submitter #45, comment 65, indicates that the profile fails to note the possibility that an increase in liver enzyme level is not necessarily a toxic manifestation but more likely an adaptation response. Submitter #45, comment 66, indicates that the clinical surveys of exposed workers were not reviewed in context of the Emmett (1985) study, which reportedly suggests that serum PCB levels are not responsible for the small serum enzyme changes that occasionally have been reported. A summary of the Emmett (1985) study is provided.

RESPONSE: These comments are addressed in the responses to comments 4.3.2.1a,b.

- d) Submitter #45, comment 71, indicates that descriptions in the first paragraph of this section (p. 52) are inaccurately presented on p. 27 (Section 2.2.2.2). Inconsistencies include referral to altered serum enzymes as not being associated with clinically detectable liver disease on p. 52 but an indicator of possible hepatocellular damage on p. 27, and results of the Maroni et al. (1981a) study as "asymptomatic hepatomegaly" on p. 52 and "well defined liver failure" on p. 27.

RESPONSE: These comments are addressed in the responses to comments 2.2.2.2c,f.

- e) Submitter #45, comment 72, refers to the statement "There was a correlation between SGOT and serum PCB levels.", which pertains to the Fischbein et al. (1979) study. The submitter concludes that this statement is inadequate due to its simplicity and should either be deleted or changed to incorporate

a more complete picture of the data available on the subject. It is indicated that the results of this study are more correctly summarized as providing evidence that high serum PCB levels may be associated with a marginally increased incidence of persons with SGOT values outside of the "normal" range, because statistical tests for correlation were not conducted. It is also indicated that recent studies by Fischbein (1985), Emmett (1985) and Lawton (1985) contradict this statement.

RESPONSE: SRC agrees with the comment and will make an appropriate revision to the statement.

- f) Submitter #49, comment 21, states that a distinction should be made between alterations in liver-associated enzymes, liver function tests and adverse health effects. It is noted that Ouw et al. (1976) and Alvares et al. (1977) are the only cited human studies that measured liver function and that elevated liver-associated enzymes do not necessarily indicate an adverse health effect. These comments also pertain to Section 2.2.1.1.

RESPONSE: This comment is addressed in the responses to comments 4.2.3.1a,b.

- g) Submitter #45, comment 73, refers to the statement "Serum PCB levels were positively associated with increased GGPT levels and blood pressure in Triana, Alabama, residents that were exposed to contaminated fish (Kreiss et al. 1981)." The submitter objects to this statement because it implies that the effect on blood pressure is attributable solely to PCBs. Although not specified, it is inferred that this objection also refers to the effect on GGPT levels. The submitter concludes that the statement should either be removed or changed to incorporate a more complete picture of the blood pressure effects data from this and other PCB studies.

RESPONSE: The submitter does not acknowledge the subsequent qualifying statement: "The significance of these effects is uncertain as the fish also contained high concentrations of DDT." As this section is concerned with hepatic effects, the summary of the Kreiss (1981) study will be rewritten to reflect only the effect on GGPT and more clearly express the mixed PCB and DDT

exposure. Comments pertaining to effects on blood pressure are addressed in responses to comments in Section 2.2.2.2.

- h) Submitter #45, comment 74, states that the summary of the Biocca et al. (1981) study should also indicate that the more potent PCB isomers tend to accumulate to a greater extent in the fat.

RESPONSE: It will be more clearly indicated in Section 4.2.2.2 that the accumulation of PCBs in lipophilic tissues is dependent on the structure-dependent metabolic rates of the individual congeners.

- i) Submitter #13(C), comment 30, Submitter #45, comment 75, and Submitter #49, comment 21, refer to the general discussion statement "Implications of enzyme induction for human health include the occurrence of disease secondary to the increased metabolism of endogenous or exogenous substances, and the interference with medical therapy due to increased metabolism of administered drugs (Letz 1983)". Submitter #13(C) indicates that the statement is speculative and should be deleted, since there is no evidence that individuals exposed to PCBs occupationally or environmentally experience any of these effects. Submitter #49 indicates that the effects are speculative, that the references cited by Letz (1983) do not support the statement, and that the reverse can also be true. Submitter #45 indicates that for the sake of completeness it should be mentioned that prior microsomal enzyme induction by PCBs has been shown to decrease the tumorigenic effects of various carcinogens (specific carcinogens and references are cited), microsomal enzyme induction is generally beneficial, the need to increase the dose of some medications due to microsomal enzyme induction is not an uncommon or difficult problem, and a number of important drugs which have been used chronically in humans are potent microsomal enzyme inducing agents.

RESPONSE: It is appropriate to speculate on implications of enzyme induction for human health in the general discussion since PCBs are enzyme inducers. SRC agrees that other possible effects of enzyme induction should be mentioned for completeness.

- j) Submitter #45, comment 76, refers to the review of Safe et al. (1985) (p.56, paragraph 3) regarding the mechanism of PCB induction of liver enzymes. The submitter states that it should be pointed out that while there is a general agreement as to the role of the Ah receptor in enzyme induction, the role for this receptor in PCB toxicity is much less clear and that this theory has become a controversial. The role of Ah receptor binding in halogenated aromatic hydrocarbon toxicity is discussed by the submitter.

