UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

March 9, 1988

SAB-EHC-88-019

OFFICE OF
THE ADMINISTRATOR

Hon. Lee M. Thomas
Administrator
U.S. Environmental Protection
Agency
401 M Street, SW
Washington, D.C. 20460

Dear Mr. Thomas:

The Halogenated Organics Subcommittee of the Science Advisory Board's Environmental Health Committee has completed its independent scientific review of the Draft Drinking Water Criteria Document for Polychlorinated Biphenyls (PCBs) and is pleased to transmit its final report to you. The Subcommittee conducted a public review of the draft criteria document at a meeting held in Washington, D.C. on November 19-20, 1987.

In general, the Subcommittee concludes that the document suffers from a failure to clearly identify its scientific objectives. Subcommittee members encountered a myriad of facts that were not critically presented in order to support subsequent regulatory decisions. For example, the document must state a scientific rationale to enable risk managers to decide whether to regulate Aroclors or PCBs in the environment. While sections of the document are improved from a previous draft, other chapters, discussed in the attached report, require extensive revision before the document as a whole represents a scientifically adequate statement of existing knowledge for PCBs.

A major recommendation of the Subcommittee is that EPA explore whether the available data on PCB congeners can be developed on a scale of toxicity, similar to the toxicity equivalency factor that EPA has already prepared for dioxins. This effort could potentially yield some scientifically interesting insights relating to uncertainties in the PCB data base, even if it represents only an approximation in which data analysis and scientific judgment are combined.

The Subcommittee appreciates the opportunity to conduct this particular scientific review. We request that the Agency formally respond to the scientific advice presented in the attached report.

Sincerely,

Norton Nelson, Chairman
Executive Committee

Richard A. Griesemer, Chairman
Environmental Health Committee

John Doull, Chairman
Halogenated Organics Subcommittee

Review of the Draft Drinking Water Criteria Document
for Polychlorinated Biphenyls (PCBs)
by the
Halogenated Organics Subcommittee
Environmental Health Committee
Science Advisory Board

I. General Comments

The regulation of PCBs in drinking water or, in fact, any environmental medium, encounters many problems, including several involving the existing scientific data base. All are described in the criteria document, but virtually none are resolved. These scientific problems include the complexity provided by 209 different congeners and isomers present in commercial PCB mixtures, each with a different toxicity; the presence of highly toxic non-PCB components such as polychlorinated dibenzofurans (PCBFs); the differential rates of removal of PCB congeners from the environment which leads to differences in congener profiles from those of the original pollutant mixtures; and the incomplete knowledge of individual PCB congener toxicity.

The draft criteria document suffers from a failure to clearly identify its scientific objectives. Thus, as reviewers, the Subcommittee members encountered a myriad of facts that were not critically applied, either directly or to support a hypothesis for subsequent regulatory decisions. It must be initially resolved whether the objective is to regulate Aroclors or PCBs in the environment. The Subcommittee believes there is a need to more precisely define what is meant by the term "PCBs", in part because Aroclors may or may not be PCB compounds and because of the varied composition of PCB mixtures.

The Subcommittee recommends that the available data on PCB congeners be developed on a scale of congener toxicity, even if this is only an approximation in which data and professional judgment are combined. Any such scale will be Any such scale will be imperfect, however. For example, it is unlikely that the adverse health consequences of thalidomide would be detected.

The draft document has improved considerably from a previous version. There are, however, some sections that require extensive revisions before it represents a scientifically adequate statement of existing knowledge. A major problem with chapters V, VI and VIII is that they are out of date. For example, in chapter V all of the recent structure activity relationships (SAR) for PCBs have been ignored even though they are discussed in detail in chapter VII. The chapter on human health effects almost completely omits a series of papers in Environmental Health Perspectives (volumes 59 and 60) and the American Journal of Ind. Medicine (volume 5) that discuss Yusho/YuCheng poisoning in Japan and Taiwan, and occupational exposures. These omissions severely compromise the quality of this chapter. In addition, it has been shown by two studies that the major etiologic agents in Yusho and YuCheng poisoning are PCDFs.[1] This does not, however, absolve PCBs as toxic agents and as contributors to some of the symptom of Yusho and Yucheng poisining.

