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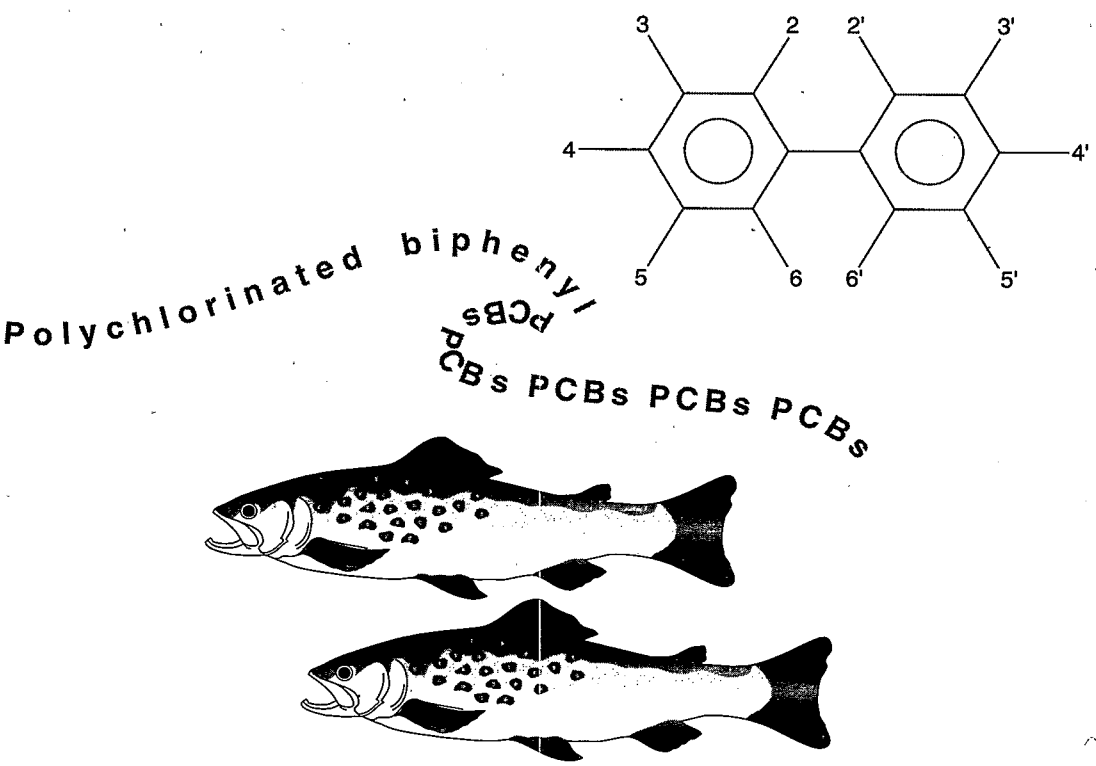
Proceedings of the U.S. Environmental Protection Agency's National Technical Workshop "PCBs in Fish Tissue"

May 10-11, 1993
Washington, DC



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

OFFICE OF
WATER

Dear Requester:

We are pleased to transmit a copy of the document titled *Proceedings of the U.S. Environmental Protection Agency's "National Technical Workshop on PCBs in Fish Tissues*, EPA/823-R-93-003, September 1993." The workshop was held on May 10-11, 1993 in Washington D.C.

The primary purpose of the workshop was to transfer current information about PCBs to states and other parties involved in risk assessment and fish consumption advisories. The workshop was structured to encourage an exchange of information between the users of the fish tissue data (such as risk assessors) and the generators of the PCB data (such as laboratory personnel). This exchange is important because the analysis of PCBs in fish tissues involves a complex set of considerations including PCB toxicity information, laboratory analytical techniques, exposure data, etc. Using case studies, the workshop also illustrated how human health assessments may be affected by the assumptions and analytical complexities associated with PCBs in fish tissues.

Additional copies of this document can be obtained by calling the Office of Water Resource Center at (202) 260-7786 or writing to the U.S. Environmental Protection Agency, Water Resource Center (RC4100), 401 M. Street S.W., Washington D.C. 20460. Please include the document title and publication number noted above.

We appreciate your interest in the workshop's Proceedings and in other EPA activities relating to fish contamination issues.

Sincerely,

Rick Hoffmann
Workshop Organizer
Risk Assessment and Management Branch
Office of Science and Technology

PROCEEDINGS
U.S. ENVIRONMENTAL PROTECTION AGENCY'S
NATIONAL TECHNICAL WORKSHOP
"PCBs IN FISH TISSUE"

May 10-11, 1993
Washington, DC

Office of Water
Office of Science and Technology
Standards and Applied Science Division
U.S. Environmental Protection Agency
Washington, DC 20460

September 1993

This document is based entirely on presentations at a workshop sponsored by the U.S. Environmental Protection Agency (EPA) as a forum to share information concerning PCB contamination of fish tissue. The material in this document has been subject to Agency technical and policy review and approved as an EPA report. The views expressed by individual authors, however, are their own and do not necessarily reflect those of the U.S. Environmental Protection Agency. Mention of trade names or commercial names in no way constitutes endorsement or recommendation for use.

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EXECUTIVE SUMMARY

On May 10-11, 1993, the U.S. Environmental Protection Agency (EPA) sponsored a "National Technical Workshop on PCBs in Fish Tissues." Polychlorinated biphenyls (PCBs) are a family of human-made chemicals that are widely distributed throughout the environment. The analysis of PCBs in fish tissues involves a complex set of considerations regarding PCB toxicity information, laboratory analytical techniques, exposure data, etc. The national technical workshop examined how human health assessments may be affected by current PCB analytical issues for fish tissues.

The primary purpose of the workshop was to transfer current information about PCBs to states and other parties involved with risk assessment and fish consumption advisories. The workshop was structured to provide for an exchange of information between the users of the PCB fish data (such as risk assessors) and the generators of the PCB data (such as laboratory personnel).

This document summarizes the proceedings of the workshop. The workshop was divided into four main parts:

Part One—Introduction to PCBs
Part Two—PCB Toxicity and Health Effects
Part Three—Analytical Methods
Part Four—Case Studies: Human Health/ Risk Assessment

Within each topic area, there were a series of individual presentations followed by questions from the audience and responses by the speakers. The Proceedings document contains a summary of each speakers presentation, a selection of key graphics, and a summary of audience questions and responses.

Part One - Introduction to PCBs

Dr. Southerland and Mr. Hoffmann of EPA welcomed the participants to the workshop and explained the contents of the workshop.

The morning session of the first day began with an overview of the major risk assessment and analytical issues for PCBs. Dr. Erickson of the Argonne National Laboratory provided background information on the chemical nature of PCBs and set the stage for subsequent discussions about PCB analytical methods. Dr. Craddock of Craddock Associates discussed temporal trends of PCBs in the environment. His talk, based on a comprehensive literature review agency studies, described PCB occurrence in various environmental compartments such as foods, human adipose tissue, shellfish, fish, and human blood sera. Mr. De Vault of EPA focused on PCB trends in Great Lake Fish. Dr. Bolger of the U.S. Food and Drug Administration reviewed the toxicology, hazards, and risks of PCBs with a focus on

pharmacokinetics. Ms. Orme-Zavaleta of EPA explained EPA's PCB criteria for water. A question and response session concluded this session.

Part Two - PCB Toxicity and Health Effects

The afternoon session elaborated on the human health effects of PCBs. Dr. Cogliano of EPA provided a regulatory update on the evidence of PCB's carcinogenicity. Dr. Cicmanec of EPA described the agency's recent review of the non-carcinogenic effects of PCBs. Dr. Barnes of EPA followed with a discussion of the use of toxicity equivalents for PCBs. Dr. Brown of General Electric reviewed the effects of occupational exposure to PCBs. He focused on work that GE has conducted on its capacitor workers who were previously exposed. Dr. Colborn of the W. Alton Jones Foundation concluded the afternoon presentations by talking about adverse effects upon wildlife and possible implications for human health. Questions and responses followed.

Part 3 - Analytical Method

The morning of the second day was devoted to PCB analytical methods and associated issues. Dr. Erickson introduced the topic and moderated the session. Mr. Schwartz of the US Fish and Wildlife Service summarized some of the challenges that PCBs present to analytical chemists, particularly for particular congeners. He also described work that FWS has been doing using principal components analysis. Mr. Sawyer of FDA described the Aroclor-based method that FDA uses to analyze its samples and compared FDA's method with other analytical approaches. Dr. Krahn of the National Marine Fisheries Service discussed the "performance-based" approach that NMFS currently employs for its congener-specific analyses. She also described a new screening method for rapidly identifying and quantifying coplanar PCBs. Dr. Swackhammer of the University of Minnesota described quality assurance and quality control aspects of EPA's Green Bay PCB study. This study collected a PCB calibration set containing 80-90 congeners and involved 8 different laboratories, federal agencies, state agencies, and academic institutions. Dr. Bush of the NY Department of Health concluded the morning session by discussing the congener-specific analyses that the Wadsworth Laboratory has conducted.

Part 4 - Case Studies: Human Health/ Risk Assessment

Four case studies were presented to illustrate different risk assessment approaches that have been used to assess the human health effects of PCBs. The studies were drawn from different geographic areas. Dr. Pollock of the California EPA described a study of chemical contaminants in fish conducted for the southern California area and the resulting fish advisories. Ms. Cox of the Tennessee Valley Authority provided an example of how to assess risks using a nomograph to display aggregate risks; she applied the risk assessment approach to screening-level fish tissue data from the TVA area. Mr. Greene from the Delaware Department of Natural Resources described a comparative risk assessment study in which his agency evaluated risks of PCBs in striped bass from the Delaware estuary. His study showed how the calculated risks might vary under four different hazard/potency scenarios. Mr. Hesse from the Michigan

Department of Health completed the presentation of case studies by explaining the efforts of the Great Lakes Sport Fish Advisory Task Force to reach agreement on a protocol for Uniform Sport Fish Consumption Advisories through the Great Lakes' region.

Dr. Southerland concluded with a summary of the workshop.

PART ONE
INTRODUCTION TO PCBs

1.1 WELCOME AND INTRODUCTION

1.1.1 Elizabeth Southerland,
Chief, Risk Assessment and Management Branch, Office of Science and Technology, EPA, Washington, DC

The Chief of the Risk Assessment and Management Branch, Betsy Southerland, welcomed attendees to the national technical workshop. She noted that a diverse group had assembled for the workshop. For example, more than a third of the attendees were from state agencies. Also, EPA and a number of Federal agencies were represented as well as people from environmental groups and industry organizations. The backgrounds of attendees were also diverse: toxicologists, chemists, biologists, managers, lawyers, etc. This demonstrated that PCBs continue to be an important topic throughout the country.

Dr. Southerland provided some historical background on the PCB workshop. The Risk Assessment Branch first became interested in PCBs from the standpoint of sediment contamination. Preliminary inventories were compiled listing contaminants found in sediments and that posed human health and ecological problems. Not surprisingly, PCBs were one of most frequently documented chemicals. It became obvious that, where there were high levels of PCBs in the sediments, the states had been forced to issue a fish consumption advisory or ban in many cases. That led to a focus on PCBs in our discussions with the states on fish consumption advisories. Since fish are an extremely valuable source of protein, Dr. Southerland emphasized that it is critical to carefully evaluate human health concerns before issuing restrictions on fish consumption.

An increasing number of States are conducting risk assessments as part of their fish consumption advisory process. However, current practice is quite divergent. In 1989, our group provided a grant to the American Fisheries Society to do an inventory of all the state government policies regarding fish consumption advisories. We asked them how they sample and analyze fish tissues, how they set the limits for consumption advisories, and how they communicated the risks. It was a very comprehensive survey. Although the FDA has explained that assumptions underlying their action levels may not be appropriate for recreational and subsistence fishermen, 34 states responded that they were using the FDA action level to trigger their advisories. Ten states said that they use the EPA cancer potency factor to do a limited risk assessment and to define the level at which they want to set fish consumption advisories. And 13 other states said that they used their own methodology without defining that any further, but were not using the EPA cancer potency, or the FDA action level. The survey also confirmed

that responsibilities for fish advisories are often spread throughout several agencies. This multiple agency involvement makes it even more difficult to arrive at a consensus about when to issue a fish advisory.

1.1.2 Rick Hoffmann,
Fish Contamination Section, Risk Assessment and Management Branch, Office of Science and Technology, EPA

As the organizer of the workshop, Mr. Hoffmann elaborated on the purpose of the workshop and some of the planning considerations for the workshop. He noted that the immediate objective of the workshop is to give a "snapshot" of key risk assessment and analytical issues related to PCBs. In prior discussions with state agency representatives, EPA was encouraged to design a workshop that would allow an exchange of PCB information across the boundaries that typically separate various programs, agencies, and academics. This information assumes a greater importance as states move towards risk-based fish advisories. A longer term objective for the Fish Contamination Section is to assess where EPA can provide further technical assistance to the states.

Mr. Hoffmann mentioned that the levels of PCBs in fish tissues are generally declining. However, there is an continuing focus on the potential health effects of PCBs, even at low concentrations. In addition, agencies need to be aware of the appropriate analytical methods and associated costs. Technical evaluations of PCB risks are often complicated by a contentious atmosphere, scientific disputes, cost-benefit debates, and other intangibles.

The workshop was designed to start with general information about PCBs and then move to specifics. Mr. Hoffmann explained that the workshop would talk about health effects, approaches to analytical methods, and then illustrate how several agencies have applied this information, using a series of case studies. He clarified what the workshop would not do. The workshop's primary focus is on human health effects, not on ecological effects or status and trends information. Secondly, the workshop would not duplicate some of the in-depth, single-focus PCB workshops that EPA has held previously. For example, EPA's Risk Assessment Forum in 1989 held a workshop on toxic equivalency factors for PCBs. In September 1992, EPA held a workshop on the neurotoxic effects of PCBs. Finally, the workshop was not designed to provide step-by-step guidance or policy judgments for site-specific risk assessments.

1.2 INTRODUCTION TO PCBS AND ANALYTICAL METHODS

Mitchell D. Erickson, Group Leader, Environmental Research Division, Argonne National Laboratory

Polychlorinated biphenyls (PCBs) are a class of 209 discrete chemical compounds, called congeners, in which one to ten chlorine atoms are attached to biphenyl.

PCBs were commonly produced as complex mixtures for a variety of uses, including dielectric fluids in capacitors and transformers. The major producer, Monsanto Corporation, marketed PCBs under the trade name Aroclor® from 1930 to 1977. Aroclors were marketed for use in transformers, capacitors, printing inks, paints, dusting agents, pesticides, and many other applications. Their chemical and physical stabilities and their electrical insulating properties led to the commercial utility of PCBs. Their chemical and physical stability also has been responsible for the PCB contamination in the environment. Because PCBs do not readily degrade in the environment after disposal or dissemination and are lipophilic, they are persistent and tend to bioaccumulate. PCBs have been shown to be nearly ubiquitous environmental pollutants, occurring in most human and animal adipose samples, milk, sediment, and numerous other matrices.

As early as 1936, occupational exposure was reported to cause toxic effects and workplace threshold limit values were subsequently set. Animal studies with both commercial mixtures and individual congeners have shown a variety of chronic toxic effects. PCB-contaminated cooking oil caused a total of 1,291 cases of "Yusho" in 1968 in western Japan. The clinical manifestations include various somatic complaints, low birth weights, chloracne, and pigmentation. The animal toxicology data have intended to indicate that PCBs are toxic. However, contamination of the commercial PCB mixtures with more toxic compounds such as polychlorinated dibenzofurans (PCDFs) confounds the data. For example, it is unclear whether the PCBs or other contaminants in the Yusho oil are responsible for the observed health effects. PCB toxicity is dependent not only on the degree of chlorination but also on the isomer. For instance, having no *ortho*-substitution but heavy substitution at the *meta* and *para* positions can assume a planar conformation that can interact with the same receptor as 2,3,7,8-terachlorodibenzo-p-dioxin (TCDD). Examples include 3,3',4,4'-tetrachlorobiphenyl, 3,3',4,4',5-pentachlorobiphenyl, and 3,3',4,4',5,5'-hexachlorobiphenyl.

The public, legal, and scientific concerns about PCBs arose from the findings that PCBs were toxic and therefore undesirable as commercial products or environmental contaminants. The evidence for this toxicity was sufficient for special citation by the U.S. Congress in the Toxic Substances Control Act as well as similar actions by other governments. However, the degree of toxicity and the nature of the effects on humans and other organisms have been and continue to be highly debatable.