RESPONSE: It will be indicated that the role of the Ah receptor in PCB toxicity is unclear.

- k) Submitter #13(C), comment 31, indicates that the reference to the Yusho and Yu Cheng patients in the discussion should be deleted.

RESPONSE: See response to comment 4.1a.

4.3.2.2 Cutaneous tissue

- a) Submitter #45, comment 77 indicates that the statement referring to the conclusion of Drill et al. (1981) that blood levels ≥ 200 ppb are associated with chloracne should be changed or qualified, because there are little or no data available to suggest that the 200 ppb level represents some type of threshold.

RESPONSE: The statement will be qualified by indicating that the available evidence cannot be used to conclude that 200 ppb represents a threshold.

- b) Submitter #49, comment 19, agrees with the statement indicating that correlations between chloracne and duration of exposure or blood PCB levels are lacking, but states that it should also be noted that the true incidence of chloracne is unknown but appears to be very low.

RESPONSE: SRC agrees with the comment and will make an appropriate addition.

4.3.2.3 Immunological effects

- a) Submitter #49, comment 22, identifies two human studies that were not cited (Emmett et al., NIOSH Health Haz. Eval. Prog. Med. Rep., #80-7, 1983; Lawton et al., Env. Health Persp., 60:165-184, 1985).

RESPONSE: Appropriate information from these studies will be added to the profile.

- b) Submitter #49, comment 23, indicates that the profile should acknowledge that there is insufficient data to support speculation that PCBs can alter incidences of infection or cancer via effects on the immune system.

RESPONSE: The profile states "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...". This speculation is appropriate because it is qualified, refers to immunosuppression in general and appears in the general discussion.

4.3.2.7 Porphyria

- a) Submitter #49, comment 24, identifies a study that was not cited that reportedly does not provide evidence for abnormal porphyrin metabolism (Colombi et al., J. Appl. Tox., 2:117-121, 1982). The submitter is unaware of data supporting the speculation of Drill et al. (1981) that exposure to PCBs can cause an attack of porphyria in patients suffering from acute intermittent porphyria, and indicates that if such data exist, it should be cited. The submitter noted that the data from Colombi et al. (1982) suggest that the converse may be true.

RESPONSE: The Colombi et al. (1982) report will be obtained, reviewed and, if appropriate, summarized for inclusion in the profile. The basis for the speculation is presented. The appropriateness of the speculation will be reevaluated upon review of the Colombi et al. (1982) data.

4.3.3 Developmental Toxicity

4.3.3.2 Oral

- a) Submitter #13(C), comment 34 indicates that the studies regarding possible behavioral effects of PCBs on human neonates (Jacobsen et al. 1984b, 1985) are inadequately evaluated with respect to exposure. Issues identified and discussed by the submitter include PCB blood levels within the range of the general population, lack of analysis for chemicals other than PCBs, and correlation of behavioral deficits with fish consumption but not cord serum PCB levels.

RESPONSE: The summaries of the human oral developmental studies will be condensed to a single general paragraph because the effects on birth weight, gestational age and behavior are inconclusive due to limitations that complicate evaluation of the studies and lack of validation. Since these are not key studies, generalization is appropriate and preferred. Limitations of the studies will be identified, including correlations of effects with consumption of contaminated fish but not serum levels of PCBs and unknown contribution of other contaminants in the fish.

- b) Submitter #49, comment 17, discusses limitations of the Fein (1984), Fein et al. (1984) and Jacobsen et al. (1984a, 1984b) studies that complicate evaluation, including failure to report maternal and cord serum PCB levels based on fish consumption. The submitter states that Jacobsen (1984b) did not find a statistically significant association between fish consumption and autonomic maturity ($p < 0.10$).

RESPONSE: These issues are addressed in the response to comment 4.3.3.2a above.

- c) Submitter #45, comments 78 and 79, reiterates shortcomings of the human studies (Fein 1984, Fein et al. 1984, Jacobson et al. 1984a) discussed in comments referred to in previous sections. Due to the shortcomings of these studies and lack of corroborating data from Rogan et al. (1986, 1987) and Taylor et al. (1984), it is recommended in comment 78 that the summaries be presented in a manner that does not mislead the lay public as to the actual limited significance of the studies.

RESPONSE: This issue is addressed in the response to comment 4.3.3.2a above.

- d) Submitter #45, comment 80, states that the profile cites the results of the Jacobson et al. (1985) study without mentioning the authors' suggestion that, while their study indicates that high cord PCB levels may be associated with developmental delay in the performance of a visual task, their results cannot be extrapolated to indicate that any permanent PCB-induced damage had occurred. The submitter states that this study should be considered flawed for failing to consider the potential effect of lead by evaluation of serum or cord lead concentrations.

RESPONSE: This issue is addressed in the response to comment 4.3.3.2a above.

- e) Submitter #13(C), comment 35 indicates that the summary of the Rogan et al. (1986) study is incomplete because the correlation of hyporeflexia with both PCB and DDE levels and results of tests conducted during the first three days of life were not reported.

RESPONSE: This issue is addressed in the response to comment 4.3.3.2a above.

- f) Submitter #13(C), comment 36, Submitter #45, comments 9 and 78, and Submitter #49, comment 18, identify a study by Rogan et al. (Am. J. Public Health, 77:1294, 1987) not included in the profile.