II. Specific Technical Comments and Recommendations

1. Concerning the contributions from contaminant toxicity, the document needs to more critically address the claims that PCDFs were absent from some Aroclor preparations. In describing a number of studies, it is indicated that the PCBs (individual congeners or mixtures) are free of dibenzofurans. Examples of such statements have already been transmitted to EPA. In many instances, it is stated that there was only "apparently" no dibenzofuran contamination, and in no instance was the claim carefully and critically documented. The draft criteria document probably provides sufficient and adequate information to partially resolve the issue of dibenzofuran contribution to observed Aroclor toxicity. Comparisons of studies using PCB mixtures, with and without dibenzofuran contamination, and comparisons of studies with purified individual PCB congeners and with mixtures should be made in the draft document. Studies such as the one recently published that indicates that the toxicity of dioxins can be diminished by co-administered Aroclors should be taken into account in assessing a role for PCDFs in PCB mixture toxicity.[2]

2. The conclusion (page III-26, line 10 and page III-42, paragraph 2, line 5) that the rat is a good model for human metabolism of PCBs is based upon a gross oversimplification since only three distinct congeners were evaluated, and the correlation is more relative than absolute. The statements should be modified or deleted.

3. The draft document is somewhat ambiguous concerning a role of metabolism in PCB toxicity. On the one hand, the less highly chlorinated congeners, and particularly those with unchlorinated vicinal carbons, are the most highly metabolized (page III-37, points 3 and 4, and pages V-53 and 55). This metabolism is erroneously associated with aspects of toxicity (page III-40, paragraph 2 and page VII-11). On the other hand, the more highly chlorinated congeners which are minimally metabolized are reported to be the most toxic.

Metabolism plays a role in PCB toxicity, and cytochromes P-450 are involved. Furthermore, PCBs can differentially induce cytochromes P-450 and thus affect their own metabolism and toxicity during chronic and subchronic exposures--a fact not discussed in the criteria document. For example, PCB exposure from food could induce hepatic cytochromes P-450, which would affect the fate of the more readily metabolized PCB congeners. The role of different forms of cytochrome P-450 in PCB metabolism should be discussed.[3]

4. Analytical measurement of PCBs in water provides no indication of an equivalent Aroclor concentration, and application of Aroclor toxicities to such equivalent contamination is without any reasonable scientific basis and cannot be used as the basis for regulatory decision making. Specific congener analysis is more precise, accurate and well-suited to PCBs exposed to physical, chemical or biotic forces. Unfortunately, not all specific congener analyses

are equal, and they are frequently not comparable. The most thorough analysis (Safe et. al., 1985) is too ambitious at this time for routine monitoring and cannot be applied retroactively to the vast data bank needed to determine trends. The inequalities of specific congener analyses can be very misleading, if not recognized. For example, Ballschmiter and Zell do not consider PCBs 84, 110, 141 and 149 in their 1980 paper. Likewise, Schwartz et. al., (1987) omit these congeners even though Sissons and Welti (1971), Webb and McCall (1972), Bush et. al., (1983) and Safe et. al., (1985) have confirmed their significant presence. In addition, PCB 95 is reported at low levels by some authors and higher levels are observed in the same PCB by others. Therefore, the problem extends beyond specific congener analysis verses Aroclor estimates. Ambiguities and disagreements should be cited to a limited extent in any precautionary statement, perhaps as a repeating footnote.

The task of resolving conflicting reports and selective congener identifications is monumental. Certainly the current document cannot resolve this issue. Nevertheless, it appears to be a disservice to state that, "10 of the 19 congeners were unambiguously from Aroclor 1016" (page IV-3). Several of these monochloro- to tetrachloro-congeners are also found in Aroclors 1232, 1242 and 1248 (Webb and McCall, 1972) as well as low levels in 1260 (Safe). This is further confirmed on page IV-6 in Table IV-1.

Also, on pages IV-8 and 9 the congener composition that is "compatible" with 24, 42 and 34% Aroclors 1242, 1254 and 1260 requires some qualification since lower chlorinated congeners might dissolve out and/or be degraded, and the sediment would be enriched in higher chlorinated congeners because of solubility and binding to particulates. Later in the same paragraph, it was stated that Lake Superior water contained 37-56% of Aroclor 1242, while years later the sediments contained 15-21%. Also, Table IV-2 shows higher 1242 in the aqueous phase compared to particulate precipitation, while 1254 and 1260 are about equal in rain and much higher in snow particulates than in the aqueous phase.

Thus, it is known that chlorobiphenyls partition in these ways, and this affects residue composition. The apparent Aroclor composition can and does seem to change. Cautioning that these things happen and that scientists must recognize that Aroclor estimates may be misleading, and subsequently trying to force a mixed residue to fit the pattern(s) of specific Aroclor(s) is inconsistent and must be rectified in the document. For example, page V-95, Table V-21 indicates grossly different compositions of Aroclor 1260 which are most likely a consequence of analytical methodology differences.

Knowing that specific congener analyses are not equal also does little good if there are not attempts to resolve the inequalities. By throwing out PCB data with some ambiguities, there would be virtually no data to assess. Moreover, the vast amount of data available would yield even more information if attempts to force a convenient fit would be avoided. The ambiguities and forced fits do not invalidate the data that are vital to the types of considerations that need to be undertaken.

