Veith, G. (coordinator), Carver, T., Fetterolf, C., Lee, G. F., Swanson, D., Willford, W., and Zeeman, M., "Polychlorinated Biphenyls," IN: A Review of the EPA Red Book: Quality Criteria for Water, American Fisheries Society, Bethesda, MD, pp 239-246 (1979).

POLYCHLORINATED BIPHENYLS

EPA Criteria

0.001 µg/ℓ for freshwater and marine aquatic life and for consumers thereof.
Every reasonable effort should be made to minimize human exposure.

Reviewers: G.D. Veith (Coordinator), T.C. Carver Jr., C.M. Fetterolf, G.F. Lee, D.L. Swanson, W.A. Willford, and M.G. Zeeman

I. Criteria

The reviewers of the PCB criteria were divided with respect to the adequacy of the 0.001 µg/liter water quality criterion. None of the reviewers judged the criterion unnecessarily restrictive for the Great Lakes from which much of the data are derived. Four reviewers concerned with the PCB contamination of the Great Lakes stressed that fish in the Great Lakes are presently so severely contaminated that PCB concentrations greater than 0.0001 µg/liter will likely result in hazardous residues in fish in the Great Lakes. Several of the reviewers questioned whether one criterion could be applied for all natural waters. The origin and nature of this issue will be addressed in the review of the Rationale for the PCB criteria.

II. Introduction

The Introduction failed to include foreign trade names for PCB's, such as Kanechlor (Japan) or Clophen (Germany). The term "molecular type" in the first paragraph is unnecessary and should be replaced by "the 12 carbon biphenyl ring structure".

The Introduction suffers from a very sketchy and outdated discussion of the physical properties of PCB mixtures and of the analytical problems associated with the measurements of PCB residues. EPA failed to provide a concise, relevant Introduction that took into account the information available at the time the Red Book was prepared. Since the Red Book was written there have been numerous extensive reviews published on the distribution, accumulation and metabolism of PCB's and this information should be incorporated in any revision of the Red Book.

III. Rationale

The rationale for the 0.001 µg/liter criterion is based on the extreme bioaccumulative property of PCB's and the hazard to human health posed by

the residues in fish. However, the rationale is not carried to a logical conclusion and is obscured by extraneous information which neither supports nor refutes the rationale. The last two paragraphs are of little or no importance to the PCB criterion for human health and should be eliminated.

The entire section on acute toxicity of PCB's to aquatic organisms is a collection of bits and pieces from the literature and no attempt was made to show relationships among the data or to explain or emphasize the significance of the data. The data of Stalling and Mayer (1972) are clearly irrelevant because the large fish they used in their study were probably several orders of magnitude less sensitive to lethal effects of PCB's than fish in the early-life stages. Because the solubility of PCB's is, at most, 250 µg/liter, the 96-hr LC50 values of 50,000 µg/liter are totally meaningless. Also, the last sentence in paragraph one on page 194 is completely untrue and a biological impossibility. The DeFoe et al. (1976) citation was not published in 1976.

If it is necessary to demonstrate that PCB's can cause lethality in aquatic communities, it would be much better if all of this information were summarized in a table with references and discussed in one or two paragraphs. Preferably, the summary should have been written by someone with knowledge of aquatic toxicity testing. If the rationale stemming from the bioaccumulation of PCB's in fish and the effects of residues on mink and on human consumers (expressed as the FDA action level) were carried to a logical conclusion, the estimated safe concentration would have to be less than 0.001 µg/liter. In fact, a criterion of less than 0.0002 µg/liter would be necessary to protect all species in all environments from residues in excess of 5 µg/g. Subsequent to the promulgation of the EPA criteria, the FDA has proposed decreasing the action level from 5 µg/g to 2 µg/g and the International Joint Commission has recommended that the PCB concentration in water be sufficiently low to prevent residues greater than 0.1 µg/g in fish. This is based largely on the studies of PCB effects on mink.