RESPONSE: Results of the Rogan et al. (1987) study will be added to the profile.

- g) Submitter #45, comment 81, indicates that the summary of the Haake et al. (1987) study would be more complete if it stated that PCB treatment antagonized TCDD-induced terata.

RESPONSE: This information is included in Section 4.4 on "Interactions With Other Chemicals."

- h) Submitter #13(C), comment 42 observes that

"consumed" in line 2, p. 63 is misspelled.

RESPONSE: The error will be corrected.

4.3.3.4 General discussion

- a) Submitter #13(C), comment 31, indicates that the reference to the Yusho incident should be deleted.

RESPONSE: The reference to the Yusho incident will be retained for the reasons discussed in the response to comment 4.1a above.

- b) Submitter #13(C), comment 33, concludes that the statement "Reports of reduced birth weight and gestational age in infants of mothers with occupational and environmental exposure to Aroclors (Taylor et al. 1984, Fein 1984, Fein et al. 1984) are inconclusive but consistent with the animal developmental effects data" implies that the human and animal studies show a similar trend. Based on an evaluation of these human studies and additional reports not cited in the profile, the submitter further concludes that any implications that PCB exposure may be resulting in decreased birth weights or early births in humans are unwarranted. The basis for these conclusions is discussed.

RESPONSE: The finding of developmental effects in animals raises the possibility that developmental effects may be of concern for humans. As the general discussion is the place to discuss similar and differential effects in humans and animals, reference to the animal studies is appropriate. The statement will be modified to indicate that developmental effects were observed in animals, but evidence for developmental effects in humans is inconclusive.

- c) Submitter #45, comments 9 and 14, agrees with the conclusion that the human developmental toxicity studies (Taylor et al. 1984; Fein et al. 1984) are inconclusive, but wonders why they are repeatedly cited and why they are cited at all, since a goal of the profile is to cite key literature. Comment 9 includes discussion pertaining to problems associated with the human developmental toxicity studies is provided. Comment 14 notes that these studies are mentioned in some sections of the

profile without the caveats that the effects are inconclusive and cannot be attributed to PCBs.

RESPONSE: This issue is addressed in Section 4.3.3.2 in the response to comment 4.3.3.2a. The summary of these studies in Section 2.2.1.2 will be generalized and appropriately caveated.

- d) Submitter #45, comment 82, indicates that the reduced birth weight and gestational age reported by Taylor et al. (1984) were not statistically significant, and therefore contradict the findings of Fein (1984) and Fein et al. (1984) and indicate that similar effects would not occur in children of mothers who were exposed to lower PCB levels via environmental contamination.

RESPONSE: This issue is addressed in the response to comment 4.3.3.2a.

- e) Submitter #49, comment 18, indicates that it should be noted that the findings of Rogan et al. (1986) are inconsistent with Fein et al. (1984), as Rogan et al. (1986) did not find associations between decreased birth weight or head circumference and serum PCB levels.

RESPONSE: This issue is addressed in the response to comment 4.3.3.2a.

- f) Submitter #3(B), comment 99, indicates that the significant divergence of views regarding the relative contributions of nursing and placental transfer in exposure to young experimental animals or humans is not discussed. The submitter notes that while it is true that nursing infants may be exposed to high PCB concentrations in the breast milk, it should be acknowledged that virtually all breast milk in the U.S. contains some detectable PCB levels which form part of the "background" exposure risk. Submitter #45, comment 83, concludes that the suggestion that intrauterine exposure to PCBs may be more harmful than lactation exposure is insupportable; the basis for this conclusion is discussed. Related comments appear in Section 4.2.2.1.

RESPONSE: SRC will make appropriate modifications

4.3.5 Genotoxicity

4.3.5.2 Nonhuman

- a) Submitter #13(C), comment 23, and Submitter #45, comment 84, indicate that the report by Wyndam et al. (1976) is irrelevant and should be deleted because the senior author of the study was unable to reproduce the results and considers the evidence for mutagenicity of 4-chlorobiphenyl to be negative. The submitters provided an affidavit from the senior author for documentation and citation. Submitter #13(C), comment 23, therefore considered the implication that PCBs may be mutagenic to be incorrect.

RESPONSE: The references to Wyndham et al. (1976) and Harbison (1986) in the text and the suggestion that the less chlorinated PCBs may be metabolized to mutagenic compounds to a greater extent than the more chlorinated PCBs will be deleted. Citations to Harbison (1986) and the affidavit will be added to Table 4.3.

- b) Submitter #45, comment 85, reviews the Peakall et al. (1972) study and concludes that the results were inconclusive; the submitter indicates that this also was the conclusion of the authors of the study.

RESPONSE: SRC agrees that the results should be indicated as equivocal rather than positive.

4.3.6 Carcinogenicity

4.3.6.1 Inhalation

- a) Submitter #13(C), comment 28 agrees with the conclusion in the general discussion that there is inadequate information to characterize PCBs as human carcinogens, but indicates that the limited relevance of the only positive human data (Bahn et al., 1976, 1977) should be discussed in the profile; specific limitations of the study were identified. Submitter #45, comments 12 and 86, indicates that the Bahn et al. (1976) study was withdrawn for revision without release of a follow-up, and cited at the expense of better studies in which no increase in cancer was observed. Submitter

#45, comment 86, reviews the study and discusses limitations. Submitter #49, comment 25, states that the Bahn et al. (1976, 1977) study is not generally accepted as sufficient evidence for carcinogenicity due to small number of tumors and cohort size; other limitations of the study are discussed.