Most PCB analyses follow a prescribed procedure, often issued by a regulatory agency. Most analyses consist of extraction, cleanup, determination, data reduction, and quality control. Sampling is an important component of the overall procedure, but it is omitted from this

presentation because of space limitations. Reliable trace organic analysis begins with the quantitative extraction of the analytes from the sample matrix. The general objective of an extraction technique is to separate the analyte (e.g., PCBs) from the sample into a matrix that is more compatible with the rest of the analytical procedure. The cleanup takes advantage of the difference in physical or chemical properties of PCBs and interferences to remove unwanted constituents. The cleanup process may be expressed in terms of enrichment, where the ratio of PCBs to interferents is increased. Ideally, a cleanup reproducibility achieves 100 percent recovery of PCBs in one fraction, with the interfering compounds relegated to other fractions.

All analytical methods are designed to determine whether the analyte is present, how much analyte is in the sample, or both. The identification and quantitation are generally accomplished in the same step. This determination step is the foundation of any method, around which all other steps (cleanup, data reduction, quality control, etc.) are centered. With PCBs, a gas chromatograph (GC) separation is almost always an integral part of the determination technique. The separation is accomplished by using either packed column (PGC) or high-resolution (capillary) (HRGC) techniques. The GC effluent is detected by using electron capture (ECD), Hall electrolytic conductivity (HECD), mass spectrometry (MS), and other detectors. In an analysis where "total PCB" is the desired output, packed column GC may provide sufficient resolution. On the other hand, if congener-specific analysis is required for a metabolism study, HRGC would be the technique of choice.

The qualitative discrimination power of a detector is a major factor in the selection of a determination technique. The discrimination is especially relevant because of the variety of PCB mixtures giving rise to complex chromatographic patterns.

Data reduction is a key element in sample analysis. In this step, the analyst converts the instrumental output into information for the user. Specifically, any PCBs present in the samples are identified and quantitated, and these results are reported to the user. Depending on the detection and output system, data may be presented to the analyst as analog chromatograms, numerical tabulations, MS-extracted ion current plots, etc. Computers and integrators can reduce the analyst's work in data acquisition and reduction; however, the judgement of a qualified analyst is critical to reliable data reduction.

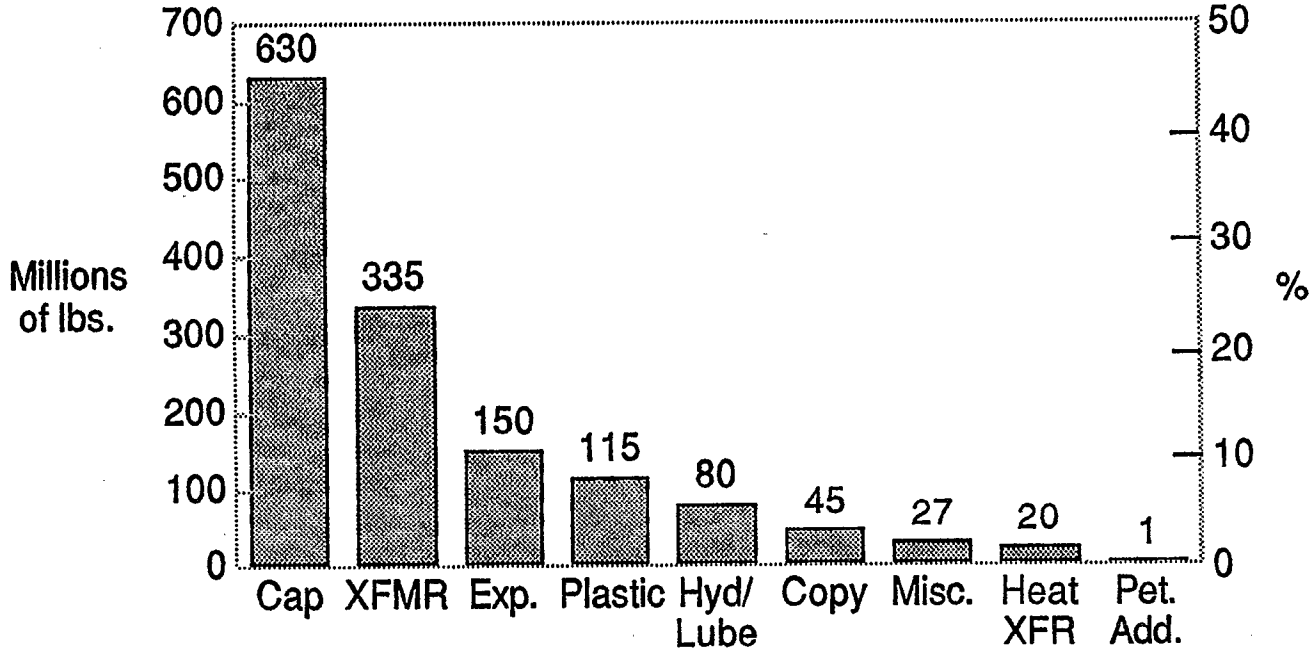
The importance of data reduction cannot be overemphasized, especially with PCBs. The first task in data reduction is to qualitatively identify the analyte, confirming its presence. Quantitation can be attempted only after a compound has been identified, although the required level of confidence in the identification can vary widely. Quantitation (or, less accurately, quantification) is the final step in a chemical analysis sequence. Some measure of signal intensity (peak height or peak area) is converted into concentration. For most detectors used in PCB analysis, the mass of analyte in a peak is proportional to the signal for the analyte, and concentrations are calculated on the basis of this relationship. With most organic compounds, quantitation is relatively straightforward. The instrumental response is calibrated by using standard solutions of the compound. The amount of unknown is measured by comparison of the signal it generates with the calibration factor or curve. Quantitation of PCBs is not nearly so

simple because the analyte is not a single compound but rather a complex mixture of 209 possible congeners. In addition, standards of all 209 congeners are not readily available for calibration. Given these problems, analysts have devised alternate quantitation methods, often based on the similarity of the sample PCB mixture to a commercial product (e.g., Aroclor). Aroclor-based quantitation schemes may be appropriate if the sample and standard "fingerprints" are similar. As the similarity diverges, the quantitative confidence diminishes.

The data report must be formatted to fulfill the analytical objectives. If individual congener concentrations are needed, the report will be complex, while if "total PCB" is sufficient, the data report may consist of a single value. The report must specify the reporting units. The analyst should include on the data report some measure of the qualitative confidence. This is often done in the text, or as a footnote.

Emphasis on quality assurance in chemical analysis has increased dramatically in the past few years with the realization that data of unknown quality are virtually useless. Since PCBs generally occur as complex mixtures of analytes, special quality control measures must be considered. The PCBs used for calibration of the analytical instrument may be a mixture (e.g., Aroclor 1254) similar to that found in the samples or a group of individual congeners. Any realistic option is a compromise from calibration with all 209 congeners. Thus, an estimate of the error induced by the compromise should accompany the data. Because of the complexity of the data, special precautions should be taken to assure both the qualitative and quantitative aspects. Many quantitation techniques involve summing the calculated responses or concentrations for many individual PCB peaks to yield a total PCB value. Any systematic error replicated through several quantitations could result in a magnified error in the reported result. The complexity of calculations also increases the chance of calculation and transcription mistakes.

U.S. PCBs 1930-1975

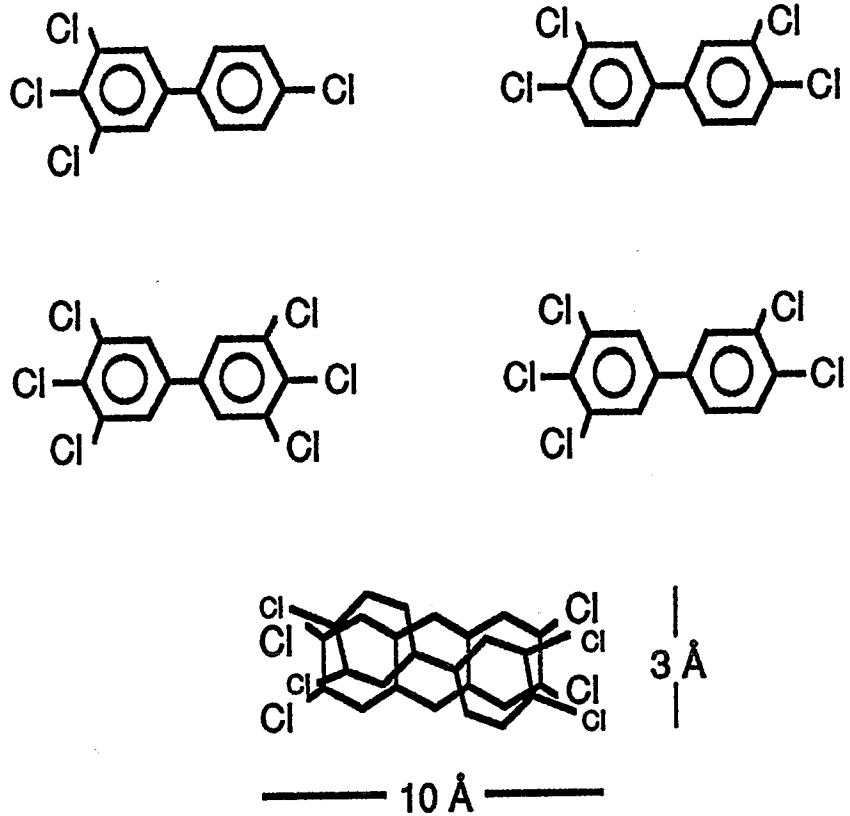


Total = 1,403 M lb.
Source: Durfee et. al., 1976

Typical Environmental Levels

Location	Air (ng/m_3)	Water/Rain (ng/L)
Remote	0.02 - 0.5	0.03 - 10
Great Lakes	0.1 - 5	10 - 150
Rural	0.1 - 2	1 - 50
Urban	0.5 - 30	10 - 250
Indoor	<10 - 620	
Indoor (Ballast)	5,900	
Stack Gas	<10 - 60,000	
Occupational	10^5 - 10^7	

Coplanar PCBs Are Like Dioxin



Coplanar PCBs in Biological Samples

Preparation of homogenous sample

Extraction with KOH (in ethanol)

Partition with hexane (in water)

Carbon chromatography

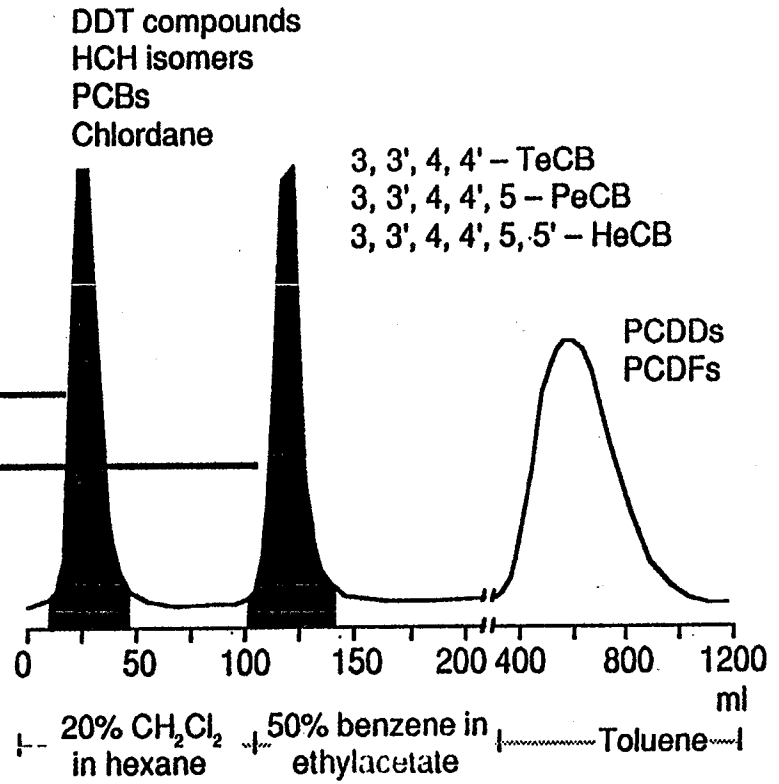
Fraction I:

Fraction II:

Clean-up with fuming sulfuric acid

HRGC/ECD determination

GC-MS confirmation



Source: Tanabe et. al., IJEAC 29 199 (1987)

1.3 TEMPORAL TRENDS OF PCBS IN THE ENVIRONMENT[1]

Written by Robert J. Fensterheim, RegNet Environmental Services, Washington, DC. Presented by John Craddock, Principal, Craddock Associates Incorporated, St Louis, MO

Based on a comprehensive literature review, data for several environmental compartments, including air, precipitation, drinking water, sediment, human milk, soil, waste, and general disposal, were considered too poorly documented to characterize temporal trends. However, adequate information was available to discuss temporal trends for the five following compartments: foods, human adipose tissue, shellfish, fish, and human blood sera. Review of the available information for these compartments reveals that there is essentially no pattern of studies that suggests an increase in the concentration of PCBs. On the contrary, a considerable number of studies document a significant decrease in PCB levels. Higher confidence levels in a trend assessment is typically reserved for studies or groups of studies where there is consistency in sampling and analysis. Although all of the studies examined are not of such quality, evidence presented in this report clearly point to an overall decrease in PCB levels throughout the environment. The overall studies show that, through 1985, there were sharp decreases in PCB concentrations in the environment as its uses were phased out. Since the mid 1980s, the rate of decline has slowed as PCB contamination levels approach trace levels in most environmental compartments.

Foods

The National Research Council in 1979 identified persistence and lipophilicity as the "most important properties of a chemical that relate to potential hazards to health and the environment." Since PCBs are highly lipophilic and will slowly biotransform, they tend to concentrate in tissues with high fat content. Thus, the temporal trends of PCBs in foods, particularly those with high fat content, and in human tissues, are critical in assessing public health implications.

PCB levels in food are regulated by the Food and Drug Administration. The FDA has set tolerances for PCBs ranging from 0.2 ppm in infant and junior foods and feed for food-producing animals to 10 ppm for paper food-packaging materials intended for use with human food. The tolerance level for fish and shellfish is 2.0 ppm. High levels of PCB contamination of food during the 1970s and the early 1980s frequently occurred because of contamination in food packaging. The use of PCBs in carbonless copy paper was cited by the National Academy as leading to contamination of paper products and foods by the recycling processes. Sawhney and Hankin note that these sources of contamination have been "essentially eliminated" since the Federal government regulated the use of PCBs. The main dietary route of human exposure to PCBs is now through consumption of PCB-contaminated fish. Thus, the majority of studies

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[1] Ed. note: This paper summarizes a report, prepared by RegNet for several trade associations, which complies and interprets PCB trends information from a variety of federal and state agencies.

identified focus on PCB levels in fish. Fish are analyzed as part of the FDA's Total Diet Study, the principal source of information for documenting trends of PCBs in the U.S. food supply. The results of this program indicate a substantial decline in PCB residues to near zero in recent years.

FDA's Total Diet Study, also known as the Market Basket Survey, began in 1961, initially to determine dietary intake of radionuclides resulting from atmospheric testing of nuclear weapons. In 1971, the program was expanded to include analyses of selected nutrients and pesticides, including PCBs. By 1982, this study included 234 food items representing 100 percent of the diet of the U.S. population. The primary purposes of the study, as currently described, are to estimate the dietary intakes of pesticides, industrial chemicals, and other toxic elements and radionuclides and to compare these intakes with established safe or recommended dietary levels. Food items are collected from retail outlets simultaneously in three cities in each of four regions in the U.S. and shipped to the Total Diet Lab in Kansas City for analysis. Results on PCB contamination from the Total Diet Study are periodically reported in published articles by the FDA researchers. The last report presenting data on PCBs was published in 1988 and includes data for the years 1982 to 1984. A more current profile of PCB trends documented in the Total Diet Study show a significant decrease in PCB intake from 6.9 ug/day in 1971 to 0.05 ug/day for the years 1987 to 1990. From 1977 to 1980, there was a slight bobble in the curve. The PCB intake rose slightly to 1.9 ug/day before dropping off again to the 0.2 level.

Human Adipose Tissue

The lipophilic properties of PCBs means they tend to collect in adipose tissue, making adipose tissue a useful method for monitoring human exposure to PCBs. Adipose is especially preferred in detecting low level or chronic exposure. Adipose tissue studies, however, are more difficult to undertake than other environmental surveys because of the intrusive nature of collecting the samples, necessitating collection from mainly autopsied cadavers and surgical patients. The NAS in 1979 identified a mean concentration of 1.2 mg/kg of PCBs in adipose tissue of the U.S. population. Robinson and others reviewed available data documenting trends of PCBs, hexachlorobenzene, and benzene hexachloride in adipose tissue in the U.S. and concluded that "while nearly the entire population has detectable levels of these chemicals, the actual concentration levels are steadily decreasing."