Since the criterion of 0.001 µg/liter is below detection limits for many monitoring programs and criteria below 0.001 µg/liter would be virtually unmanageable for PCB's, it seems more reasonable to include in the criterion the use of residue levels in fish. If the criterion used 0.001 µg/liter in water as well as the 0.1 µg/g PCB residues in fish, the effectiveness of the water quality criterion would be much greater. A criterion based on residues in fish rather than water could be enforced in streams and impoundments through the use of live-car bioaccumulation studies or monitoring of natural populations, and the concern over appropriate bioconcentration factors would be lessened.

IV. References Cited

There are numerous errors in the cited references. The corrections are indicated by the underlined summary below:

1. Armour and Burke. 1970. J. Assoc. Offic. Anal. Chem.

2. Cecil et al...Environ. Contam. Toxicol.

3. DeFoe et al...J. Fish. Res. Board Can. Paper not published in 1976.

4. Friend, M., ...biphenyl:interaction.

5. Lillie et al...Poultry Sci. (for both entries).

6. Mayer, F.L., Jr. et al. 1977...Arch. Environ. Contam. Toxicol. 5: 501-511.

7. Nisbet, I.C.T. and A.F. Sarofim...Perspect. 1: 21.

8. Platonow...Can. J.

9. Risebrough, R.W. 1970...Environment.

10. Stalling and Mayer. 1972. Environ. Health Perspect. 1: 159.

11. Vos, J.G...liver necrosis...Appl.

There were many inconsistencies in abbreviations of Environment and Toxicology.

V. Reviewers' Discussion

The presentation of information in support of the EPA criteria for PCB's is essentially a list of isolated data, the relevance of which is very poorly discussed. This review should have been devoted to key facts and their specific significance in deciding criteria. Discussion should have centered upon how the criteria were derived (safety indexes, application factors, detection limits, etc.). One reviewer (G. Fred Lee), based on his examination of PCB total concentrations in water and in aquatic organisms derived from those waters from a variety of locations throughout the U.S., stated that the 0.001 µg/liter total PCB criterion was too strict if the objective of the criterion is to prevent bioconcentration of PCBs in fish and other aquatic life to levels of 5 ppm in fish flesh. Lee pointed out that this criterion should be based on available forms of PCBs and not the total content since, in some waters, appreciable parts of the PCBs are associated with suspended particulate matter and are not totally available to aquatic organisms for bioconcentration.

VI. Recommendations for Improvement of this Section

On the basis of the data presented in the Rationale and other data which should have been included in the Rationale, four of the seven reviewers concluded that a criterion calculated from bioaccumulation factors and acceptable tissue concentration would be considerably less than 0.001 µg/liter.

The proposed revision is as follows:

Criteria

0.0001 µg/liter or at concentrations such that levels in fish (whole fish, wet weight basis) do not exceed 0.1 µg/g for protection of freshwater and marine life and for consumers thereof including fish-eating birds and mammals.

Rationale

It is suggested the toxicity of PCB's to aquatic organisms be summarized in tables and discussed briefly. Other sublethal effects on fish could be summarized as follows:

1. Fish brain, liver, kidney, and muscle ATPases have been shown to be inhibited by PCB's (Cutkomp et al. 1972; Davis et al. 1972; Desaiah et al. 1972; Koch et al. 1972; Yap et al. 1971). Inhibition of these important enzymes under field conditions could disrupt normal functions in fish, i.e., nervous condition, metabolism, osmoregulation, etc. Disruption of these normal homeostatic and integrative processes could lead to stress and decreased survival.

2. PCB's induce fish hepatic microsomal enzymes (Gruger et al. 1977; Hill et al. 1976; Lidman et al. 1976). These membrane-bound enzymes are important in the metabolism (degradation or activation) of lipophilic drugs, hormones, carcinogens, and pesticides. Induction of these microsomal enzymes can be important in activation of mutagens (Ames et al. 1973), carcinogens (Conney et al. 1977; McLean 1977) and activation or degradation of insecticides (Matsumura 1975; Nakatsugawa and Morelli 1976). PCB's may alter drug and hormone metabolism (Alvares et al. 1977; Fishbein 1974). PCB's have been implicated in possible activation of carcinogens or promotion of tumors (Kimura et al. 1976; Nishizumi 1976; Ito et al. 1973) and are even suspected of being carcinogenic themselves (Bahn et al. 1976; Fishbein 1974; Kimbrough and Linder 1974; Kimbrough et al. 1975; Ito et al. 1973).