RESPONSE: Limitations will be added to the summary of the study. The limited relevance of the study is implied in the conclusion that the available human data do not indicate a consistent tumorigenic effect.

- b) Submitter #13(C), comment 29, and Submitter #49, comment 27, identify a recently published epidemiological study that is not included in the profile: Bertazzi et al. (1987; Am. J. Ind. Med., 11:165). Other uncited epidemiological studies were also identified: "The Greater New Bedford PCB Health Effects Study 1984-1987" (Submitter #13[C], comment 29), and Brown (1987), an unpublished NIOSH study that is an update of the Brown and Jones (1981) data (Submitter #49, comment 26). The aforementioned studies are discussed by the submitters.

RESPONSE: Summaries of these studies will be added to the profile.

4.3.6.2 Oral

- a) Submitter #13(C), comment 24, and Submitter #45, comment 88, observed that the summary of the Kimbrough et al. (1975) study did not report that tumor incidences in tissues other than the liver were sometimes decreased with PCB treatment, and that overall tumor incidence was less in the treated rats than in the controls. Submitter #13(C), comment 24, considers this information relevant to the general discussion (Section 4.3.6.4).

RESPONSE: A statement indicating that decreased incidences of extrahepatic tumors have been observed in studies of carcinogenic 60% chlorine PCB mixtures will be added to the discussion.

- b) Submitter #13(C), comments 26 and 27, and Submitter #49, comment 8, address the omission of negative

carcinogenicity data for non-Aroclor mixtures from the profile. The submitters observe that and/or question why the profile cites the Schaeffer et al. (1984) study as providing positive evidence for carcinogenicity of a 60% chlorine commercial PCB mixture (Clophen A-60), but neglects to mention that Clophen A-30 was negative in the same study; the significance of these and other data are discussed with respect to carcinogenicity of PCBs as a function of increasing average degree of chlorination. Submitter #13(C), comment 27 also provides discussion leading to the conclusion that if non-Aroclor studies are to be used in the profile, both positive and negative results should be included.

RESPONSE: The omission of negative carcinogenicity data for non-Aroclor PCBs is consistent with the intent of the following Overview (Section 4.1) statement: "Reference to Kanechlors is made occasionally to support statements made about Aroclors because effects produced by Kanechlors are similar."; this statement will be revised to include reference to Clophens. The omission of non-Aroclor PCB carcinogenicity is appropriate because EPA concluded that Aroclors are carcinogenic; the Guidance To Contractors indicates that summaries should be provided for those studies which contribute to the weight of evidence for carcinogenicity.

- c) Submitter #45, comment 7, states that the profile "ignores the article by Young (1985), certain data provided in Kimbrough et al. (1975), and statements made by Norback and Weltman (1985), all of which clearly indicate that the liver tumors observed in rats fed PCB mixtures of 60% chlorine do not act like malignant tumors". Submitter #49, comment 29, indicates that the liver tumors in the Kimbrough (1975), Schaeffer (1984), Norback and Weltman (1985) and Ito (1974) studies were not aggressive and did not metastasize. Submitter #49, comment 9, indicates that reference to the late-developing, non-metastasizing and non-life shortening nature of the tumors in the Norback and Weltman (1985) study should be included in the profile. Submitter #63, comment 2, also indicates that the unaggressive nature of the nodules in the Norback and Weltman (1985) study should be noted.

RESPONSE: The summary of the Norback and Weltman

(1985) study in Section 4.3.6.2 states: "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." Specific statements regarding the nature of the liver tumors in the other studies is inconsistent with the intended level of detail for non-key studies, particularly for studies of non-Aroclor PCBs (i.e., Ito, 1974 and Schaeffer, 1984). A general statement regarding the nature of the liver tumors in studies of carcinogenic 60% chlorine PCB mixtures will be added to the discussion.

- d) Submitter #45, comment 7, states that the profile ignores evidence from the Young (1985), Kimbrough et al. (1975) and Norback and Weltman (1985) studies that carcinogenic 60% chlorine PCB mixtures appear to have antitumorigenic effects on extra-hepatic tumors. Submitter #45, comment 8, concludes that by ignoring this information, the profile "apparently intentionally leads the reader to inevitable conclusions which exaggerate the likely qualitative cancer risk that PCBs pose to humans."

RESPONSE: This issue is addressed in the response to comment 4.3.6.2a.

- * e) Submitter #45, comment 89, argues that EPA's use of combined incidences of neoplastic nodules and hepatocellular carcinomas from the Norback and Weltman (1985) study as the basis for the quantitative risk assessment is inappropriate.

RESPONSE: No action is required.

- f) Submitter #49, comment 9, discusses limitations of the Norback and Weltman (1985) study, including the uncertain role of partial hepatectomy in the development of liver tumors and use of one progressive dose level.

RESPONSE: The summary of the Norback and Weltman (1985) study is sufficient for a carcinogenicity section of an ATSDR profile.