The principal source of information for documenting trends of PCBs and other substances in human adipose tissue is the National Human Adipose Tissue Survey known as NHATS. The primary purpose of the NHATS program is to establish baseline levels for the presence of toxic chemicals in human tissue, adipose tissue, and to make statistical comparisons of the residue levels for the population and sub-populations, including trends over time. Samples collected during 1982 were analyzed using high resolution gas chromatography and mass spectrometry, a technique which more sensitively detects volatile organic compounds. Samples taken during 1984 were split and analyzed using both of these methods to allow comparison of the two different analytical techniques. Thus, two sets of data exist for the 1984 samples. The high

resolution gas chromatographic method allowed for detection of each homolog rather than measuring PCBs as if PCB is one compound. The high resolution gas chromatographic method, furthermore, has an average detection limit for each homolog ranging from 0.03 ug/g of lipid compared to 0.33 in the electron capture method. The data reveals an upward trend in the percentage of population having a detectable level of PCBs. The 1972 data show approximately 90 percent of adults in this country having detectable levels. This level increased to 100 percent in 1981 and 1983. Adipose tissue levels were obtained from two Canadian cities between 1979 and 1981, and 100 percent of the samples analyzed in the Canadian cities were found to have quantifiable levels, confirming what was found in this country. However, the results are somewhat disputed when you look at the more sensitive high resolution gas chromatographic method used in 1982, 1984, and 1986 composites. For 1982 samples, PCBs were detected in only 38 out of 44 composites, about 83 percent, with all of the non-detectable samples coming from persons in the 0 to 14 year old age group. A higher but still less than 100 percent detection was also seen with the 1984 composites using the high resolution gas chromatographic method. These results showed 98 percent had detectable PCB levels, while the electron capture method reported 100 percent detection. More notable than the level of detection is that the actual levels of PCB contamination reported by the electron capture method appear to be greater determined using the more sensitive high resolution gas chromatographic technique.

Another significant finding from the NHATS program is that PCB levels in adipose tissue over time show a downward trend in the percentage of the population with PCB levels greater than 1 ppm or greater than 3 ppm. The percentage of persons having greater than 1 ppm PCBs in adipose tissue showed a significant decreasing trend from a high of 62 percent in 1972 to 2 percent in 1984. The percentage of persons having greater than 3 ppm of PCBs also declined from a high of near 10 percent in '78 to 0 in the '83-84 time frame.

Blood Sera

Analysis of PCB levels in blood sera is a valuable means to study PCB levels in humans also. Although blood samples are less sensitive than other human tissue samples such as adipose tissue for detecting small exposures to PCBs, the analysis of blood sera gives a direct indication of the level at which the internal body organs are exposed. According to ATSDR, PCBs adipose levels correlate with blood sera levels readily, although low level exposure over the long term is better detected in adipose tissue. For those studies where multiple years of sampling were conducted, downward trends were seen, suggesting that PCBs are not stored in blood as they are in adipose tissue but tend to readily dissipate from blood sera after elimination of the exposure.

A study of Michigan residents found a decrease in serum PCB levels in persons consuming greater than 10 kg of fish per year, from 56 ng/ml in 1974 to 21 in 1980. The study authors note that this decline followed a reduction in the amount of PCB contaminated fish consumed per year. For non-fish eaters, PCB levels declined also from a median of 15 ng/ml in 1973 to 6.6 ng/ml in 1983. In Japan, a study of persons accidentally exposed to PCBs concluded that, within five years after exposure, PCB levels in the blood were recorded at almost the same levels as those of unexposed individuals. This decrease in blood sera PCB

levels was also found in occupationally exposed Japanese workers. The results cited are consistent with results obtained from the Greater New Bedford Harbor PCB health effects study. This study was prompted by the discovery of high levels of PCBs in seafood taken from New Bedford Harbor, Massachusetts.

Shellfish and Fish

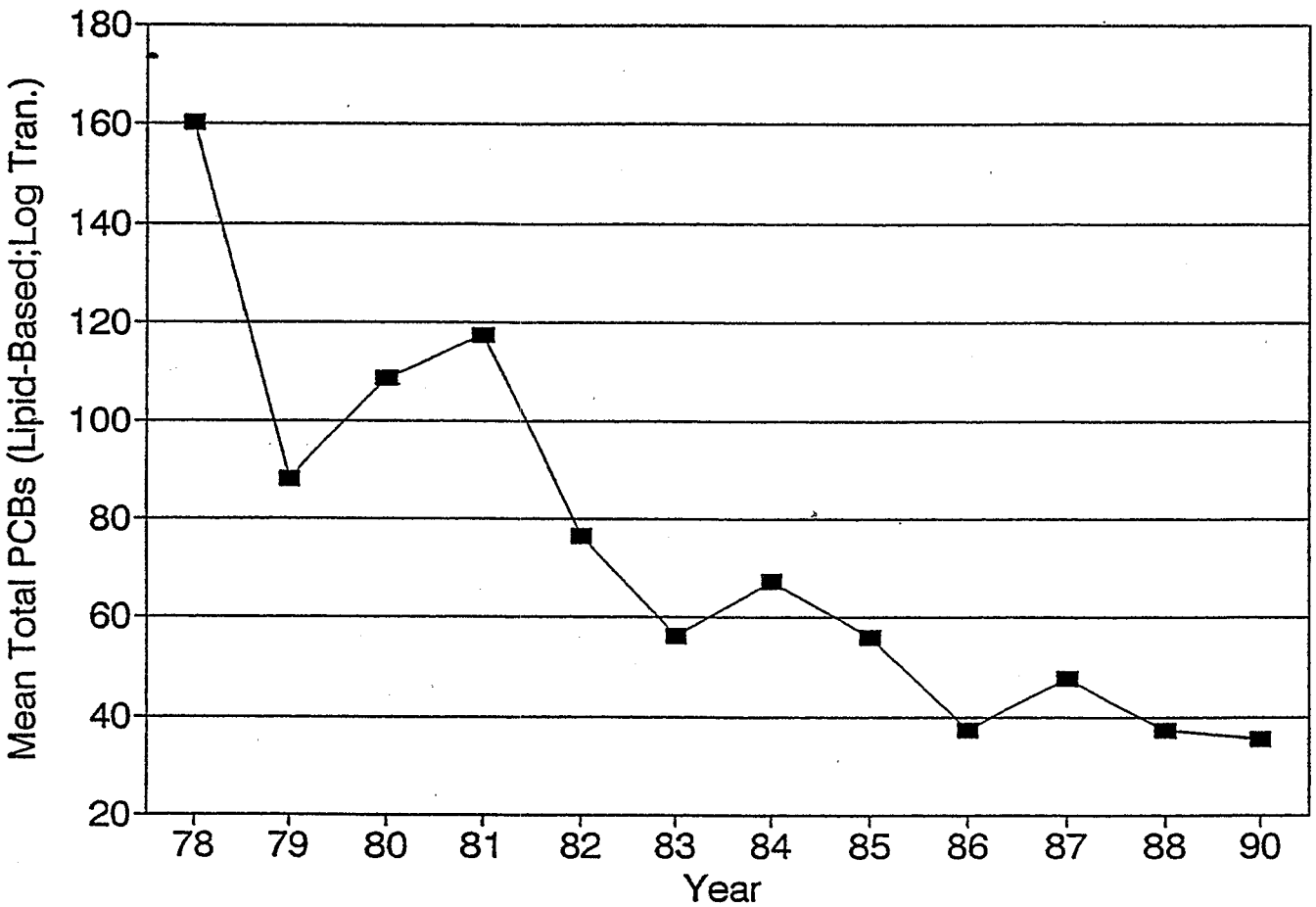
The National Academy of Sciences in 1979 estimated that 50 to 80 percent of PCBs present in the environment are contained in North Atlantic waters. Because of PCBs' high octanol/water partition coefficient and low water solubility, PCBs readily adsorb to suspended particulates and bottom sediment. PCB levels in sediments represent a time-averaged indication of contamination at the sampling site or an indicator of historical PCB inputs rather than a representation of contamination in the mobile aquatic environment.

The analysis of organisms is considered the most accurate measure of PCB contamination in the aquatic environment. Ideal bioindicators generally have the following characteristics: they accumulate PCBs in proportion to the average levels present in the ambient waters; they are sedentary in order to be representative of the area from which they are collected: they are abundant in the study area; they tolerate the presence of high levels of the pollutant without being toxicologically affected; they are of reasonable size, giving adequate tissue for analysis; they should be easy to sample and be hardy enough to survive in the laboratory; and they are long lived enough to permit time integration of the pollutants over several months or years. Shellfish and, in particular, bivalves such as oysters, mussels, and clams are useful in evaluating contaminant trends, because contaminant levels in tissues of a single organism change fairly rapidly, that is, within months, in response to changes in water quality. Mussels provide an especially good indication of spatial and temporal contaminant trends, because they are sessile and abundant in many geographical areas. These characteristics also allow researchers to assess environmental contaminant levels for a specific locality and time frame.

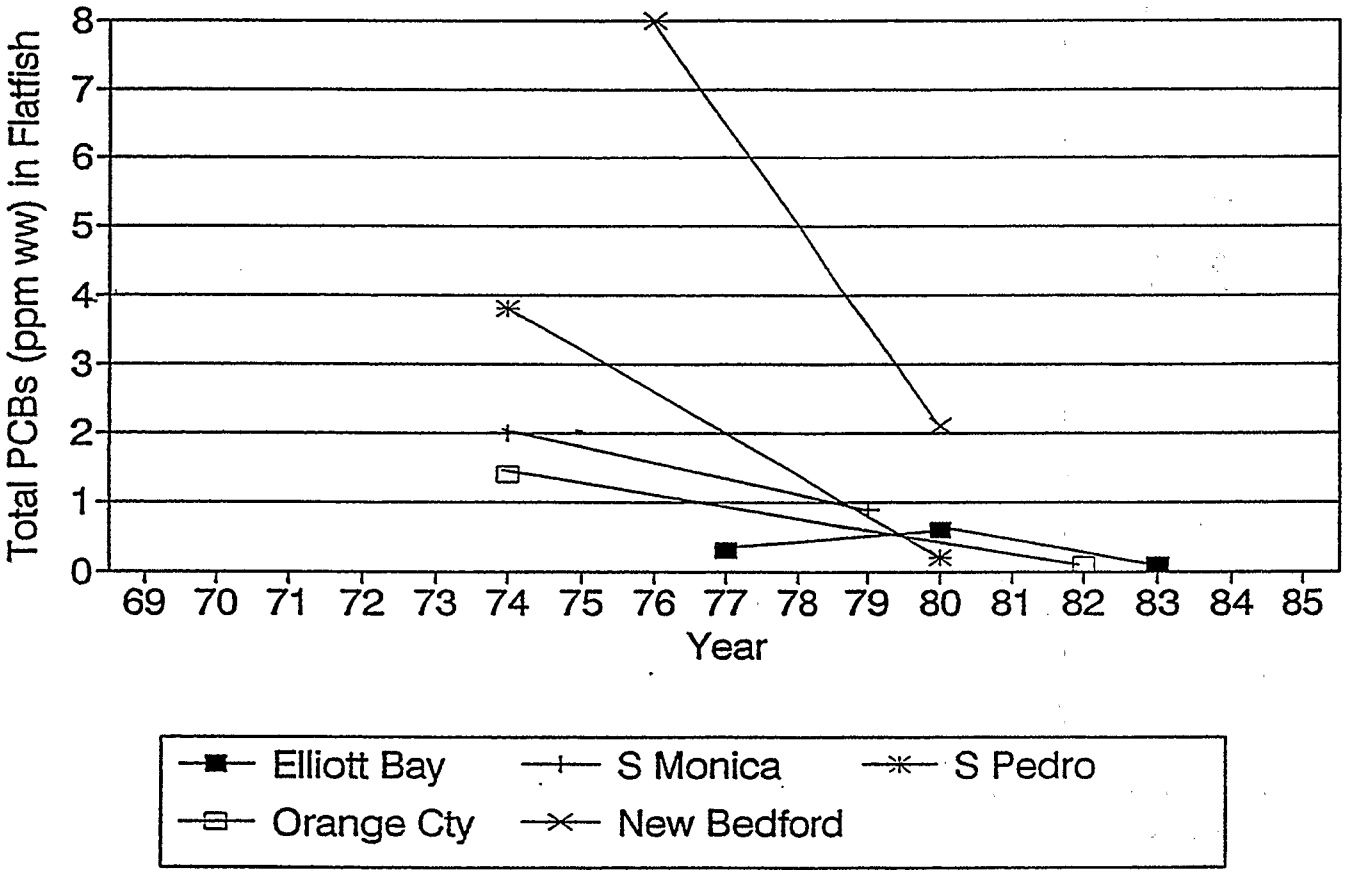
In 1988, NOAA conducted a historical assessment of trends in PCB contamination in shellfish and fish, which examined available data from studies on fish and shellfish conducted in the U.S. in an attempt to identify long-term trends in PCB contamination. The survey was based on a synthesis of approximately 35,000 pieces of historical data from many different studies, covering over 540 species collected between 1940 and 1985. Data on PCB levels in fish and shellfish were contained in over 11,000 records. The study found that PCBs have been detected in all estuaries sampled, including remote, non-industrial areas. The highest concentrations were found to occur in fish samples near the urban areas. The results of data compiled for NOAA '88 did not allow the study authors to make conclusions regarding a national trend in PCB contamination in the U.S. among fish and shellfish as a whole. However, for specific species such as the striped bass and menhaden, NOAA's 1988 historical study was able to develop 15 to 20 histories of PCB contamination. Within geographical areas such as Chesapeake Bay and San Francisco Bay, long-term declines in PCB contamination were documented. In fact, site-specific sampling has yielded very few instances where PCB levels increased in the short or long term.

In conclusion, PCBs concentration in the environment have undergone a significant decline over the past 15 years. The most dramatic declines appear to occur in the late 1970s and the mid 1980s time frame which corresponds to the period following the regulatory controls imposed by the Toxic Substances Control Act. Declines in PCB levels were documented in environmental compartments of public health significance, most notably foods for human consumption, human adipose tissue, shellfish and various fish species. Most of the reports that we have screened suggest that these declines will continue through natural degradation processes.

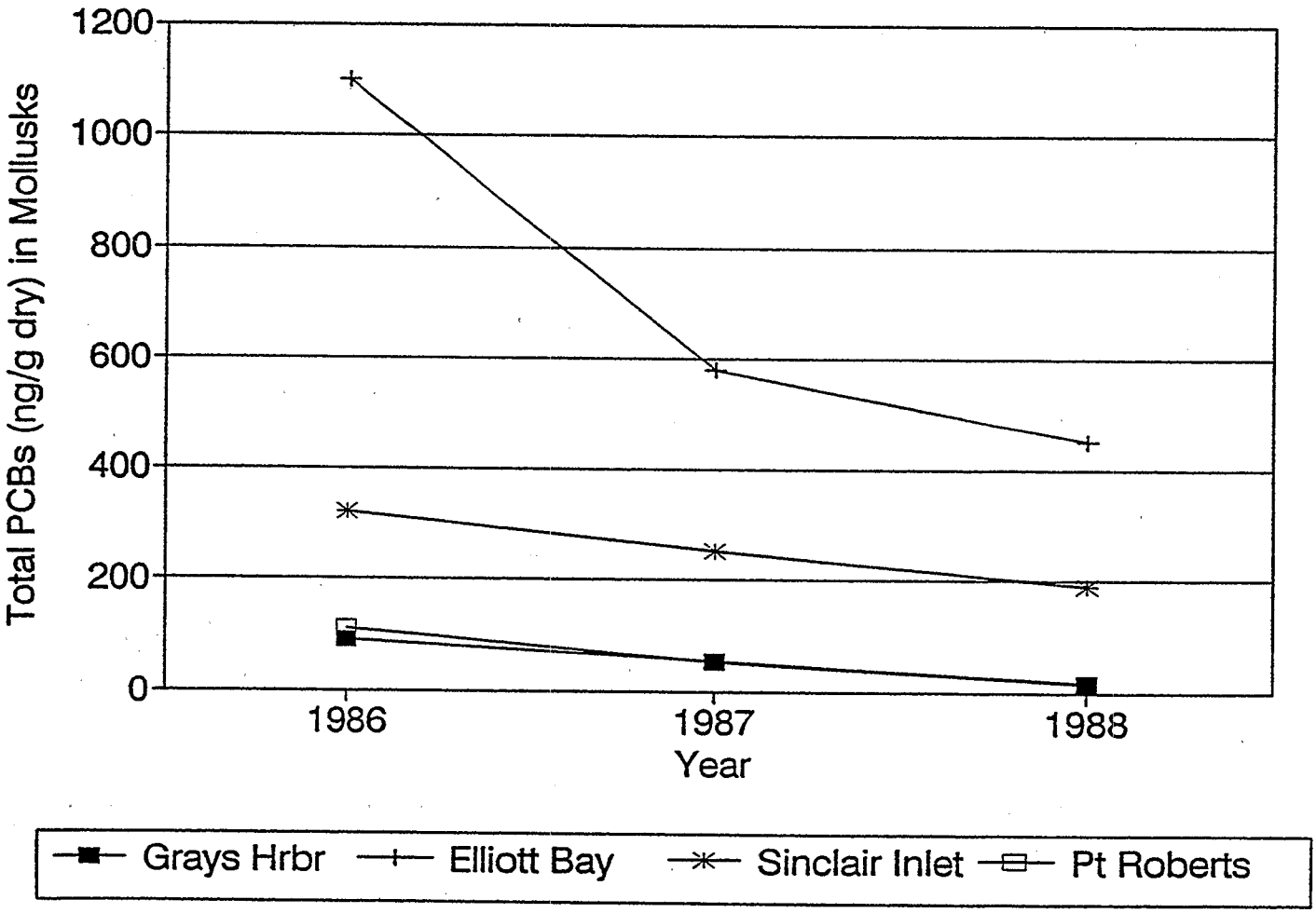
Trends in PCB Contamination
Lower Hudson River Striped Bass