In summary, the Subcommittee recommends that a simple two-footnote qualification system be developed stating that: 1) when Aroclor estimates are used, there should be references to an appendix page stressing the problems, inferences and possible valuable information; and 2) when specific congener analyses are used, subsequent pages should present some of the ambiguities and appropriate precautions.

5. There is evidence for PCB metabolite binding to protein, DNA and RNA (page III-40) and DNA damage by metabolites (page III-41). However, the mutagenicity data presented in the document show that the PCBs tested do not induce gene mutations in either prokaryote or eukaryote test systems. Similar studies testing the ability of PCBs to induce clastogenic effects, i.e. chromosome aberrations resulting from chromosome breakage and re-arrangements, were also negative. Thus, the conclusion, to date, would be that the PCBs studied provide no evidence for genotoxicity, namely no induced DNA damage.

On the other hand, there is a possibly conflicting result in the studies with Drosophila. Here, exposure to purified Clophen-A-50 (at certain doses) has resulted in significant increases in exceptional XO flies. This means that either X or Y chromosomes were lost in development of the male germ line. Such chromosome loss could result either from chromosome breakage or non-disjuction. Non-disjunction may be induced by damaging the spindle fibers (tubulin protein), the centrosomes and/or other elements of the mitotic apparatus such that the chromosomes are improperly segregated in meiosis. Thus, a mutagenic, but not genotoxic, endpoint is possibly induced by some PCBs leading to cellular aneuploidy (unbalanced chromosome numbers). The Subcommittee recommends that this phenomenon be discussed because it may provide additional insight into the mechanism of carcinogenesis.

6. In reaching a regulatory decision for PCBs in drinking water, the Subcommittee recommends that a modified version of Option I (see attached issue paper provided by the Office of Drinking Water) be adopted. It is not necessary to derive criteria for drinking water for each PCB isomer/congener but, rather, only for the more toxic ones. A scale of toxicities for PCB isomers/congeners should be prepared and an "equivalency approach" developed, using the most toxic PCBs as the basis for comparison. All available data on PCB congener toxicity should be used in deriving a toxicity scale, including cytochrome P-450 and non-Ah receptor effects and induction data. Although the Subcommittee recognizes that some of these data cannot be considered "toxicologic," it concludes that this will not negate derivation of a reasonable approximation. A similar approach is currently used by EPA and other governmental agencies for halogenated dibenzofurans and dibenzodioxins. Once such a scale of toxicities is developed it can be used as a guide in selecting congeners of major significance for regulatory decisions. This approach will have the advantage over Option III in that any PCB mixture can be analyzed and decisions made and defended.

References

1. Bondiera, et. al., Chemosphere 13 (1984), 507; and Kunita, et. al., American Journal of Ind. Med., 5 (1984), 45.

2. Bulletin of Environmental Contam. Toxicol., 39 (1987), 791.

3. Biochem. Pharmacol., 30 (1981), 577-588, and 29 (1980), 729-736; and Biochemistry 20 (1984), 7379-7384.

Note to the Reader

Dr. Stephen Safe, a consultant to the Halogenated Organics Subcommittee, did not formally vote to approve this Subcommittee report because of a prior involvment in the preparation of the draft criteria document. He did participate in the public meeting in which the Subcommittee reviewed the draft document but served in the capacity as a resource to clarify specific technical issues.

U.S. Environmental Protection Agency
Science Advisory Board
Environmental Health Committee
Halogenated Organics Subcommittee
Roster for November 19-20, 1987 Review of the Draft Final
Drinking Water Criteria Document for Polychlorinated Biphenyls

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Drinking Water Criteria for Polychlorinated Biphenyls (EPA)

I. Background:

Appreciable levels of PCBs were detected in ground water samples from wells near highly industrialized and landfill areas of New Jersey. Surface water, sediments and fish from a good number of rivers in the U.S. and in the Great Lakes were found to contain PCBs. PCBs were also detected in tap water samples of a few communities which obtain their water from the highly contaminated Hudson River. However, none of the above ground water and municipal tap water surveys identified the specific Arochlor mixture in drinking water samples. There is only one published report which identified Aroclor 1016 mixture, at levels as high as 100 ng/l, in samples from a small upstate New York public water supply system. The two reservoirs of this waterworks, where Aroclor 1016 was also detected, used the Hudson River as their source of water. Higher chlorinated Aroclor mixtures were present in the Hudson River and in one of the reservoirs but not detected in the finished drinking water samples from this community.