- g) Submitter #45, comment 90, indicates that the negative carcinogenicity findings of the NCI (1978) bioassay provide additional data that should be considered in reevaluating the opinion that all Aroclor mixtures should be considered as being equally toxic.

RESPONSE: ATSDR concurs with the EPA conclusion that current data are inadequate to differentiate between the carcinogenicity of PCB mixtures with any reasonable degree of confidence.

- h) Submitter #13(C), comment 31 and Submitter #45, comments 87 and 91, agree that there is sufficient toxicological evidence to separate Kanechlors from Aroclors, and indicate that references to the Yusho incident should be deleted (see related comments in Section 4.1). Submitter #49, comment 28, indicates that inclusion of the Yusho data is inconsistent with the rest of the profile which eliminates such data. Submitter #49, comment 28, discusses limitations of the Amano et al. (1984) and Kuratsune (1986) Yusho studies.

RESPONSE: As indicated in the response to comment 4.1a, the references to the Yusho incident will be moved to the general discussion.

- i) Submitter #45, comment 91, refers to the conclusions that the Kimura and Baba (1973) and Ito et al. (1974) Kanechlor studies are inadequate for assessing carcinogenicity. The submitter notes that although the rats were fed "high doses of various Kanechlors over a period of time less than that required for a chronic study, prevailing theories in chemical carcinogenesis would suggest that the increased doses used in these studies would decrease tumor latency while increasing tumor incidence. This runs counter to the ideas that these studies were not chronic bioassays and that they provide little evidence concerning the carcinogenicity of the PCB mixtures."

RESPONSE: The EPA conclusion that these studies are not useful for assessing the carcinogenic potential of these PCB mixtures is appropriate. It is appropriate to delete the summaries of these studies because they provide inconclusive carcinogenicity data for non-Aroclor PCBs.

- j) Submitter #13(C), comment 43 states that "...polychlorinated quinones." in line 32, p.69 should be "...polychlorinated quaterphenyls."

RESPONSE: The error will be corrected.

4.3.6.3 Dermal

- a) Submitter #45, comment 92 indicates that, for completeness, the findings of Berry et al. (1979) showing that PCBs afford protection against the development of papillomas should be included in the profile.

RESPONSE: The results from this study will be reviewed and added to the profile if deemed to be appropriate. SRC objects, however, to any statement that would imply that exposure to PCBs is beneficial.

4.3.6.4 General discussion

- a) Submitter #45, comment 93, indicates that the discussion of the NCI bioassay should be removed because it is speculative rather than descriptive. It is stated that "decidedly different results would have been obtained if the experiments of Schaeffer et al. (1984) or those of Norback and Weltman (1985) had been performed for the traditional two year period rather than the 27-29 month duration used in these two studies."; discussion supporting this statement is provided. Referring to a review of the animal carcinogenicity studies provided as an appendix to the comments, the submitter concludes that the profile "...failed to evaluate critically all of the evidence..." and "...there is considerable scientific evidence that is counter to the conclusions and statements rendered in this subsection of the profile."

RESPONSE: Speculation is appropriate in a discussion section. The intent of this discussion is to indicate the reasoning behind EPA's assessment of carcinogenicity, particularly the issue of biological significance versus statistical significance. The submitter's speculation regarding the Schaeffer et al. (1984) and Norback and Weltman (1985) studies does not appear to be inconsistent with the discussion (i.e., the suggestion that

liver tumors can be detected only in long-term experiments).

4.4 INTERACTIONS WITH OTHER CHEMICALS

- a) Submitter #13(C), comment 44 indicates that phenobarbital, rather than pentobarbital, should be used on line 42, p.73.

RESPONSE: The investigators (Chu et al. 1977; Villeneuve et al. 1972) of these studies used pentobarbital, not phenobarbital.

- b) Submitter #45, comment 94, and submitter #49, comment 30, observe that many studies are available reporting that PCBs have promoting effects, initiating effects, antitumorigenic effects and/or no effects on tumorigenesis with other carcinogens.

RESPONSE: Section 4.4 does report the effects of PCBs on the carcinogenicity of other compounds.

- c) Submitter #45, comment 94, indicates that the summary of the Haake et al. (1987) study failed to note that Aroclor 1254 antagonized the teratogenicity of TCDD.

RESPONSE: The submitter is mistaken. The summary of the Haake et al. (1987) study in Section 4.4 indicates that Aroclor 1254 antagonized the teratogenicity of TCDD.

5. MANUFACTURING, IMPORT, USE AND DISPOSAL

5.2 PRODUCTION

- a) Submitter #45, comment 95, indicates that the basis for the estimate of the sale of 1 billion pounds of PCBs in North America since 1970 is unclear and should be verified.

RESPONSE: The source of the 1 billion pound estimate is IARC (1978) which obtained the estimate from the Interdepartmental Task Force on PCBs (1972). The statement in the profile is incorrect and should read "sold in North America by 1970" rather than "sold in North America since 1970". The estimate seems reasonable since North America is being considered rather than just the United States.

5.4 USES

- a) Submitter #45, comment 96, states that the profile is "...misleading in describing the typical size of capacitors utilizing PCBs. No discussion is provided as to the average size of a capacitor or to the amount of PCBs typically contained in 'small' or 'medium' sized capacitors."