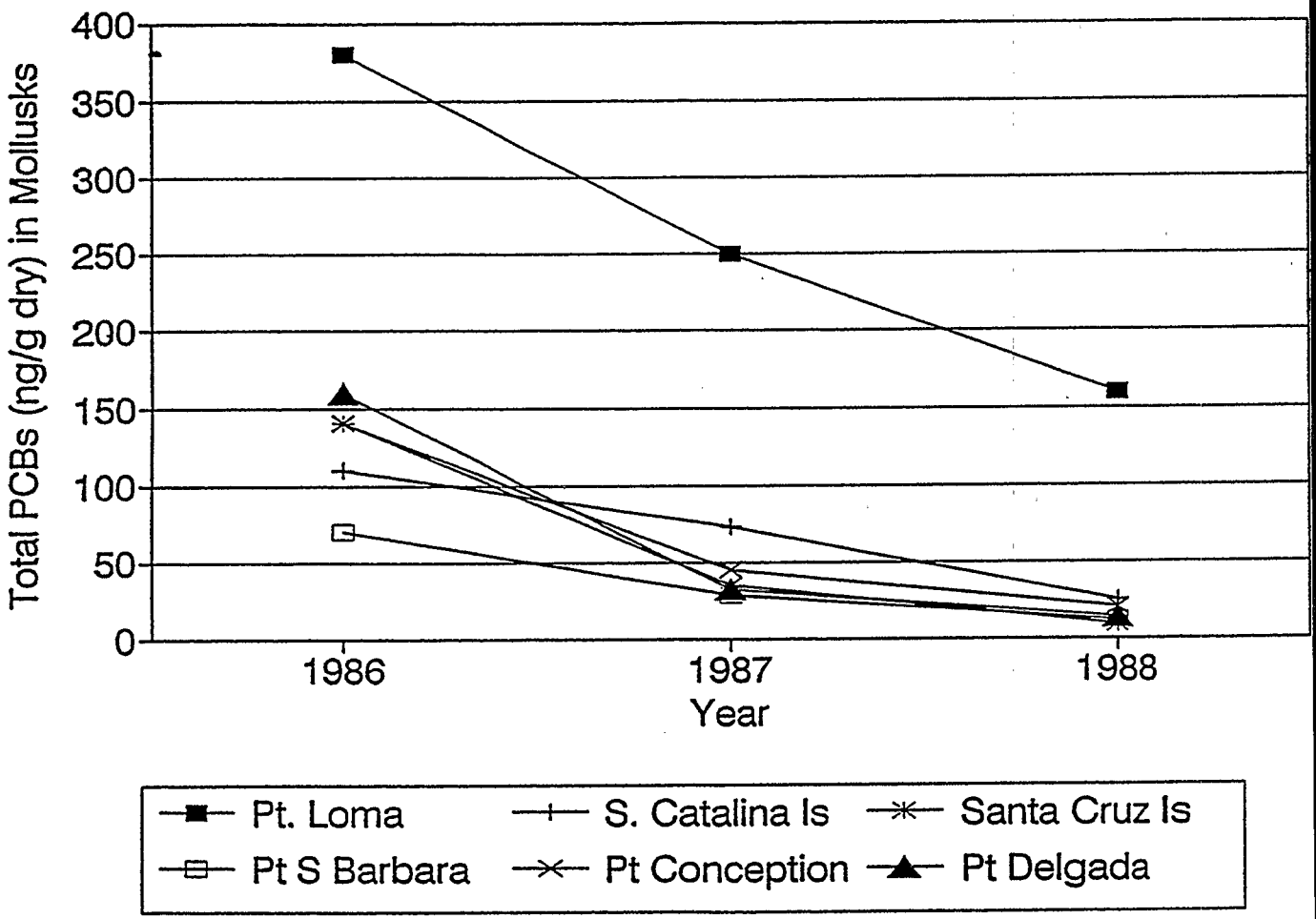
PCB Levels in Flatfish
Various Sampling Sites



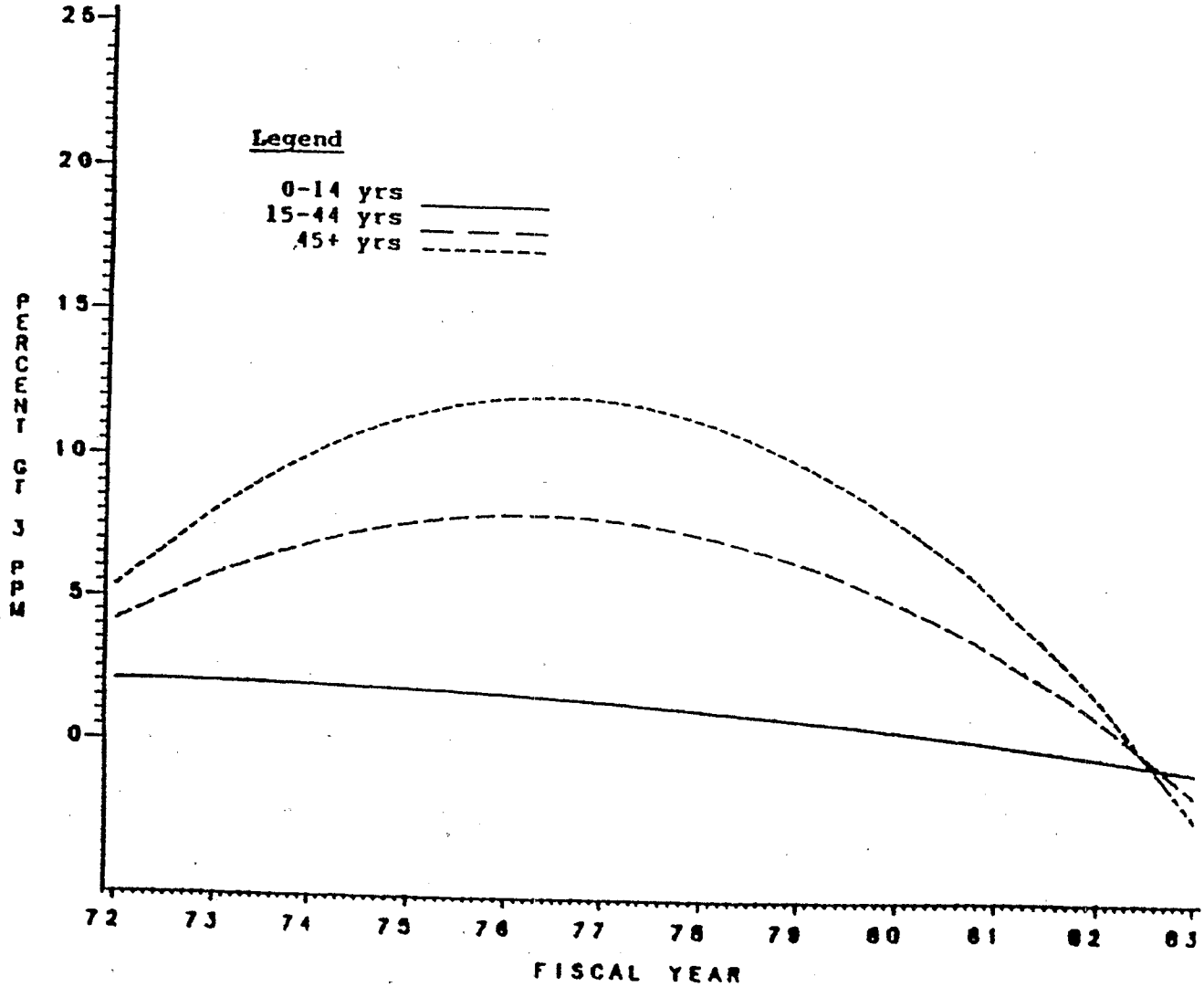
1986-88 Mussel Watch Data
Sites in Washington State



1986 - 88 Mussel Watch Data
Sites in California

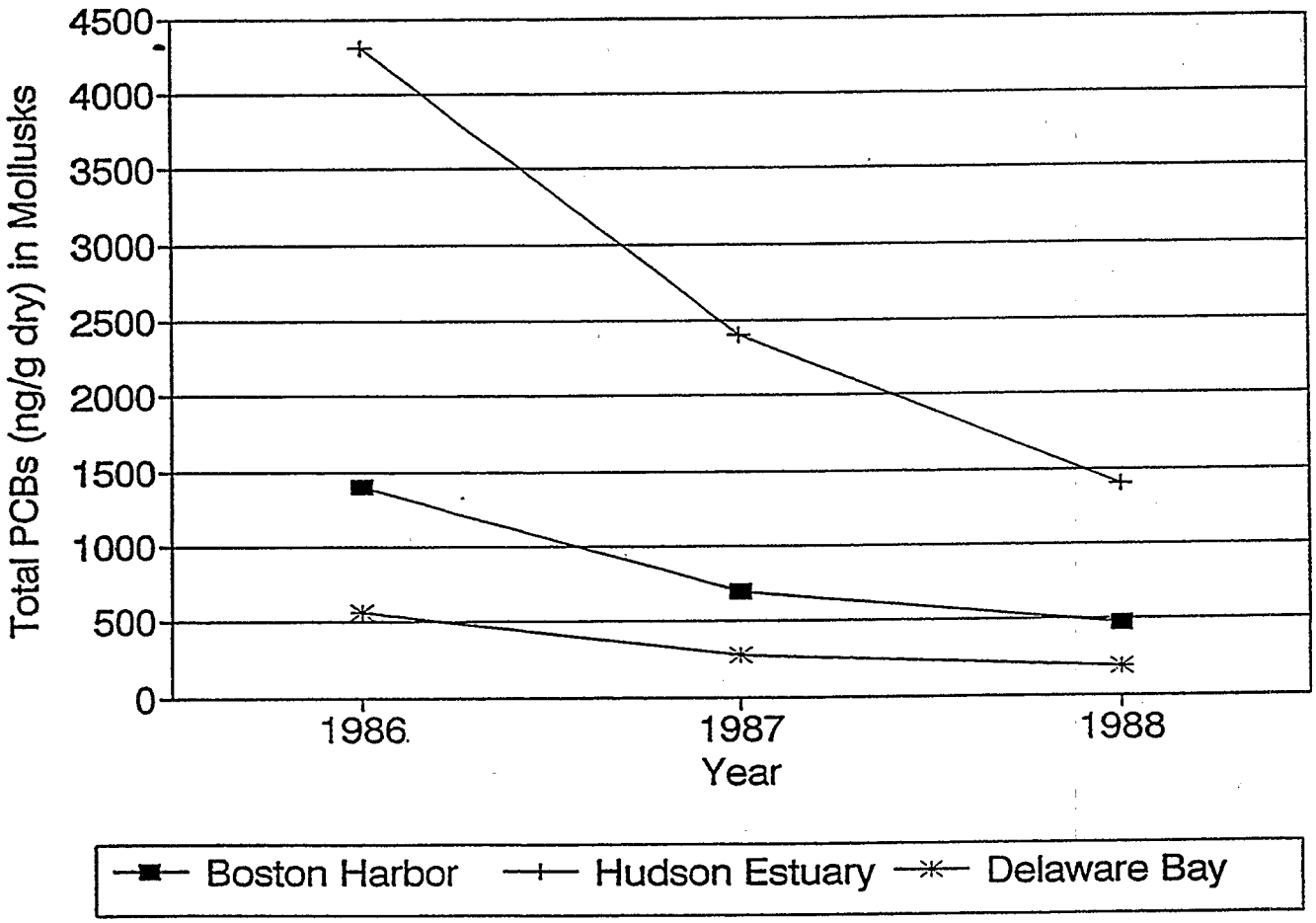


PCB Levels Greater Than 3 ppm by Age Group, 1972 - 1983



(Reprinted from EPA, Office of Toxic Substances, Baseline Estimates and Time Trends for Beta-benzene hexachloride, Hexachlorobenzene, and Polychlorinated Biphenyls in Human Adipose Tissue 1970-1983. Washington, DC, September 1985.)

1986 - 88 Mussel Watch Data
Sites With Significant PCB Decreases



1.4 PCB TRENDS IN GREAT LAKES FISH

David De Vault, U.S. EPA's Great Lakes Program Office, Chicago, IL

PCB contamination is ubiquitous across the Great Lakes and residues occur in fish tissue from all areas of the Basin (Figure 2). Lakes Superior and Michigan represent the least contaminated and one of the most contaminated of the Lakes, respectively. These two lakes may also be used to illustrate the overall success of PCB regulation (Lake Superior), and an area where we need to do additional work (Lake Michigan).

PCB concentrations across the Great Lakes have declined significantly as a result of bans on manufacture and use implemented in the mid 1970's. Concentrations in the Lake Superior water column (Figure 5) and lake trout have declined from around 1 ng/1 in 1980 to less than 0.2 ng/l in 1992. Concentrations in whole lake trout similarly declined from nearly 2 ug/g in 1980 to 0.5 ug/g in 1990 (figure 6). In both cases, the declines are consistent with first order loss kinetics, and the decline continues through the most recent data available. This is supported by a PCB mass budget for Lake Superior (Figure 7), which estimates inputs to the Lake at around 200 kg/yr and losses, primarily through volatilization, at around 800 to 900 kg/yr. PCB loading to Lake Superior appear to be below that required to maintain existing concentrations and further declines in concentrations are expected.

PCB concentrations in several Lake Michigan fish species have declined in response to regulatory actions (Figure 8). However, these declines have slowed or stopped in recent years in several species. Lake Michigan lake trout (Figure 9) declined significantly from 1974 through 1982. However, from 1986 through 1990 concentrations declined only slightly, if at all. During this period, concentrations were above the loss rate calculated from the 1974-1982 data, further suggesting a leveling off of the downward trend. The Lake trout data represent fish that are approximately 6 years old and concentrations have been relatively stable since 1986, suggesting (using an very simplistic load-exposure scenario) that the PCB loadings to southern Lake Michigan have been relatively constant since the early 1980s. Fillets from fall run coho salmon (Figure 10) show a similar situation, with a definite leveling of concentrations beginning in 1983. Coho salmon are stocked in Lake Michigan and are in the lake for approximately 18 months before they return to the tributaries to spawn. They are taken in the Great Lakes Fish Monitoring Program during the fall spawning run. Using the same simplistic relationship between loads and exposure that was used for lake trout, the coho data would also suggest that PCB loadings have been relatively stable since the early 1980s.

Dated sediment cores provide a more direct measure of relative net loadings than fish, which are subject to food chain and other exposure variations. Core data from the southern basin of Lake Michigan (Figure 11) indicate that concentrations in sediments increased rapidly through the 1940s, 1950s, and 1960s, reflecting PCB manufacture and use. Concentrations then declined from the mid 1970s, when use and production bans were implemented, through the early 1980s. Concentrations in sediments from about 1982 through 1989 were virtually constant, reflecting constant loading rates. Thus three independent data sets indicate that PCB loading to southern Lake Michigan decreased beginning in the mid 1970s through the early 1980s, and that

loadings have been relatively constant since then. Unfortunately, those loadings are sufficient to maintain tissue residues at unacceptably high concentrations, as illustrated by Sport Fish Consumption Advisories for several Lake Michigan species.

PCB congener data (normalized as a percentage of congener 153) shows that congener profiles for lake trout from Lakes Superior, Michigan, Huron, and Ontario, as well as, walleye from Lake Erie are quite similar (Figure 12,13). The similarity in congener profiles from open lake samples across the Great Lakes suggests a similar source, such as the atmosphere. That the source of PCBs is reflected in the congener profile in fish tissue is illustrated by the very different profiles seen in Green Bay walleye, where the source is contaminated sediments in the Fox River (Figure 14).