3. The PCB's have been shown to alter fish hematological responses and thereby are implicated in changes of fish immunological systems (Camp et al. 1974; Ito 1973; Johansson et al. 1972; Larsson 1973; Nestel and Budd 1975). PCB's have been shown to suppress avian and mammalian immune responses (Fishbein 1974; Harris et al. 1976; Koller and Thigpen 1973; Vos 1972; Vos and deRoij 1972; Vos and Driel-Grootenhuis 1972; Wassermann et al. 1973) and immunosuppression has been linked to increased incidences of disease and tumor formation (Cerilli and Hatton 1974; Friend and Trainer 1970; Kripke and Borsos 1974; Simmons et al. 1975).

Therefore, it should not be too surprising that PCB's residue or treatments may be related to increased incidences of fish disease (Couch 1975; Hansen et al. 1971; Perkins et al 1972; Schimmel et al. 1974; Sherwood and Mearns 1977; Wedemeyer et al. 1976; Wellings et al. 1976) and tumor formation (Falkmer et al. 1977; Ljungberg 1976; McCain et al. 1977; Sonstegard 1977).

The proposed FDA action level for PCB's is 2 µg/g (Fed. Reg. 1977). Platonow and Kolstad (1973) have demonstrated that a steady diet of 0.64 µg/g of Aroclor 1254 nearly eliminated reproduction in ranch mink. The recommended maximum limit of PCB in fish is 0.1 µg/g (for complete discussion, see International Joint Commission 1975).

The field and laboratory bioaccumulation data can be summarized in tables.

Since environmental concentration factors in excess of 1.0×10^6 and possibly as much as 2.0×10^7 have been demonstrated in the Great Lakes, a water concentration of no more than 0.0001 µg/liter (based on a 10^6 concentration factor) is required to prevent levels of 0.1 µg/g in fish. Water concentrations of PCB's near 0.0001 µg/liter can only be analyzed with great difficulty if at all. The use of a 0.1 µg/g criterion in fish in addition to being justified in itself for protection of fish-eating mammals, is also justified as providing a usable means of analyzing and indicating when the concentration of PCB's in water has exceeded the 0.0001 µg/liter criterion.

Literature Cited

Alvares, A.P., A. Fishbein, K.E. Anderson, and A. Kappas. 1977. Alterations in drug metabolism in workers exposed to PCBs. Clin. Pharmacol. Ther. 22: 140-146.

Ames, B.N., W.E. Durston, E. Yamasaki, and F.D. Lee. 1973. Carcinogens are mutagens: a simple test system combining liver homogenates for activation and bacteria for detection. Proc. Nat. Acad. Sci. USA 70: 2281-2285.

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

Camp, B.J., E. Hejtmancik, C. Armour, and D.H. Lewis. 1974. Acute effects of Aroclor 1254 (PCB) on *Ictalurus punctatus* (Catfish). Bull. Environ. Contam. Toxicol. 12: 204-208.

Cerilli, J. and D. Hatton. 1974. Immunosuppression and oncogenesis. Am. J. Clin. Pathol. 62: 218-223.

Conney, A.H., E.J. Pantuck, K.C. Hsiao, R. Kuntzman, A.P. Alvares, and A. Kappas. 1977. Regulation of drug metabolism in man by environmental chemicals and diet. Fed. Proc. 36: 1647-1652.

Couch, J.A. 1975. Histopathological effects of pesticides and related chemicals on the livers of fishes. Pages 559-584 In: The pathology of fishes. W.E. Ribelin and G. Migaki (Eds.) Univ. Wisc. Press, Madison, WI.

Cutkomp, L.K., H.H. Yap, D. Desaiah, and R.B. Koch. 1972. The sensitivity of fish ATPases to PCBs. Environ. Health Perspect. 1: 165-168.

Davis, P.W., J.M. Friedhoff, and G.A. Wedemeyer. 1972. Organochlorine insecticide, herbicide and polychlorinated biphenyl (PCB) inhibition of NaK-ATPase in rainbow trout. Bull. Environ. Contam. Toxicol. 8: 69-72.