RESPONSE: The profile does not describe the typical size of a capacitor; therefore, it can't be misleading in describing something it doesn't discuss. As noted in the profile (page 76, paragraph 2), a thorough review of PCB use can be found in EPA (1976). The brief discussion of transformers and large capacitors in section 5.4 is intended simply to inform the reader of the general method of filling these electrical devices with PCBs.

- b) Submitter #19, comment 3, states that Aroclors 1260 and 1262 are still occasionally used as a slide mounting medium; it is recommended that this use and exemption should be mentioned in the profile.

RESPONSE: This recommendation by Submitter #19 seems appropriate. The exemption and use of the Aroclors as a slide mounting medium will be noted in section 5.4.

5.5 DISPOSAL

- a) Submitter #45, comment 97, states that "The statement that the TSCA regulations promulgated on April 18, 1978 required PCB disposal by incineration is incorrect." Discussion is provided.

RESPONSE: The statement in the profile (page 76, paragraph 3) is correct. The regulation required PCB incineration UNLESS "clearance is obtained from the EPA to dispose of the materials in another manner". In comment 97, Submitter #45 states that "most PCB waste was not disposed of through incineration following promulgation of these regulations". While this is most likely correct, Submitter #45 does not provide documentation for this statement. Submitter #45 appears to be objecting to the statement in the profile "because it implies that all PCB disposal from 1978 to at least 1983 was by incineration". The statement in the profile does not imply this at all.

6. ENVIRONMENTAL FATE

6.1 OVERVIEW

- a) Submitter #45, comment 98, indicates that the statement that Aroclors with a high degree of chlorination are resistant to biodegradation is somewhat inconsistent with statements made in Section 6.3.2. Discussion is provided.

RESPONSE: The statement in the overview and the statements in section 6.3.2 are not inconsistent. The reviews of PCB biodegradability clearly show that the higher chlorinated congeners are resistant to biodegradation, where resistant refers to extremely slow biodegradation. Submitter #45 refers to the Brown et al (1987) study (section 6.3.2, paragraph 4, line 14), which observed anaerobic biotransformation of the higher chlorinated congeners, as a possible inconsistency with the statement in the overview. Actually, extremely slow anaerobic degradation in sediments is completely consistent with the overview statement. Potential anaerobic biotransformation in sediments is important because this is only known route by which the higher chlorinated PCBs may be degraded at such anaerobic environmental sites. Even though the transformation may be extremely slow, it is the only route by which degradation is occurring and, therefore, it will be the ultimate degradation process.

6.2 RELEASES TO THE ENVIRONMENT

- a) Submitter #49, comment 40, indicates that the profile fails to mention that sewage waste discharge may be the major source of PCBs to aquatic systems, particularly in major urban-industrial areas.

RESPONSE: Submitter #49 fails to cite any source which documents their comment. The literature reviewed during the preparation of the profile did not mention sewage waste discharge as a major source of PCB release to the aquatic environment. If documentation can be located to support this statement, it should definitely be incorporated into the document.

6.3 ENVIRONMENTAL FATE

6.3.1 Transport and Partitioning

- a) Submitter #49, comments 41 and 42, indicates that statements in the first paragraph are over-generalized. Discussion is provided leading to the conclusions that

desorption of PCB congeners is not a simple function of $\log K_{ow}$ but depends upon $\log K_{ow}$, solubility, vapor pressure and particle size and organic content (comment 41), and that the "sink" concept must be modified because it is only the PCBs in the very top layers of sedimentary deposits that are available for redistribution (comment 42).

RESPONSE: Although statements in the paragraph are generalized, they are believed to be correct. Submitter #49 is objecting to the statement that the lower chlorinated components of an Aroclor will sorb less strongly than the higher chlorinated components. Numerous Koc studies have shown that the lower chlorinated PCB congeners adsorb less strongly than the higher chlorinated congeners. In comment 41, Submitter #49 discusses the importance of particle size distribution in adsorption, which is correct. However, when the same particle size distribution is present, the lower chlorinated congeners will adsorb less strongly than the higher chlorinated congeners. An in-depth discussion of all adsorption/desorption parameters is beyond the scope of this profile. In comment 42, Submitter #49 objects to the concept that aquatic sediments can act as an environmental sink for PCBs. Yet, section 6.3.1, paragraph 1, line 10 notes two studies that have proven this concept on an environmental level. Submitter #49 notes that only PCBs in the top layers of sedimentary deposits are available for redistribution while the PCBs in the lower layers may be sequestered. This may be true and could be noted in the revised profile.

6.3.2 Transformation and Degradation

- a) Submitter #45, comment 99, concludes that excessively high PCB bioconcentration factors were reported in the profile. Discussion with references is provided.

RESPONSE: Submitter #45 is confusing concentration and bioconcentration factors. A bioconcentration factor is a ratio of the concentration in the organism to the concentration in the water. Bioconcentration factors are not expressed in terms of ppm.

- b) Submitter #49, comments 43 and 44, indicates that the first part of paragraph 4 contains over-generalized and misleading statements. Specifically, the submitter disagrees with the indications that Aroclors are composed of particular isomer groups (comment 43) and

that particular Aroclors may biodegrade rapidly, slowly or be resistant to biodegradation (comment 44). In reference to the latter comment, the submitter states that "... , some of the congeners that are constituents of particular Aroclors can be said to be degraded to such an extent that the Aroclor ceases to exist as a conceptual entity on a gas chromatographic tracing."