The indication that there is an atmospheric source, or sources, to southern Lake Michigan is further suggested by atmospheric samples collected over the Great Lakes (Figure 7). These data indicate relatively little variation across the basin, with the exception of Lake Michigan, where there is a strong north or south gradient. Concentrations over the southern portion of the Lake are nearly an order of magnitude above background and are twice the levels found in the next most contaminated area (Detroit/St. Clair River).

Thus there is substantial evidence suggesting that PCB loadings to southern Lake Michigan are being maintained at unacceptably high levels due to atmospheric sources. We are attempting to identify the ultimate source of these loadings, and suspect the highly industrialized Chicago-Northwestern Indiana region.

Some concern has been expressed that, although total PCBs have decreased, concentrations of the planar PCBs may not be decreasing at equivalent rates. Figure 17 illustrates trends in mean concentrations of several planar congeners in Lake Michigan Lake trout. Figure 18 presents the log fit of these data to time and illustrates that, with the exception of congener 77, the declines in lake trout are similar to that observed for total PCB.

Data Acknowledgements

Steven Eisenreich, University of Minnesota, Gray Freshwater Biological Institute, Navarre, Minnesota: Figure 5 - *PCBs in The Lake Superior Water Column*; Figure 7 - *PCB Budget for Lake Superior-1992*; and Figure 11 - *Lake Michigan Sediments-Site 18*.

Robert Hesselberg, U.S. Fish and Wildlife Service, Ann Arbor, Michigan:
Figures 16 and 17 - *Lake Michigan Lake Trout, Planar PCBs*.

Fig. 2

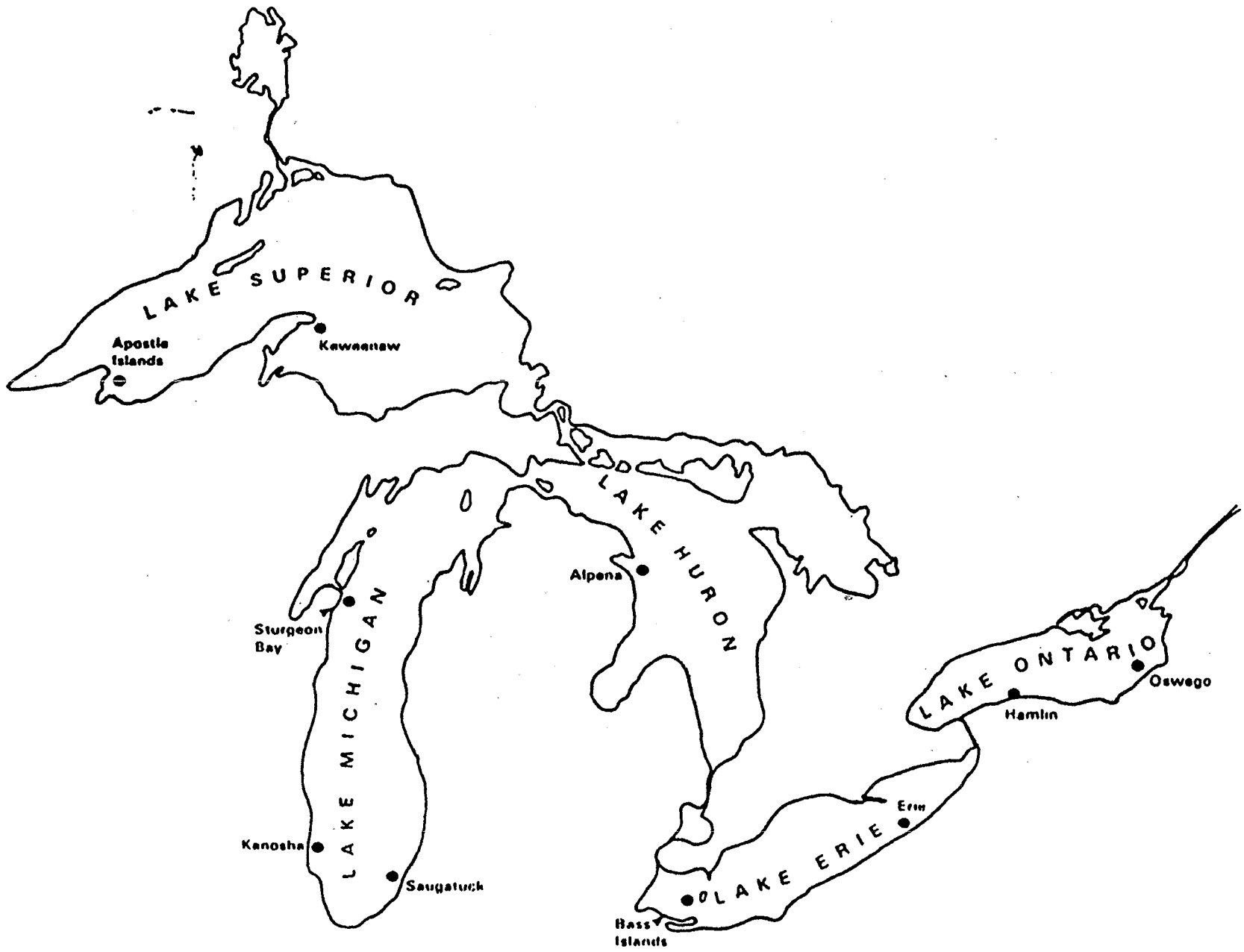

LAKE SUPERIOR
Apostle Islands
Keweenaw
LAKE HURON
Alpena
LAKE MICHIGAN
Sturgeon Bay
Kenosha
Saugatuck
LAKE ONTARIO
Oswego
Hamlin
LAKE ERIE
Erie
Bass Islands

Fig 5

PCBs In the Lake Superior Water Column

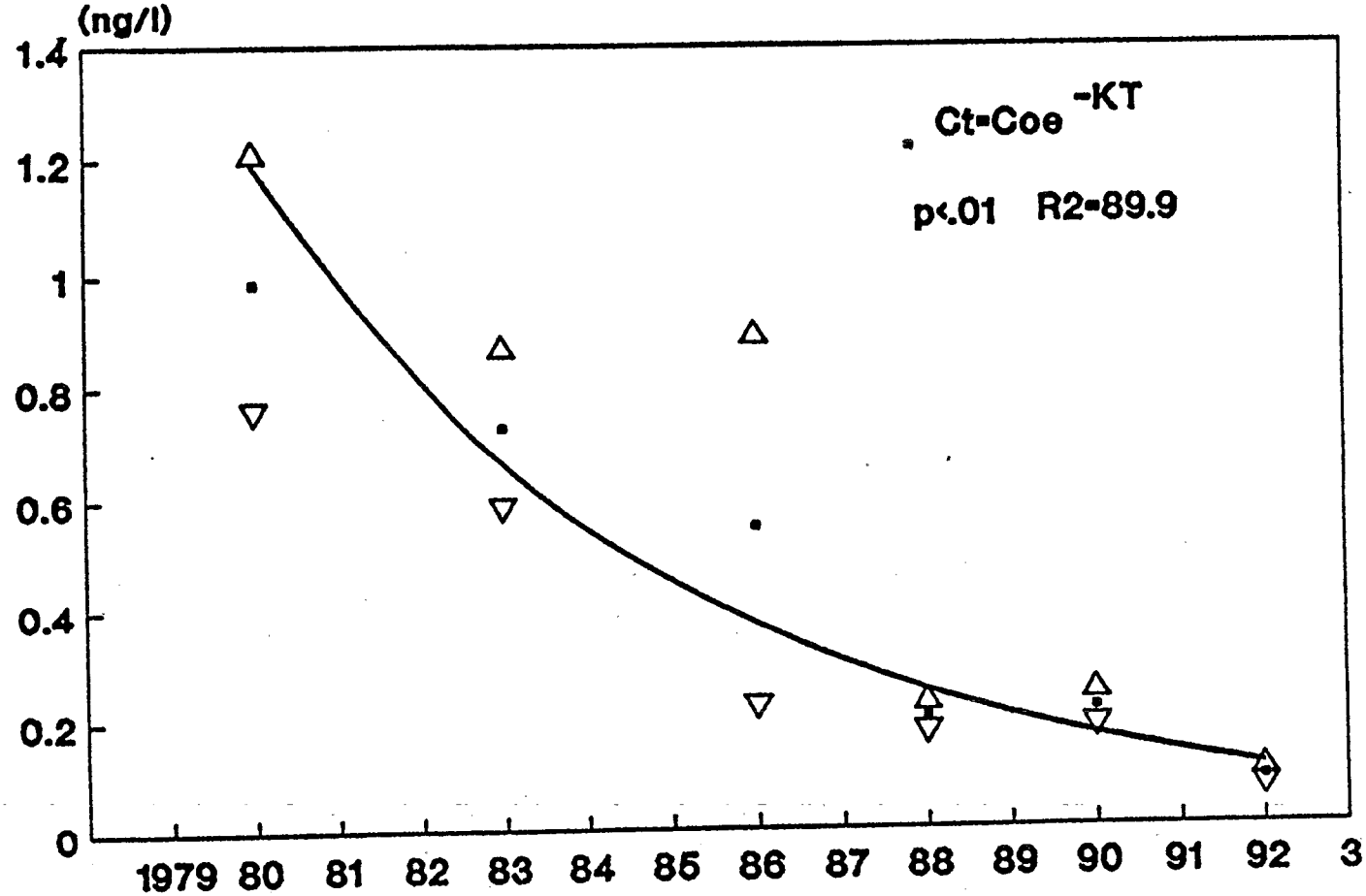
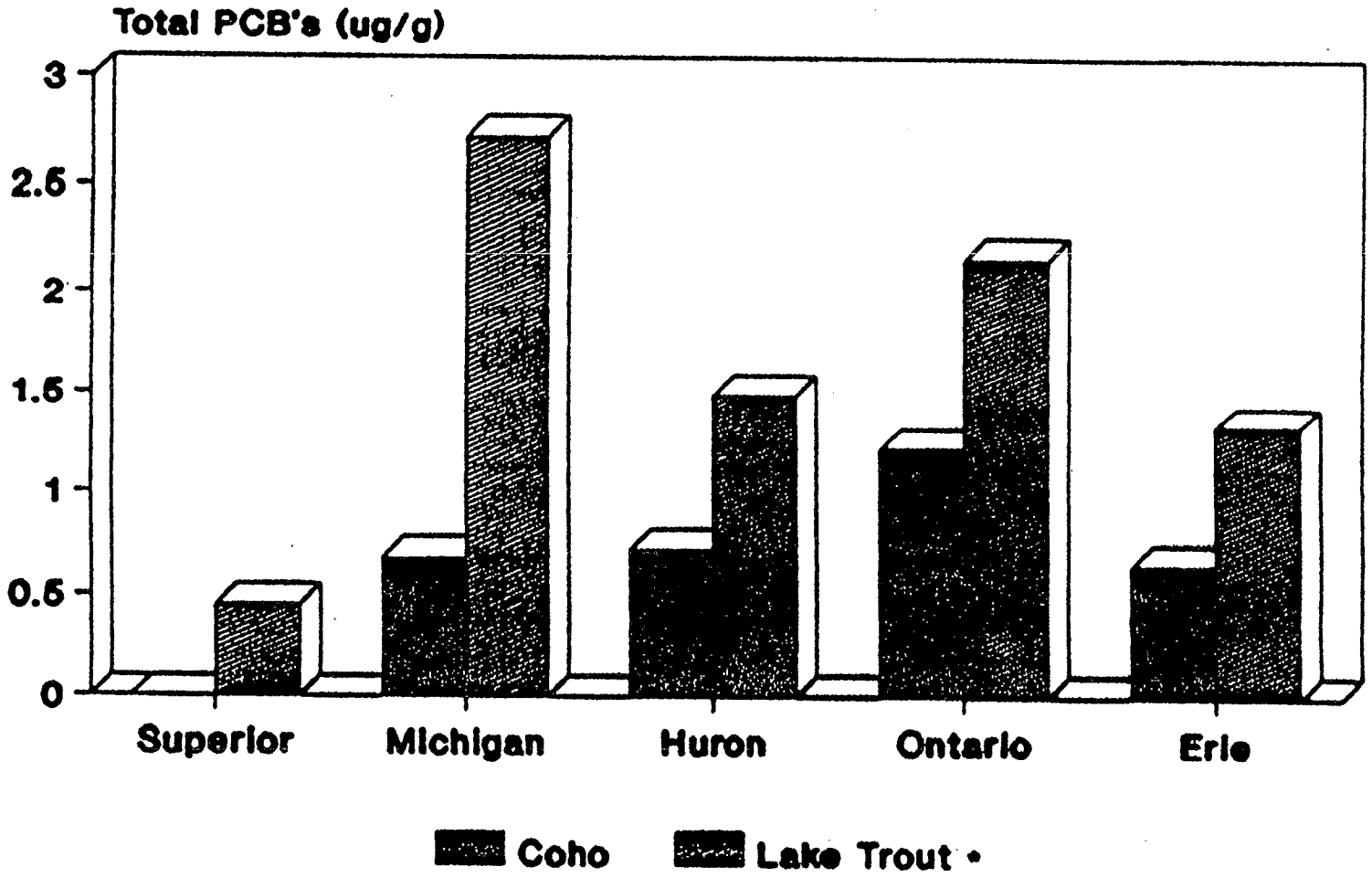


Fig 4

PCBs In The Great Lakes



Erie-walleye

Fig 6

Lake Superior Lake Trout
Total PCB (ug/g)