Desaiah, D., L.K. Cutkomp, H.H. Yap, and R.B. Koch. 1972. Inhibition of oligomycin-sensitive and -insensitive Mg-ATPase activity in fish by PCBs. Biochem. Pharmacol. 21: 857-865.

Falkmer, S., S. Marklund, P.E. Mattsson, and R. Christoffer. 1977. Hepatomas and other neoplasms in the Atlantic hagfish (*Myxine glutinosa*): a histopathologic and chemical study. Ann. N.Y. Acad. Sci. 298: 342-355.

Federal Register. 1977. Pages 17487-17494. April 1, 1977.

Fishbein, L. 1974. Toxicity of chlorinated biphenyls. Ann. Rev. Pharmacol. 14: 139-156.

Friend, M. and D.O. Trainer. 1970. PCB: interaction with duck hepatitis virus. Science 170: 1314-1316.

Gruger, E.H. Jr., M.M. Wekell, P.T. Numoto, and D.R. Craddock. 1977. Induction of hepatic aryl hydrocarbon hydroxylase in salmon exposed to petroleum dissolved in seawater and to petroleum and PCBs, separate and together, in food. Bull. Environ. Contam. Toxicol. 17: 512-520.

Hansen, D.J., P.R. Parrish, J.I. Lowe, A.J. Wilson Jr. and P.D. Wilson. 1971. Chronic toxicity, uptake and retention of Aroclor 1254 in two estuarine fishes. Bull. Environ. Contam. Toxicol. 6(2): 113-119.

Harris, S.J., H.C. Cecil, J. Biteman and R.J. Lillie. 1976. Antibody response and reduction in bursa of Fabricius and spleen weights of progeny of chickens fed PCBs. Poultry Sci. 55: 1933-1940.

Hill, D.W., E. Hejtmancik, and B.J. Camp. 1976. Induction of hepatic microsomal enzymes by Aroclor 1254 in *Ictalurus punctatus* (Channel Catfish). Bull. Environ. Contam. Toxicol. 16: 495-502.

International Joint Commission. 1975. Great Lakes water quality 1974, Appendix A. Pages 47-54 In: Water Quality Objectives Subcommittee Report, International Joint Commission, Windsor, Ont.

Ito, N., H. Nigasaki, M. Arai, S. Makiura, S. Sugihara, and K. Hirao. 1973. Histopathologic studies on livers tumorigenesis induced in mice by technical PCBs and its promoting effect on liver tumors induced by benzene hexachloride. J. Nat. Cancer Inst. 51: 1637-1646.

Ito, Y. 1973. Studies on the influence of PCB on aquatic organisms - II. Changes in blood characteristics and plasma enzyme activities of carp administered orally with PCB. Bull. Jpn. Soc. Sci. Fish. 39: 1135-1138.

Johannsson, N., A. Larsson, and K. Lewander. 1972. Metabolic effects of PCB on the brown trout (*Salmo trutta*). Comp. Gen. Pharmacol. 3: 310-314.

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

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

Kimura, N.T., T. Kanematsu, and T. Baba. 1976. PCBs as a promotor in experimental hepatocarcinogenesis in rats. Z. Krebsforsch. Klin. Onkol. 87: 257-266.

Koch, R.B., D. Desaiah, H.H. Yap, and L.K. Cutkomp. 1972. PCBs: Effects of long-term exposure on ATPase activity in fish, *Pimephales promelas*. Bull. Environ. Contam. Toxicol. 7: 87-92.

Koller, L.D. and J.E. Thigpen. 1973. Reduction of antibody to pseudorabies virus in PCB exposed rabbits. Am. J. Vet. Res. 34: 1605-1606.

Kripke, M.L. and T. Borsos. 1974. Immunosuppression and carcinogenesis - A review. Israel J. Med. Sci. 10: 888-903.

Larsson, A. 1973. Clinic - chemical methods applied to fish blood with reference to effects of chlorinated hydrocarbons. Pages 619-628 In: General physiology - locomotion, respiration, transport and blood. L. Bolis et al. (Ed.) North-Holland Pub. Co., Amsterdam.

Lidman, U., L. Förlin, O. Molander, and G. Axelson. 1976. Induction of the drug metabolizing system in rainbow trout (*Salmo gairdneri*) liver by PCBs. Acta Pharmacol. Toxicol. 39: 262-272.