RESPONSE: The second sentence in paragraph 4 will be amended to: "In general, the results show that mono-, di-, and trichlorinated biphenyls (major components in Aroclors 1221 and 1232)...", to make the intended meaning clearer. The components of the various Aroclors are clearly listed in Table 3.3; the second sentence in paragraph 4 is not attempting to define the Aroclors as Submitter #49 appears to believe. Submitter #49 is also objecting to the concept that the less chlorinated biphenyls biodegrade more rapidly than the higher chlorinated ones. Yet the reviews cited in paragraph 4 have shown this to be true. Submitter #49 is correct in the concept that differing degradation rates of an Aroclor's components will change the make-up of the remaining mixture.

7. POTENTIAL FOR HUMAN EXPOSURE

7.2 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

7.2.2 Water

- a) Submitter #49, comment 45, indicates that the data in the first paragraph show that PCB concentrations in ocean waters vary tremendously, indicating that they reflect local PCB inputs and do not represent "background" levels.

RESPONSE: When the monitoring data from the southern North Sea is excluded (due to anthropogenic influence), the concentrations do not vary tremendously. The concentration range would then be only about one order of magnitude. Averaging of those data would then be a good indication of background levels. Background levels do not have to be global in nature, but can, and usually are, localized in nature. The first paragraph of section 7.2.2 can be amended to make the meaning clearer and note the anthropogenic influences. Submitter #49 is correct in noting that paragraph should be more consistent.

- c) Submitter #45, comment 100, indicates that the profile fails to put the water monitoring data into perspective by failure to compare with the U.S. EPA (1987a) drinking water criterion for carcinogenicity at the 10^{-4} risk level.

RESPONSE: Section 7.2.2 is intended to outline levels monitored in the environment, and not to discuss health risk assessment.

8. ANALYTICAL METHODS

8.1 ENVIRONMENTAL MEDIA

- a) Submitter #70, comment 2, states that the method referred to in the second paragraph should be EPA 608 instead of 680.

RESPONSE: The EPA method number will be checked and changed if incorrect.

9. REGULATORY AND ADVISORY STATUS

9.2 NATIONAL

9.2.1 Regulations

- a) Submitter #13(C), comment 38, recognizes that the OSHA standards for PCBs are not presented.

RESPONSE: The OSHA standards will be added.

9.2.2 Advisory Guidance

9.2.2.2 Water

- a) Submitter #45, comment 100, indicates that the profile fails to put the drinking water criteria for carcinogenicity into perspective by not comparing with the monitored concentrations of PCBs reported in Section 7.2.2, by not comparing with the drinking water standards for chloroform and arsenic, and by not indicating that epidemiologic evidence can be used to invalidate the PCB cancer risk estimate. Other comments pertaining to the latter issue are referred to in Section 1.6.

RESPONSE: The intent of this section is to tabulate advisory guidelines.

9.2.3 Data Analysis

- a) Submitter #13(C), comment 39 states that reference to Clophen A-30 as an animal carcinogen should be deleted as Clophen A-30 was not carcinogenic in the only study that examined its potential carcinogenicity (Schaeffer et al. 1984). Submitter #45, comment 6, also observes that there was no evidence for carcinogenicity of Clophen A-30 in this study.

RESPONSE: EPA concluded that the results of the Clophen A-30 study provide limited evidence of carcinogenicity because the incidence of neoplastic nodules was significantly increased. The evidence from this study and the studies of Aroclors 1254 and 1260, Kanechlor 1254 and Clophen A-60 were considered collectively, with structure-activity considerations, to provide a basis for recommending that PCB mixtures of any composition should be regarded as having the potential to be probable human carcinogens and therefore be placed in the category B2.

- * b) Submitter #45, comment 101, Submitter #49, comment 8, and Submitter #63, comment 1 disagree with the EPA position that all PCB mixtures should be considered to have equal carcinogenicity; discussion is provided. These comments also pertain to Sections 2.2.1.2 and 4.3.6.2. Submitter #49 notes that this assumption is at variance with an extensive body of scientific knowledge and differs from the approach taken by other regulatory bodies (e.g., OSHA, the State of California). Areas discussed by submitter #49 include lack of suitable data for direct estimation of PCB cancer potency in humans, uncertainty associated with species to species and experimental dose to low dose extrapolations, the EPA SAB's recommendation for a congener-specific approach, negative carcinogenicity data for PCBs containing <60% chlorine (Ito et al. 1973; Schaeffer et al. 1984), and the fact that Aroclor 1260 accounted for a minority of total domestic PCB production. Submitter #63 argues that each Aroclor mixture should have its own carcinogenic potency since the less chlorinated mixtures are clearly less carcinogenic than more highly chlorinated mixtures. Submitter #63 calculated potency (q_1^*) values for Aroclor and Clophen PCB mixtures with 30, 42, 54

and 60% chlorination from four studies (Kimbrough et al. [1975], NCI [1978], Schaeffer et al. [1984] and Norback and Weltman [1985]).

RESPONSE: SRC merely reported the EPA risk assessment.