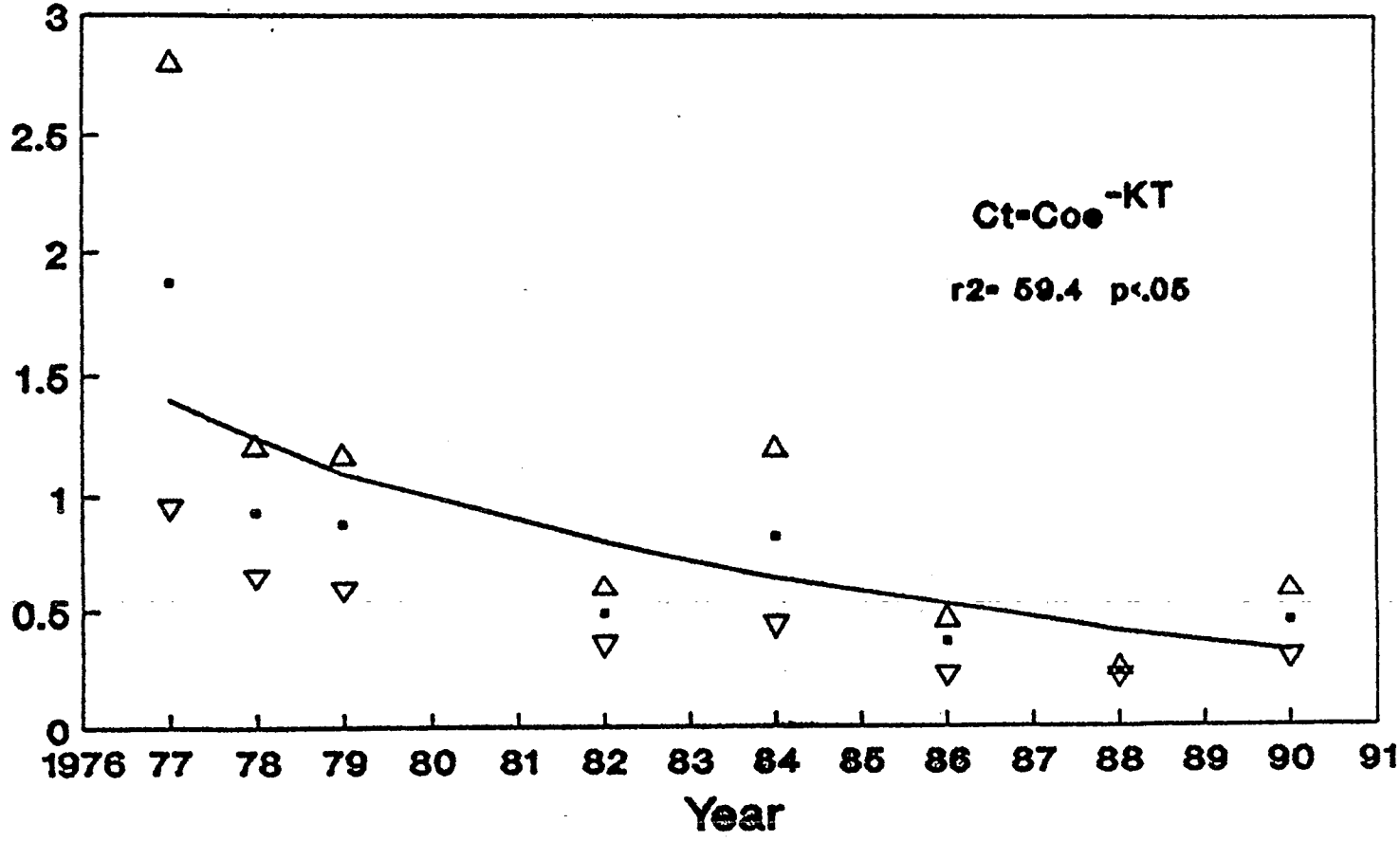
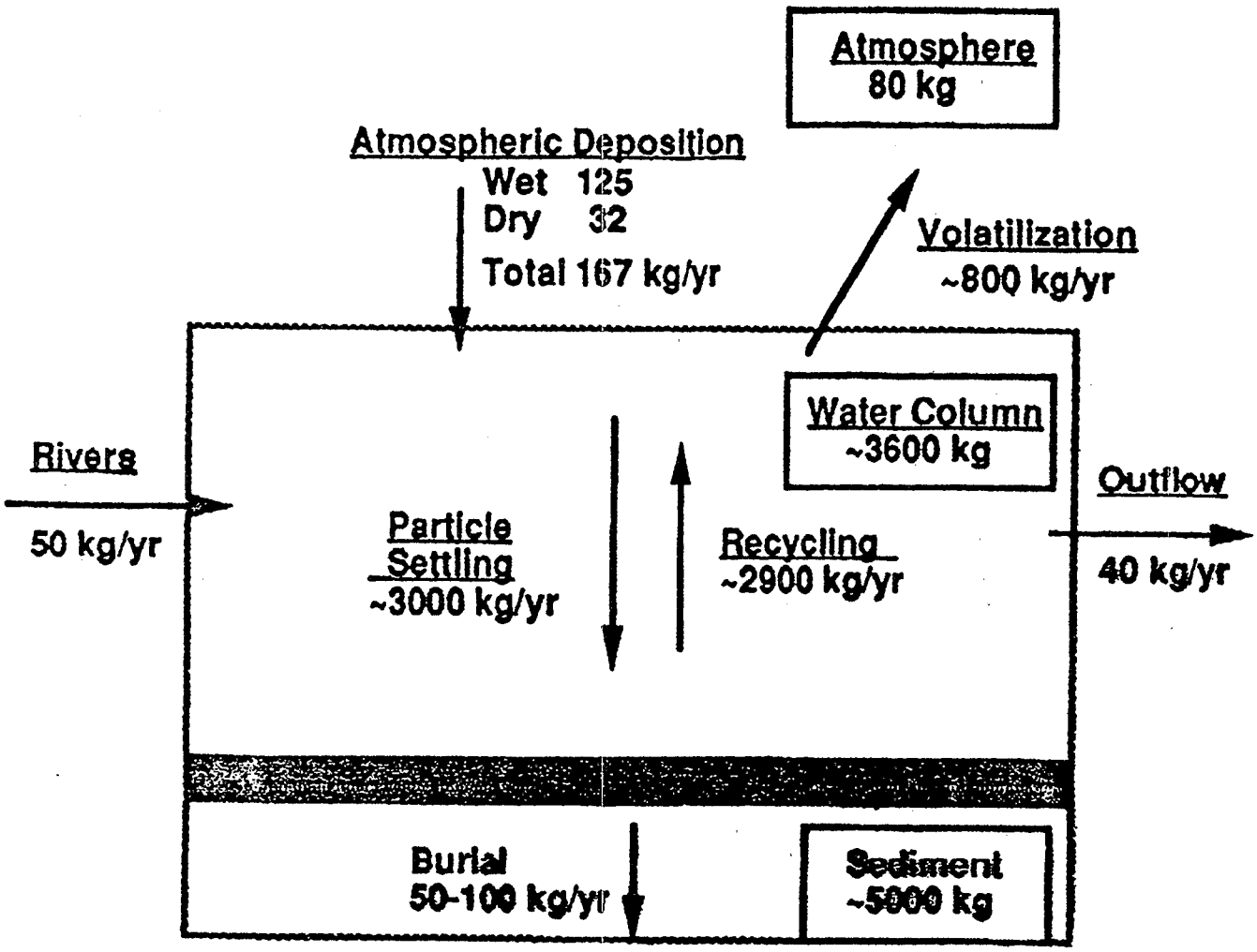


Fig 7

PCB BUDGET FOR LAKE SUPERIOR - 1992



Water Column - 1980 ~12000 kg
- 1992 ~ 4000 kg
Water Column Loss Rate ~ 700 kg/yr

Water Column Loss ~ Volatilization

Fig 8

Lake Michigan Fish
Total PCB (ug/g)

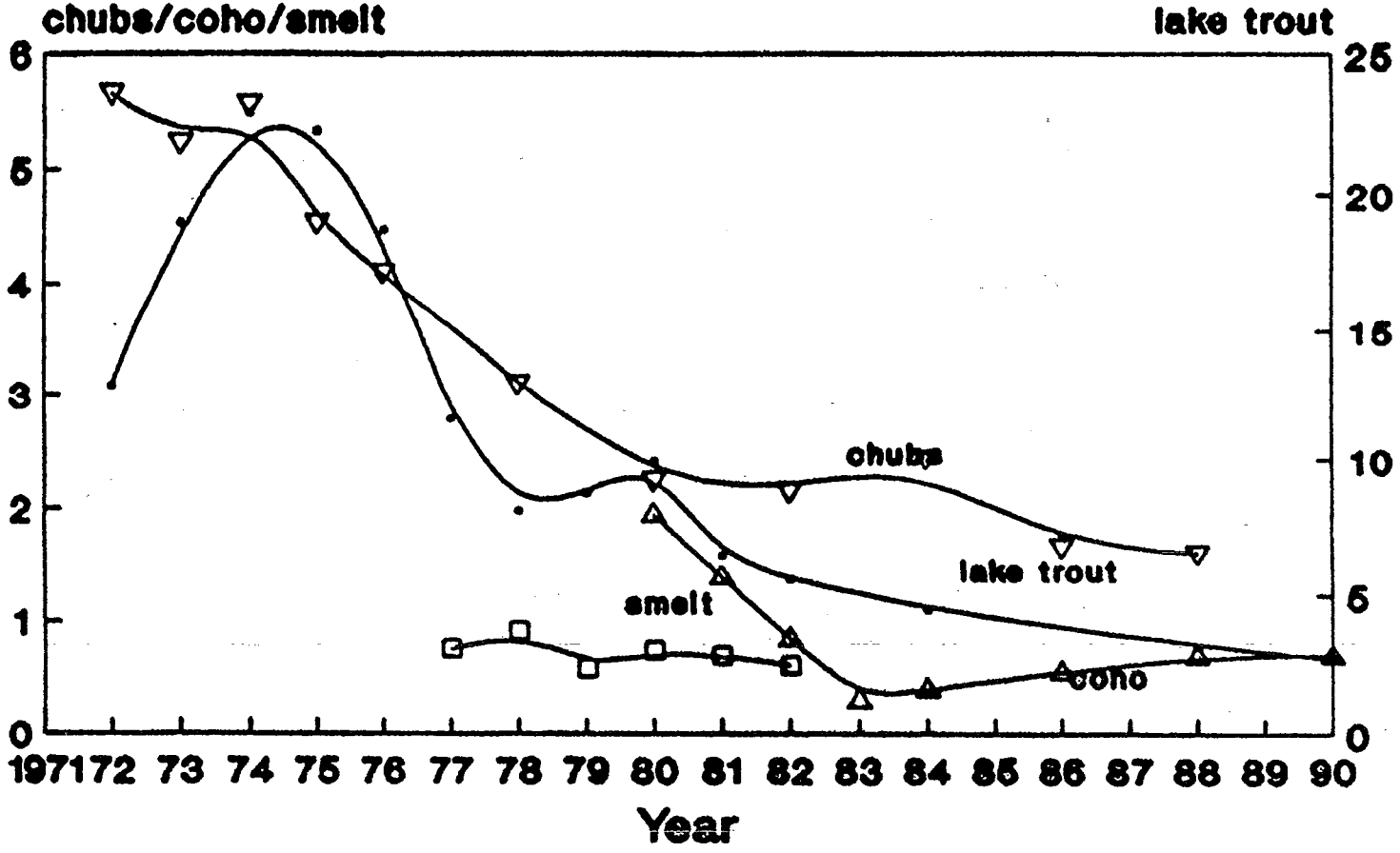


Fig 9

Lake Michigan Lake Trout
Total PCB (ug/g)

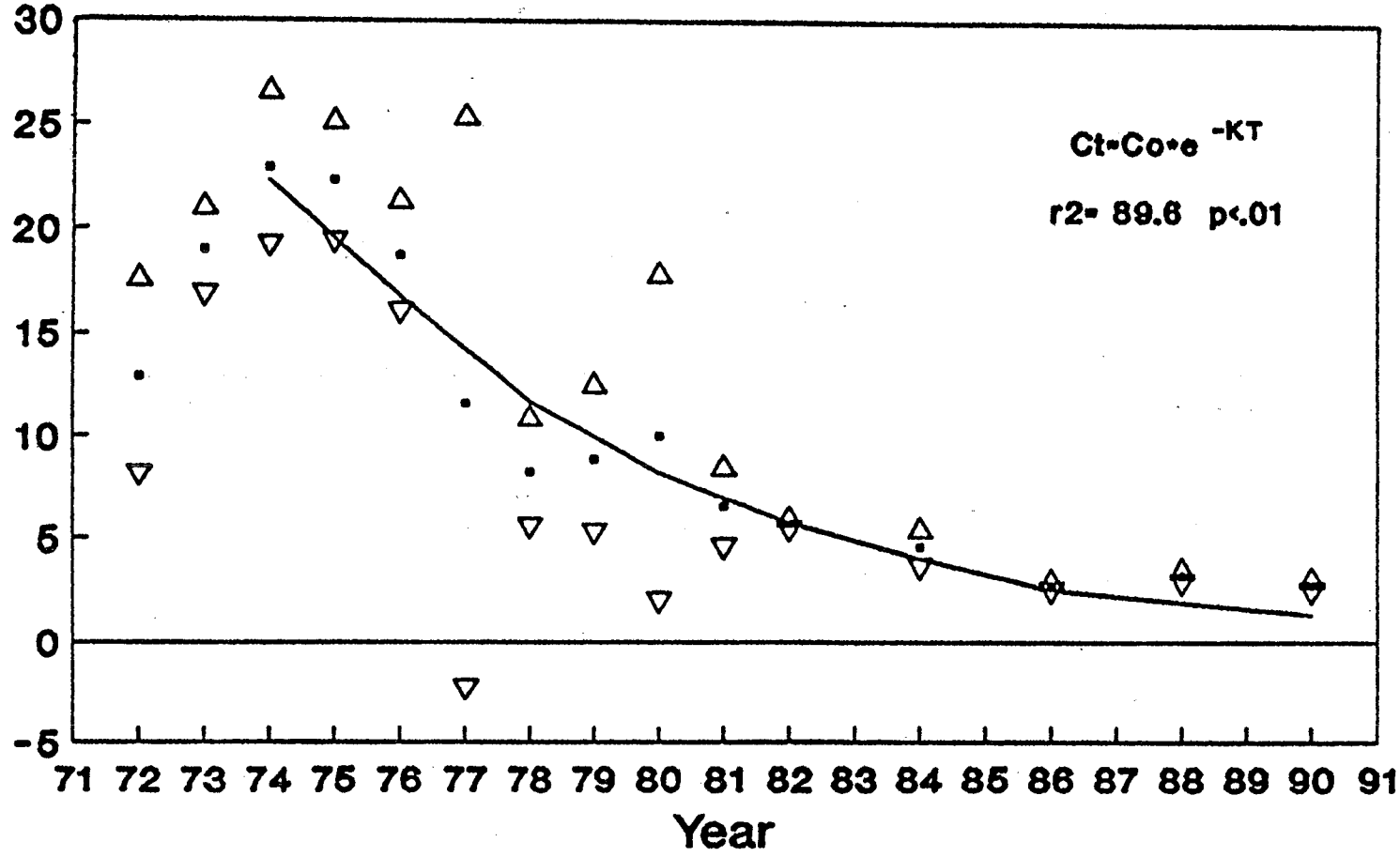
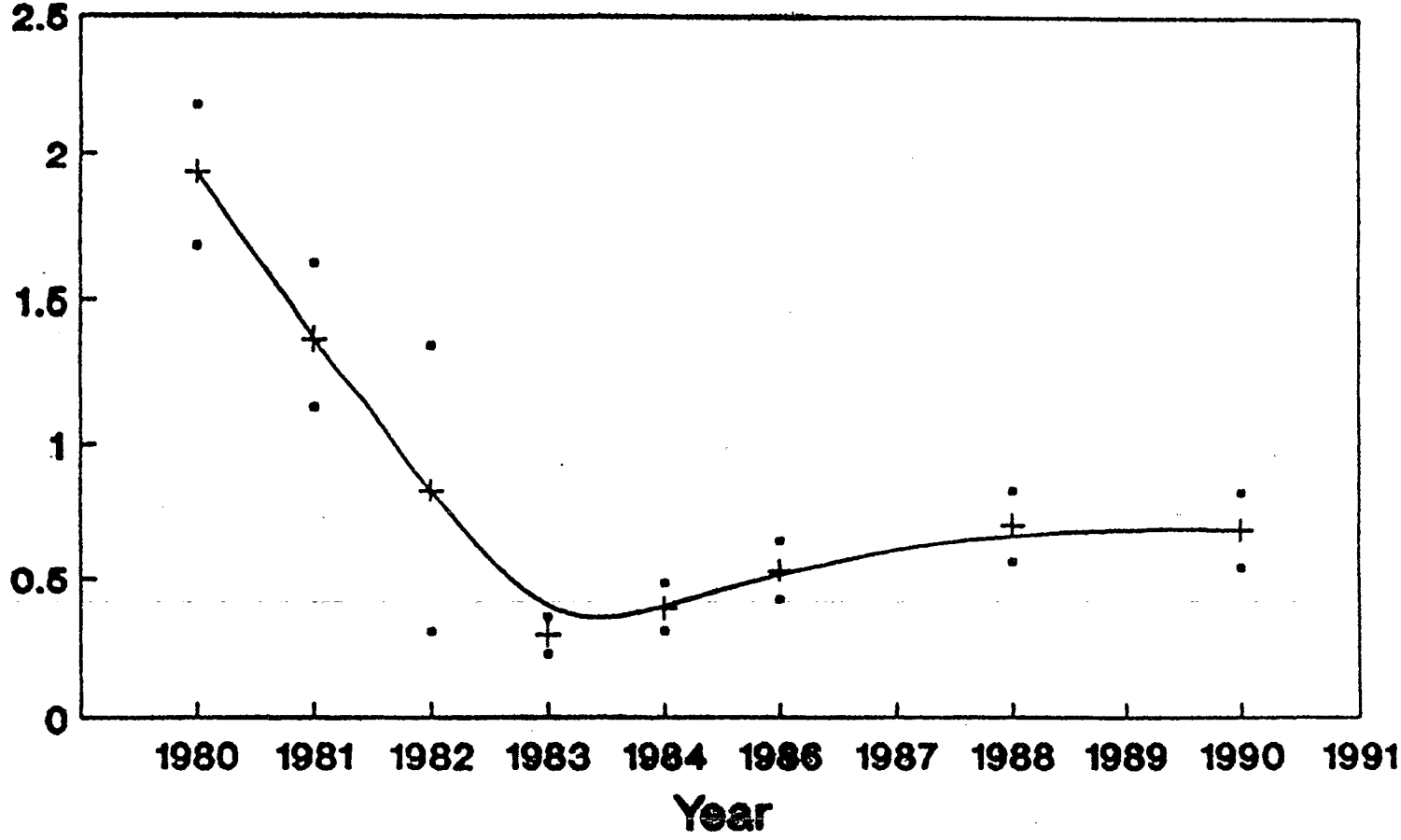