Polychlorinated biphenyls pose special problems with respect to establishing meaningful drinking water regulations. There are 209 different PCB isomers and it seems only 100 individual isomers have been identified at significant levels in commercial mixtures. Although toxicological studies have been performed on only a small number of the Aroclor mixtures, it is evident that there are significant differences in toxicity between different isomers and congeners. In particular, toxicity appears to increase with increasing chlorine content, and isomers which are axially substituted (positions 3,4,and 5) are more toxic than species that are substituted in positions 2 and 6. Consequently, the toxicity of PCB mixtures depends on the isomer-specific composition of the mixture, as illustrated by the differing chronic toxicities of various commercial PCB formulations. In addition, different PCB preparations may differ considerably in the content of toxic contaminants, such as polychlorinated dibenzofurans.

For these reasons, toxicity data derived from a particular commercial PCB formulation are not directly applicable to other formulations, and may not even be applicable to different batches of the same formulation. More importantly, toxicity data from studies of commercial PCB formulations may have little relevance to the toxicity of PCBs in drinking water because the composition of environmental mixtures is markedly changed from the parent contaminant as a consequence of differing solubility and stability characteristics of the PCB isomers. Since the toxicity of a mixture could be dominated by a few relatively minor but highly toxic constituent isomers or contaminants, measurement of total concentration is not an adequate index for assessing the toxicity of PCB mixtures.

II. Issue:

Based on the information on the toxicity of PCBs (mixtures, isomers and congeners) and on their solubility and stability in drinking water, is it possible to develop meaningful acceptable concentrations of PCBs in drinking water?

III. Options

Option I

° Consider evaluating the toxicity of individual isomers and derive criteria for drinking water for each isomer, if the data permit. This is a scientifically sound method for addressing the toxicity of PCB mixtures. This approach is not feasible at present, both because isomer-specific toxicity data are not available and because isomer specific analysis of water is not feasible on a routine basis.

Option II

° Assume that all PCB mixtures in the environment are composed entirely of the most highly toxic isomer (3,4,5,3',4',5' hexachlorobiphenyl) and use this to estimate acceptable level of PCBs in drinking water. This will be the most conservative, approach. While this would be certainly protective, this isomer is a minor component of most formulations and has low solubility in water. This option may not be protective of the carcinogenic potential of PCBs because of the lack of data on the carcinogenic potential of this isomer.

Option III

° Assume that a mixture of PCBs in water retains an average toxicity that is not greatly different from that of the parent formulation. Based on this assumption, acceptable levels could be derived for commercial formulations as if they were individual chemicals. One disadvantage to this approach is that it is usually difficult to identify which specific PCBs formulation(s) is (are) the source of PCBs in drinking water.

IV. Recommendation:

Option III is recommended. The key assumption upon which this option rests (that PCBs in water retain an average toxicity similar to the parent formulation) may not be true. However, it is unlikely to underestimate risk since the more toxic higher chlorinated isomers would have least water transport potential. Changes in the acceptable levels of PCBs in drinking water or in the basic regulatory approach may be possible in the future as additional data and techniques become available.

V. Points Of Interest:

1. PCB cancer potency: Comparison with the human evidence (Discussion to be added to document)

The Agency's cancer potency for PCBs (calculated from the Norback and Weltman rat study and reported in the May 1987 Drinking Water Criteria Document to be 7.7 per mg/kg/d continuous lifetime exposure) compares favorably to the number of cancer cases seen following the rice-oil incident in Japan. Although more cancer cases may be reported in the future, a rough calculation can be made from currently available information.

The Drinking Water Criteria Document (page VI-14, attributed to Kuratsune) reports the average amount of PCBs consumed during the riceoil incident to be about 2 grams. Dividing this by 70 kg (the weight of a typical adult) and by 25,600 days (the number of days in a typical 70-year lifespan), the average daily exposure is estimated to be about 0.0011 mg/kg/d. Multiplying this by 7.7 per mg/kg/d (the Agency's cancer potency) shows the risk to be 847 per 100,000. In an exposed population of 1761 (page VI-31, attributed to Kuratsune) approximately 14.9 excess cancer cases are expected. This projection is not inconsistent with the 7.39 excess liver cancer cases reported to date (page VI-31, 9 observed minus 1.61 expected).

Several major sources of uncertainty in this comparison should be noted:

a. The Agency's potency estimate is a plausible upper bound, which would tend to overestimate the number of cancer cases.

b. The rice oil was contaminated with polychlorinated dibenzofurans at a level 250 times more concentrated than in the commercial PCB product Kanechlor 500. To the extent that these dibenzofurans are responsible for the observed cancer cases, a projection based on based on the cancer potency of PCBs alone would tend to underestimate the number of cancer cases.

c. Calculating an average daily exposure prorated over an entire lifetime is very problematical, since the exposure was intense but of short duration. In the absence of evidence to the contrary on PCBs, this approach is consistent with the Agency's cancer guidelines. Nevertheless, it remains a substantial source of uncertainty.