- * c) Submitter #49, comment 11, indicates that ATSDR does the reader a disservice by citing only the conservative EPA carcinogenic potency estimate. The submitter characterizes this estimate as a "worst case" estimate applicable to only one Aroclor formulation that accounted for only a minority of total PCB production. Other PCB potency estimates, including one performed by the U.S. FDA, all smaller than the U.S. EPA estimate, are summarized in tabular form.

RESPONSE: As the Guidance to Contractors requires that other federal estimates of carcinogenic potency be included, the FDA estimate will be included if still recommended by FDA. The only other federal estimates are those of various offices of the EPA (OTS, OHEA), which are superceded by the estimate verified by the CRAVE workgroup.

- d) Submitter #49, comment 9, concludes that since the Norback and Weltman (1985) study used Aroclor 1260, the carcinogenic potency estimate based on this study is not applicable to other Aroclors. Other factors which make direct use of this study problematic are identified and discussed.

RESPONSE: EPA assumes that the potency estimate based on Aroclor 1260 is representative of other PCB mixtures because there is no information regarding which constituents of any PCB mixture might be carcinogenic.

- * e) Submitter #63, comment 2, objects to acceptance of the U.S. EPA (1987a) argument that combined incidences of neoplastic nodules and hepatocellular carcinomas from the Norback and Weltman (1985) study should be used as the basis for the quantitative cancer risk assessment; discussion is presented. It is noted that inclusion of nodules in the risk analysis may lead to an overestimation of risk by 1.5- to 15-fold, and concluded that "At the

very least, q_1^* values derived with and without nodules should be presented and emphasis placed on values excluding nodules."

RESPONSE: No action is required.

- * f) Submitter #49, comment 10, states that "EPA's use of the linearized multi-stage model for epigenetic compounds may be inappropriate and a threshold method of potency estimation might be better applied." The submitter recognizes that U.S. EPA (1987a; 1988) acknowledges this and says that, lacking evidence to support a threshold, the regulatory authority and requirement exists to apply the linearized model. However, since EPA recently reassessed and lowered risk estimates for dioxins based upon the epigenetic argument, the submitter concludes that the profile should take a similar approach and recalculate PCB risks.

RESPONSE: SRC merely reported the verified EPA cancer risk assessment.

9.3 STATE

- a) Submitter #49, comment 5, states that "...the list of carcinogens recently promulgated by the State of California under the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65) includes only polychlorinated biphenyls containing 60% or more chlorine by weight."

RESPONSE: SRC refers this comment to ATSDR for purposed of compiling state regulations and guidelines.

APPENDIX A

- * a) Submitter #45, comment 20, states that "ATSDR has ignored valuable criticisms from its peer review group." Examples were cited that pertained to organization of the profile, condensing and deemphasizing the human developmental toxicity studies, and correctness of the q_1^* .

RESPONSE: Criticism regarding the organization of the profile is a generic issue. The human developmental toxicity studies were condensed in response to peer review comments; current revisions include additional condensing and deemphasis (see comment 4.3.3.2a). The issue of the correctness of the q_1^* has been resolved (see comment 1.6i).

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TOXICOLOGICAL PROFILE ON SELECTED PCBs

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	29	4.3.1.2a; 4.3.6.2c
	30	4.4b
	31	2.2.3.2a
	32	2.2.3.2b
	33	2.2.3.2c
	34	2.3.3.3a
	35	2.3.3.3b
	36	2.3.3.3e
	37	2.3.3.3f
	38	4.3a
	39	4.3b
	40	6.2a
	41	6.3.1a
	42	6.3.1a
	43	6.3.2b
	44	6.3.2b
	45	7.2.2a
#61	1	A.g
#62	1	A.h
#63	1	9.2.3b

	2	4.3.6.2c; 9.2.3e
#66	1	A.d
	2	1.6f
#70	2	8.1a

APPENDIX

IDENTIFICATION OF SUBMITTERS

Submitter #3(B) is the Division for Environmental Hazards and Health Effects. PHS. CDC. DHHS.

Submitter #13(C) consists of Geraldine Cox of CMA, Michael Hertel of the Utility Solid Waste Activities Group, Douglas G. Bannerman of the National Electrical Manufacturers Association, and Raymond D. Harbison and Stephen M. Roberts of the University of Arkansas School of Medicine.

Submitter #19 is Monona Rossol of Arts, Crafts and Theater Safety, Inc. New York NY.

Submitter # 23 (B) is Lloyd R. Robinson, Jr., Environmental Engineer, Birmingham, Alabama.

Submitter #45 consists of Anne Rogers of Nutter, McClennen and Fish, Boston, MA and the AVX Corporation.

Submitter #49 consists Paul B Galvani of Ropes and Gray, Boston, MA., Attorney for Aerovox Incorporated.

Submitter #61 is Leslie S. Ritts, of Morgan, Lewis and Bockius, Washington, DC., Attorney for Federal Pacific Electric Company.

Submitter #62 is Wendy B. Jacobs of Foley, Hoag and Eliot, Boston, MA., attorney for Cornell-Dubilier Electronics, Inc.

Submitter #63 is Health Risk Associates, Berkeley, CA.

Submitter #70 is Santos Rohena Betancour, Environmental Quality Board of the Commonwealth of Puerto Rico.