Fig 10

Coho Salmon Fillets

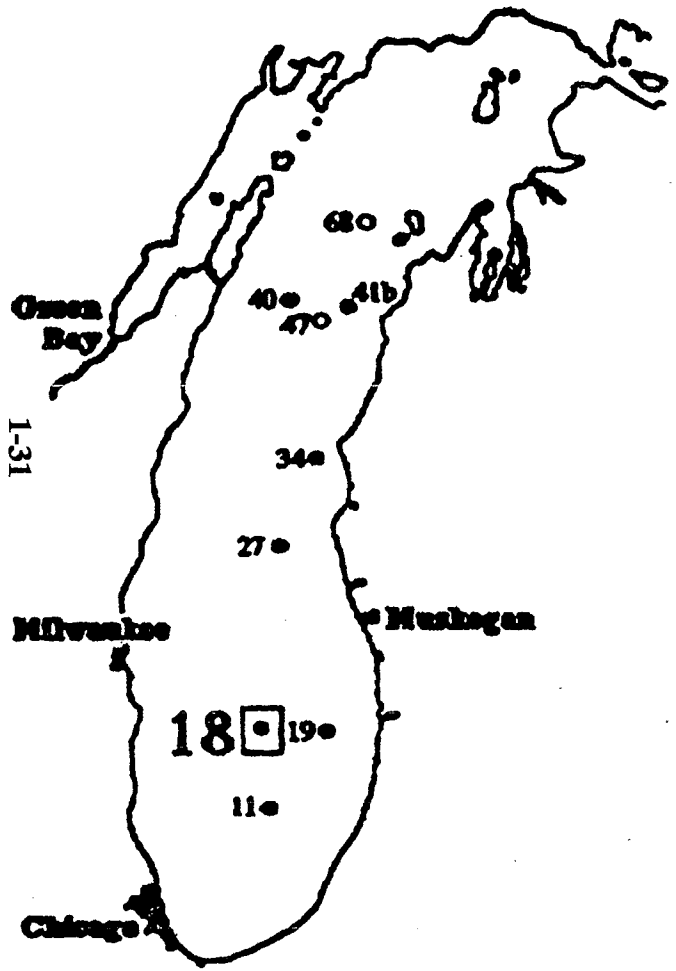
Total PCB (ug/g)



Mean and 95% CI

Lake Michigan Sediments--Site 18

Fig 11



● 1991 Sampling Sites
○ 1992 Sampling Sites

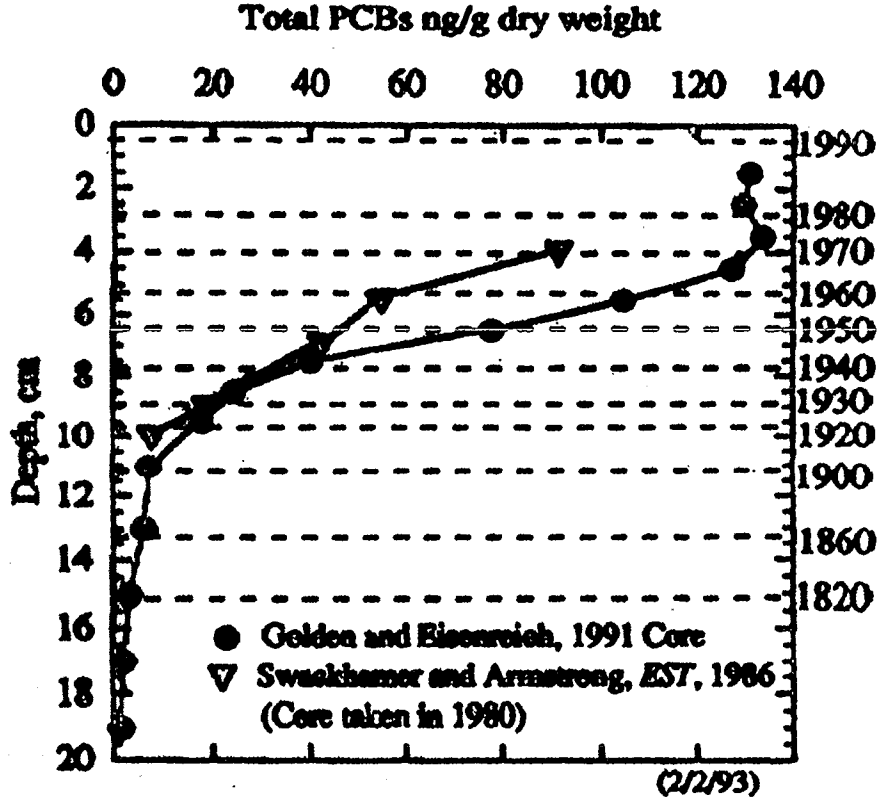


Fig 12

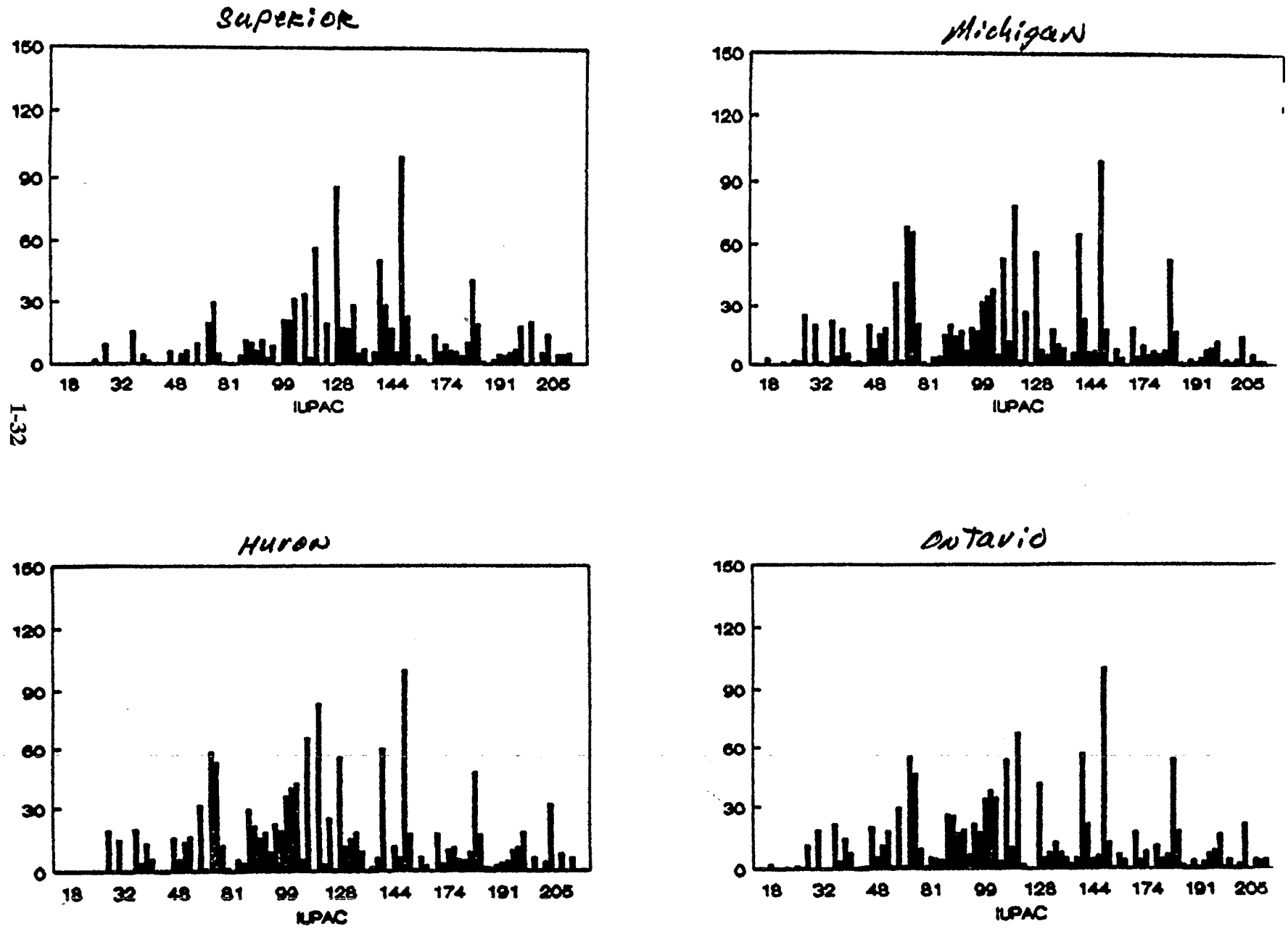

Superior
Michigan
Huron
Ontario
150
120
90
60
30
0
18 32 48 81 99 128 144 174 191 205
IUPAC

Fig 13

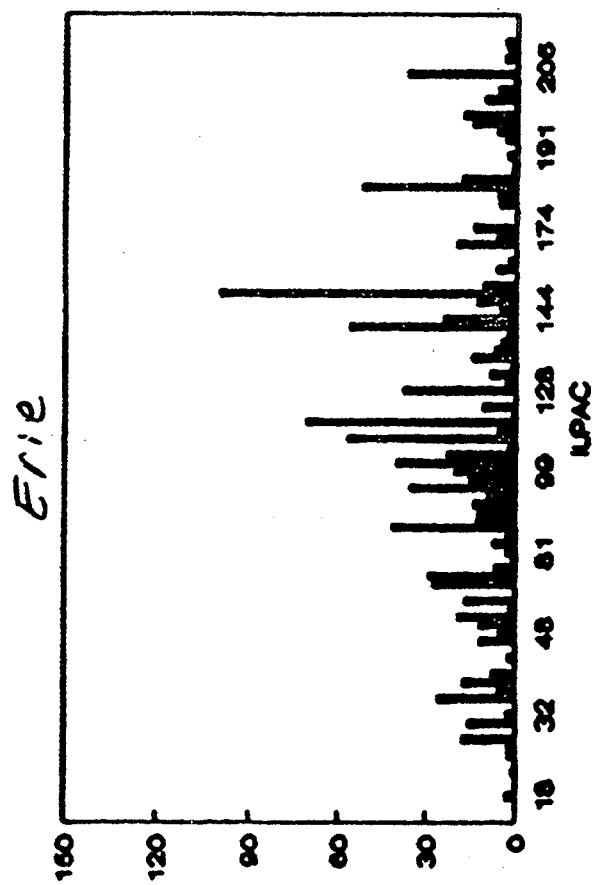
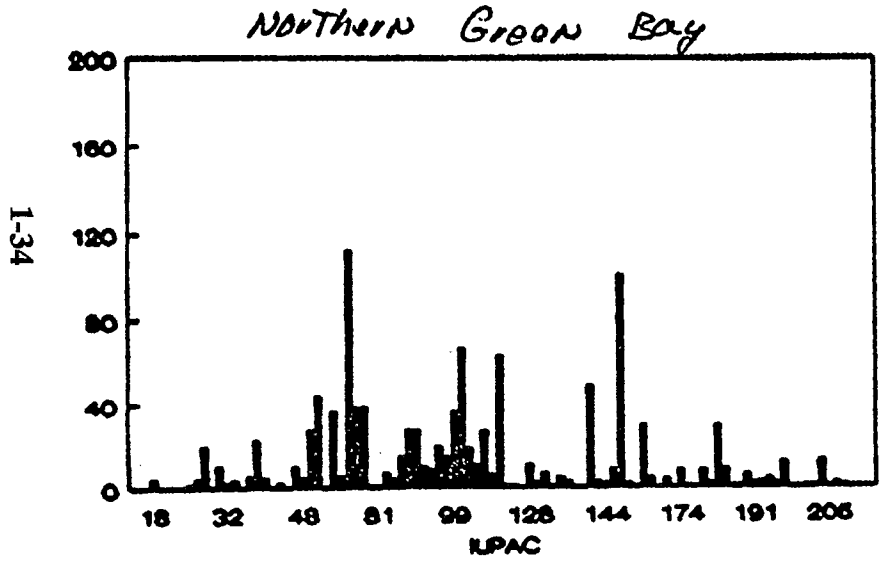


Fig 14


Northern Green Bay
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160
120
80
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0
18
32
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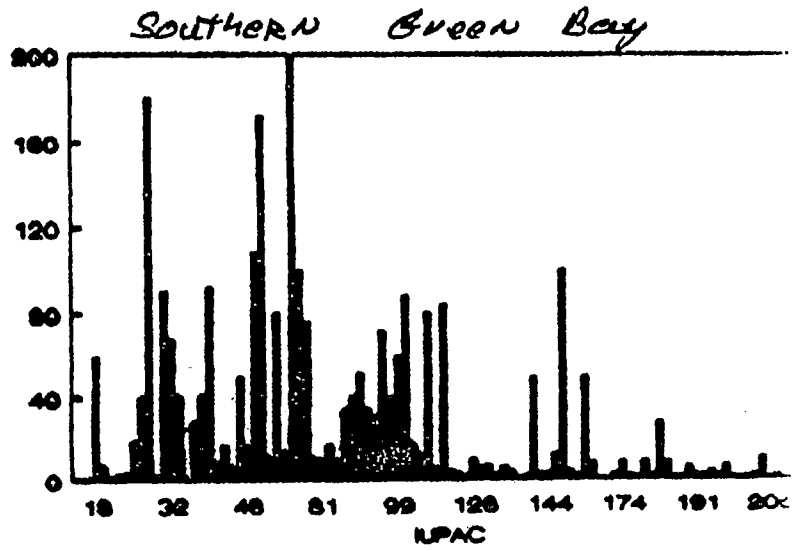
81
99
126
144
174
191
206
IUPAC


Southern Green Bay
200
160
120
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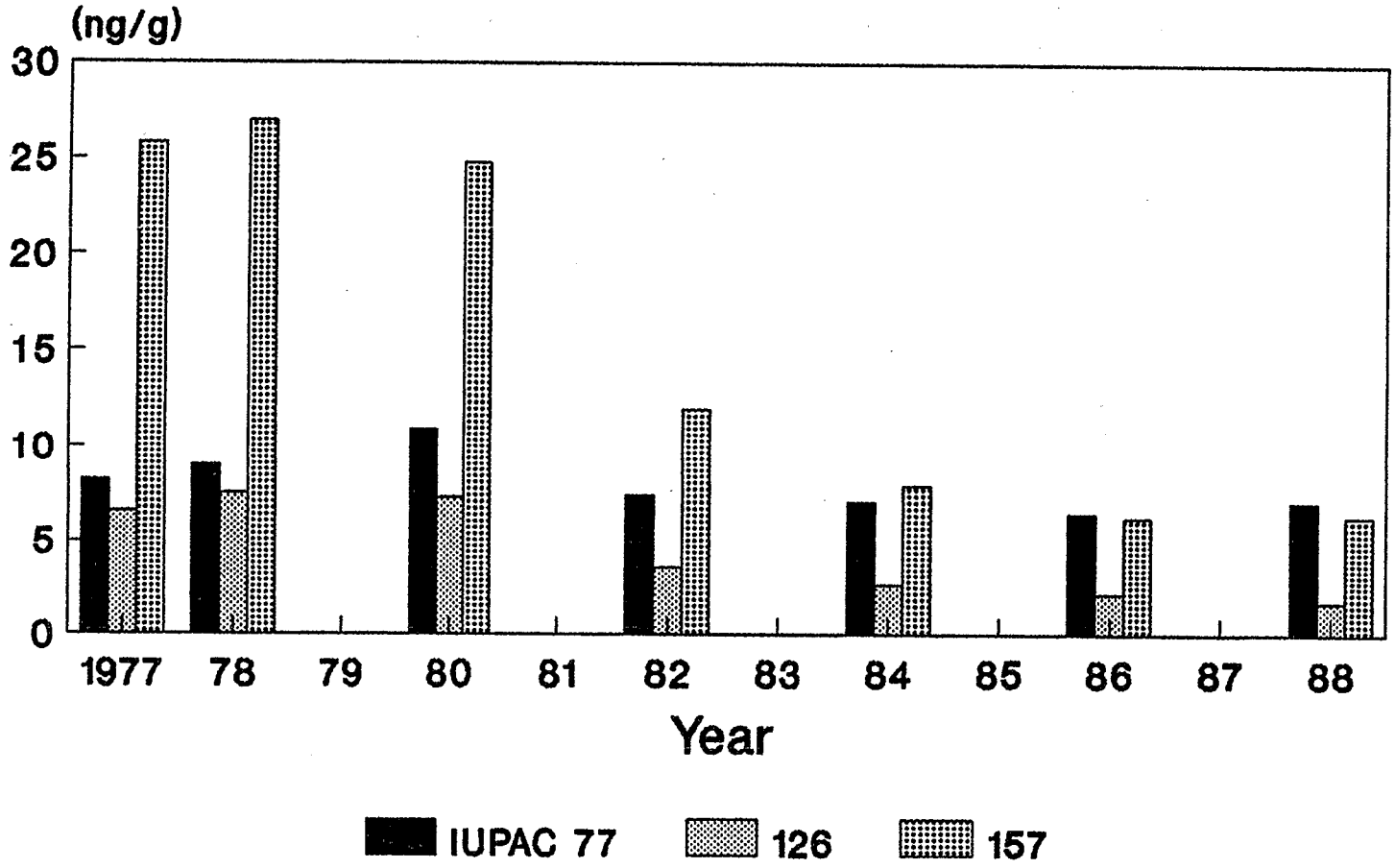
174
191
IUPAC

Fig 17

Lake Michigan Lake Trout
Planar PCBs



R. Hesselberg, USFWS

Fig 18

Total and Planar PCB Trends

Lake Michigan Lake Trout

Log #77	= 4.52 - .029(yr)	ns	r2=35%
Log #105	= 16.7 - .137(yr)	p<.01	r2=91%
Log #126	= 13.4 - .146(yr)	p<.01	r2=91%
Log #156	= 16.7 - .155(yr)	p<.01	r2=89%
Log #157	= 15.4 - .157(yr)	p<.01	r2=90%
Log Total PCB	= 12.6 - .132(yr)	p<.01	r2=88%

1977-1988

1.5 OVERVIEW OF PCB TOXICOLOGY

Michael Bolger, Chief, Contaminants Standards Monitoring and Program Branch, Center for Food Safety and Applied Nutrition, U.S. FDA, Washington, DC

The following is a brief presentation of the toxicology and hazard and risk of PCBs, with a focus on pharmacokinetics. PCBs, as a class, are highly lipophilic. Absorption of PCB congeners is determined by their relative lipophilicity and is dependent on the ability of PCBs to cross fatty membranes. Lesser chlorinated congeners are more readily absorbed. With increasing chlorination, congeners are more lipophilic; however, absorption decreases because viscosity increases, and solubility decreases, thus the congeners literally become stuck in membrane structures. Absorption of PCBs is greater orally than by the dermal route because of size and lipophilicity considerations. In terms of the absorption of PCBs via inhalation, very little work has been done. However, one would surmise that the same generalizations presented above would apply somewhat in the lungs.