Ljungberg, O. 1976. Epizootiological and experimental studies of skin tumors in northern pike (*Esox lucius*) in the Baltic Sea. Prog. Exp. Tumor Res. 20: 156-165.

Matsumura, F. 1975. Pages 167-169 In: Toxicology of pesticides. Plenum Press, New York, NY.

McCain, B.B., K.V. Pierce, S.R. Wellings, and B.S. Miller. 1977. Hepatomas in marine fish from an urban estuary. Bull. Environ. Contam. Toxicol. 18: 1-2.

McLean, A.E.M. 1977. Diet, DDT, and the toxicity of drugs and chemicals. Fed. Proc. 36: 1688-1691.

Nakatsugawa, T. and M.A. Morelli. 1976. Microsomal oxidation and insecticide metabolism. Chap. 2 In: Insecticide biochemistry and physiology. C.F. Wilkinson (Ed.) Plenum Press, New York, NY.

Nestel, H. and J. Budd. 1975. Chronic oral exposure of rainbow trout (*Salmo gairdneri*) to a PCB (Aroclor 1254): Pathological effects. Can. J. Comp. Med. 39: 208-215.

Nishizumi, M. 1976. Enhancement of diethylnitrosamine hepatocarcinogenesis in rates by exposure to PCBs or phenobarbital. Cancer Lett. 2: 11-16.

Perkins, E.J., J.R.S. Gilchrist, and O.J. Abbott. 1972. Incidence of epidermal lesions in fish of the North-East Irish Sea area, 1971. Nature 238: 101-103.

Platonow, N.S. and L.H. Kolstad. 1973. Dietary effects of polychlorinated biphenyls on mink. Can. J. Comp. Med. 37: 391-394.

Schimmel, S.C., D.J. Hansen, and J. Forrester. 1974. Effects of Aroclor 1254 on laboratory-reared embryos and fry of sheepshead minnows (*Cyprinodon variegatus*). Trans. Am. Fish. Soc. 103: 582-586.

Sherwood, M.J. and A.J. Mearns. 1977. Environmental significance of fin erosion in Southern California demersal fishes. Ann. N.Y. Acad. Sci. 298: 177-189.

Simmons, R.L., H.H. Balfour, C. Lopez, S.M. Mauer, C.M. Kjellstrand, T.J. Buselmeier, and J.S. Najarian. 1975. Infection in immunosuppressed transplant recipients. Surg. Clin. North Am. 55: 1419-1430.

Sonstegard, R.A. 1977. Environmental carcinogenesis studies in fishes of the Great Lakes of North America. Ann. N.Y. Acad. Sci. 298: 261-269.

Vos, J.G. 1972. Toxicology of PCBs for mammals and for birds. Environ. Health Perspect. 1: 105-118.

Vos, J.G. and L.V. Driel-Grootenhuis. 1972. PCB-induced suppression of the humoral and cell-mediated immunity in guinea pigs. Sci. Total Environ. 1: 289-302.

Vos, J.G. and T. deRoij. 1972. Immunosuppressive activity of a PCB preparation on the humoral immune response in guinea pigs. Toxicol. Appl. Pharmacol. 21: 549-555.

Wassermann, M., D. Wassermann, E. Kedar, M. Djavaherian, S. Cucos, and S. Ventura. 1973. Effect of organochlorine compounds on serum proteins. Bull. Environ. Contam. Toxicol. 10: 42-50.

Wedemeyer, G.A., F.P. Meyer, and L. Smith. 1976. Environmental stress and fish disease. T.F.H. Publications, Inc., Neptune, NJ: 192 p.

Wellings, S.R., C.E. Alpers, B.B. McCain, and B.S. Miller. 1976. Fin erosion disease of starry flounder (*Platichthys stellatus*) and English sole (*Parophrys vetulus*) in the estuary of the Duwamish River, Seattle, Washington. J. Fish. Res. Board Can. 33: 2577-2586.

Yap, H.H., D. Desaiah, L.K. Cutkomp, and R.B. Koch. 1971. Sensitivity of fish ATPases to PCBs. Nature 233: 61-62.