After absorption, PCBs are distributed throughout the body by lipoprotein carrier molecules. Partitioning from the blood to the tissues occurs rapidly. Chronic exposure to PCBs results in concentrations in fatty tissues of the body. The most abundant storage site is the adipose tissue, followed by the liver and skin. The distribution of PCBs is modulated by body composition. That is, mobilization of storage depots occurs when fat stores are metabolized as is seen with reduction in body weight and lactation. Elimination of PCBs can occur both actively and passively. The major route of PCB elimination is dependent on metabolic changes that effectively increase water solubility and increase elimination. Direct oxidation, introduction of an oxygen molecule into the ring structure of PCBs, can also occur. Metabolism also occurs by the mixed function oxygenase (MFO) system. For example, the action of the MFO system results in the formation of an arene oxide intermediate which can be converted into dihydrodiol by epoxide hydrase. The arene oxide intermediate can also be converted into a phenol, which in turn can be conjugated with glucuronic acid. Further action by MFO can result in the formation of diols. The arene oxide intermediate can be converted via reduced gastrointestinal into a thioether, which is particularly important in terms of metabolism in the lungs. Finally, dechlorination, that is removal of the chlorine molecule from the ring structure, does occur. In passive elimination, diffusion occurs across the gastrointestinal wall, and partitioning into the sebum, sweat, or other bodily secretions including milk occurs with active elimination, molecule weight determines the route. In other words, smaller molecules will be eliminated via the urine, larger molecules via the feces. Metabolism is most effective in congeners with two adjacent, unsubstituted carbon atoms. Less chlorinated congeners are metabolized more rapidly than higher chlorinated congeners. Also, congeners with chlorine substituted on one ring are metabolized more rapidly than those with chlorines substituted on both rings. In active elimination, the most important step is the initial oxidative step by the MFO system which results in the formation of an epoxide intermediate. Dechlorination and direct insertion of hydroxyl groups occurs at the 3 and 3' position. One MFO enzyme is CYP1A, which is primarily induced by dioxin and related compounds that includes the coplanar PCBs, prefers the 2 or 2' ortho position. The other is CYP2B which is induced primarily by phenobarbital and related compounds and prefers the 4 or 4' para position. In terms of metabolic efficiency,

mammals are more efficient than birds, birds more efficient than fish, and within mammals, the dog is particularly efficient, more so than other mammals including humans.

With acute exposure to PCBs, a range of systemic effects can occur including effects on the liver, kidneys and gastrointestinal, or neurological system. The latter includes decreases in brain dopamine levels and changes in behavior. In rodents, adverse effects on male fertility and decreases in implantation and fetal weight and survival and decreases in weaning survival have been noted. With intermediate exposure—5 weeks to 8 months—such effects as thymic atrophy, decrease in natural killer cells, effects on lymph nodes, increase in rates of infection, and decreases in antibody levels have been reported. In the monkey, PCB exposure results in decreases in brain and hypothalamic dopamine, levels. Intermediate exposure in the rat results in thyroid, hepatic, skeletal, dermal, and cardiac effects and decreases in body weight. Developmental toxicity has been reported in the rat, rabbit, guinea pig, monkey, and mink, with increases in neonatal death, decreases in litter size, increases in fetal and neonatal deaths, and increase in resorption/absorption. For reproductive effects, several mammalian species show changes in the estrus cycle and decreases in rate of conception, reproductive rates, and litter size. With chronic exposure, the major effects include decreased survival, body weight gain, and spermatogenesis and dermal, hematological, gastrointestinal, and thyroid effects.

Studies of PCB structure-activity relationships (SAR), generally, have focused on the dioxin-like congeners that are non-ortho substituted. They bind with the AH receptor, which is an index of dioxin reactivity. The molecular structure is relatively flat with little to no rotation, resulting in a stacking type of interaction in the receptor binding domain. The interaction with this receptor eventually results in the expression of "a messenger RNA" which includes the activation of the MFO system. Thus you have a molecule that actually activates its own metabolism. The induction of various types of proteins are supposedly involved in the pleiotropic and/or the toxicological responses seen with dioxins and dioxin-related compounds. Chlorine substitutions in ortho substituted congeners tend to twist and bend the molecule making it less "dioxin like" and as a result binding with the AH receptor is poor, if at all. The binding interaction is known as "cleft-type" such as seen with the thyroxine carrier protein, prealbumin. T_4, which is structurally similar to the hormonal-like PCB congeners, has two ring structures which are juxtaposed 90 degrees to each other. The relevance of prealbumin binding is that this may prove useful in terms of a description of relative reactivity of the different PCB congeners, particularly the ortho-substituted congeners. This in turn could prove useful in the development of a toxicity equivalency factor (TEF) approach for "non-dioxin- like" PCB congeners which is important in that it is likely that the most persistent PCB residues found in human tissue will bind to prealbumin.

The SAR studies conducted on prealbumin binding indicate that laterally substituted PCB congeners have the greatest activity. In addition, at least one lateral substitution will result in prealbumin binding and ortho substitution does not diminish binding appreciably. Neither biphenyls or fully substituted congeners demonstrate any binding activity.

Recent work with coplanar PCBs suggests that the dioxin-like TEFs developed to date tend to overestimate the actual potency of the coplanar congeners, depending on the target tissue. It appears that the TEFs may be tissue-specific. The available SAR information on developmental neurotoxicity, suggests that a thyroid hormone antagonistic property is important and may prove useful in explaining the mechanisms of action of specific ortho substituted congeners. This anti-thyroidal activity, whether it occurs directly at the receptor through an alteration of thyroid metabolism or by changing the activity of the thyroid (T_3 or T_4) system, results is an alteration in neurotransmitter concentrations. There is even some speculation that a biochemical hypothyroid status at the cellular level occurs.

The SAR studies of the neurotoxicity of PCBs, clearly indicate the importance of specific molecular properties, specifically ortho or ortho-para substitutions. These studies show that activity is not related to cellular accumulation, hydrophobicity, or metabolism and that activity is related to prealbumin binding. The 2,2' substitution is more active than the 2,2',4,6,6' or the 3,5 substitutions where there is more lateral substitution and, with no activity seen with planar PCBs. It appears that these PCB congeners prefer the T_3 family of proteins and that they are thyroid hormone antagonists.

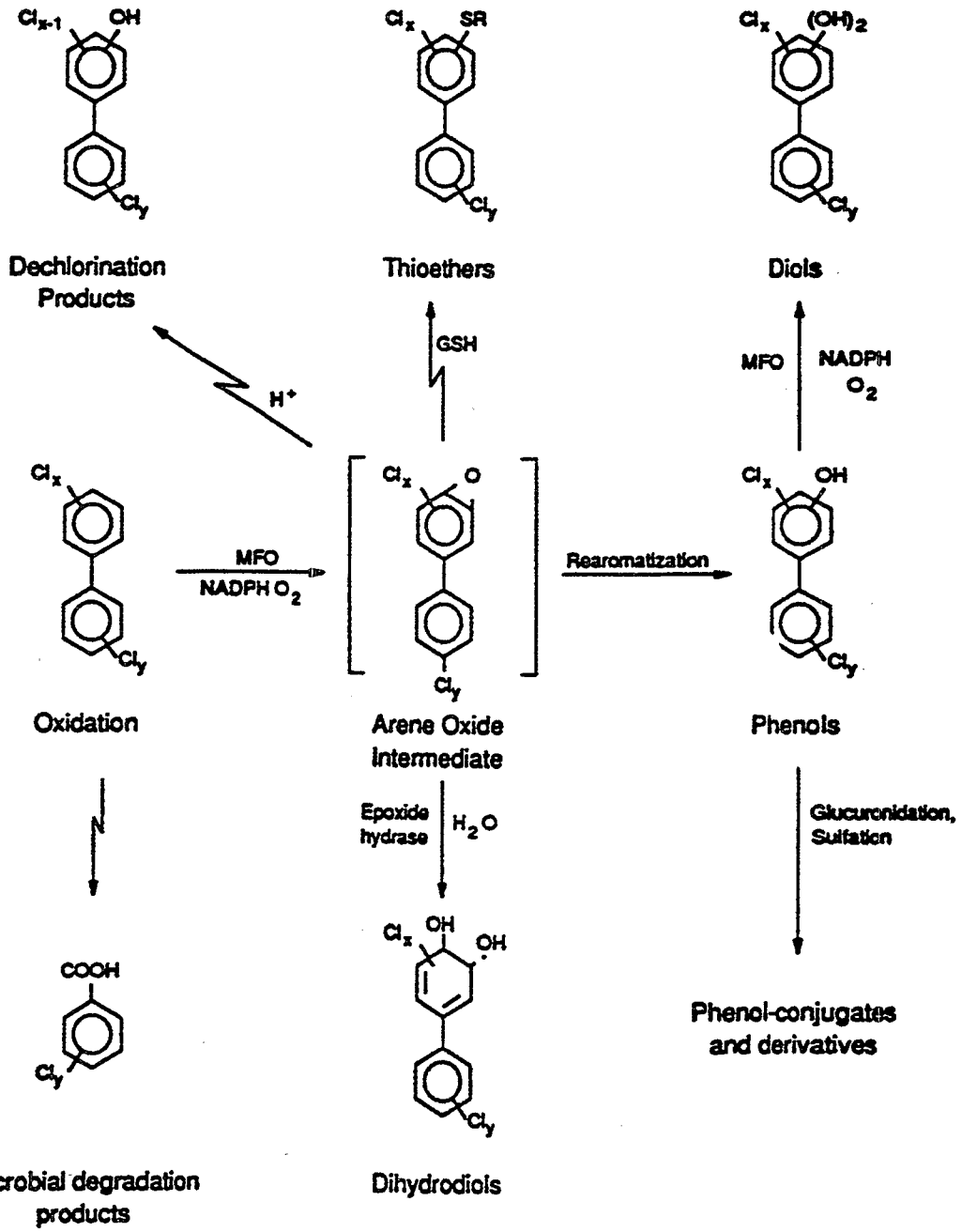
One of the mechanisms that has been suggested for the action of ortho substitution PCB congeners is an effect, on dopamine metabolism, which would explain some of the neuro-developmental effects seen in the rat or primate studies and possibly those observed in human studies. What has been determined to this point is that ortho substituted congeners (2,2' or the 2,2',4,6 congeners), which are non-planar, exhibit the greatest effects on dopamine content. Planar "dioxin-like" congeners exhibit no activity. Chlorination in the para position increases potency, whereas inversed congener chlorination is not correlated with reduced potency and complete chlorination substitution does reduce potency.

A review of what is known of the toxicity of PCBs indicates that doses, ranging from 0.01 to 100 mg/kg b.w./day result in a variety of adverse effects including, lethality, and gastrointestinal, hematological, developmental, immunological effects, and systemic cancer. The lowest observed effect level has been reported for an immunological end point which suggests that the immunological effect is a more sensitive end-point than cancer. However, this is somewhat misleading in that this could be an artifact of the quality of the studies. If additional carcinogenic bioassays of PCB mixtures were conducted, lower dose-response carcinogenic effects would probably be observed depending on the size of the study and particularly on the number of animals used in each study group. In addition, the methodology used to extrapolate the dose response information from animal studies to humans for cancer is inherently more conservative that the methodology used for non-cancer endpoints. This results in a lower risk number for cancer that it does for other end-points.

A range of reference doses (RfDs) for PCBs have been developed on the basis of several toxicological end-points which have been noted in animal studies. In terms of reproductive effects, decreased conception rate, and infant survival, the corresponding reference doses range from 2×10^{-2} to 1.4×10^{-4} mg/kg b.w./day. In terms of developmental toxicity, an RfD of 1.4

x 10^{-5} mg/kg b.w./day has been developed. The corresponding RfD for cancer risk at an upper bound estimate of 1 in a million is 1.3 x 10^{-7} mg/kg b.w./day. Thus, there is at least several orders of magnitude difference between the corresponding developmental and cancer risk reference doses. In terms of human studies, the RfDs developed from the no observed effect levels or estimated no observed effect levels and an uncertainty factor are about ten-fold greater than the corresponding RfD for the one in a million cancer risk.

In summary, based on the spectrum of toxicity of PCB mixtures and congeners, their pharmacokinetics, and structure-activity information, it appears that there are at least two general classes of PCBs, "dioxin-like" and "hormonal-like". A spectrum of RfDs has been developed that range from 10^{-2} to 10^{-7} mg/kg/day, depending on whether systemic, developmental, reproductive, immunological, or carcinogenic effects are the end-point of concern.



* Source: Safe 1984

PCB TOXICITY

Acute Exposure	Species	Effect	Exposure Duration	LOEL mg/kg/day
Death	rat	LD50	1x	1010
	mouse	LD50	2 wk	130
	mink	LD50	1x	750
Systemic	rat	hepatic, renal	1x	1.0 - 4000
	pig	GI	11 d	100
Neurological	rat	↓ brain dopamine, behavior	1x	500 - 2500
Developmental	rat	neurobehavioral, ↓ fetal weight and survival	10 d ges	4 - 15
		↓ weaning survival	9 d ges	100
	mouse	renal	1 d ges	244
	rat	↓ fetuses	9 d lac	8
Reproductive	rat	male fertility, ↓ implants	9 d lac	8

PCB TOXICITY

Intermediate Exposure

	Species	Effect	Exposure Duration	LOEL mg/kg/day
Death	rat	↓ survival	8 mo	72.4
	mouse	↓ survival	6 mo	48.8
	monkey	100% mortality	2 mo	4
	mink	↓ survival	8 mo	1.9
Immune	rat	thymus, ↓ natural killer cells	5 wk	10
	rabbit	thymus	8 wk	0.18
	g. pig	lymph nodes	8 wk	0.4
	mouse	↑ infections	5 wk	13
	monkey	↓ antibody levels	8 mo	0.1
Neurological	monkey	↓ brain, hypothalamus DA	5 mo	0.8

PCB TOXICITY

Intermediate Exposure	Species	Effect	Exposure Duration	LOEL mg/kg/day
Systemic	rat	thyroid, adrenal	5 mo	0.09 - 0.25
		hepatic	2 mo	0.30
		skeletal	10 wk	0.10
		↓ BW gain	5 wk	25
	mouse	hepatic	6 mo	4.9
		dermal	5 mo	26
	monkey	dermal, GI, hematopoietic	2 mo	0.1 - 4.0
		hepatic	7 mo	0.1
		cardiac	3 mo	12
	pig	GI, ↓ BW	3 mo	9.2
	mink	GI	8 mo	1.9
		↓ BW	28 d	1.8

PCB TOXICITY

Intermediate Exposure	Species	Effect	Exposure Duration	LOEL mg/kg/day
Developmental	rat	↑ neonatal death, ↓ motor function ↓ thyroid function	42 d	1.3 - 13.5
		↓ litter size	6 mo premat	1.5
		neurobehavioral, learning	21 d postnat	2
		hepatic	4 mo	1.5
		↓ pre-, post- weaning survival	1 mo	30
	rabbit	↑ fetal death	28 d gest	12.5
		hepatic	11 wk	28.0
	g. pig	↑ fetal death	43 d gest	2.5
	monkey	resorption, absorption	2 mo	4.3
		↑ fetal death	8 mo	0.1
	mink	↑ neonatal death	6 mo	0.18

PCB Toxicity

Intermediate Exposure

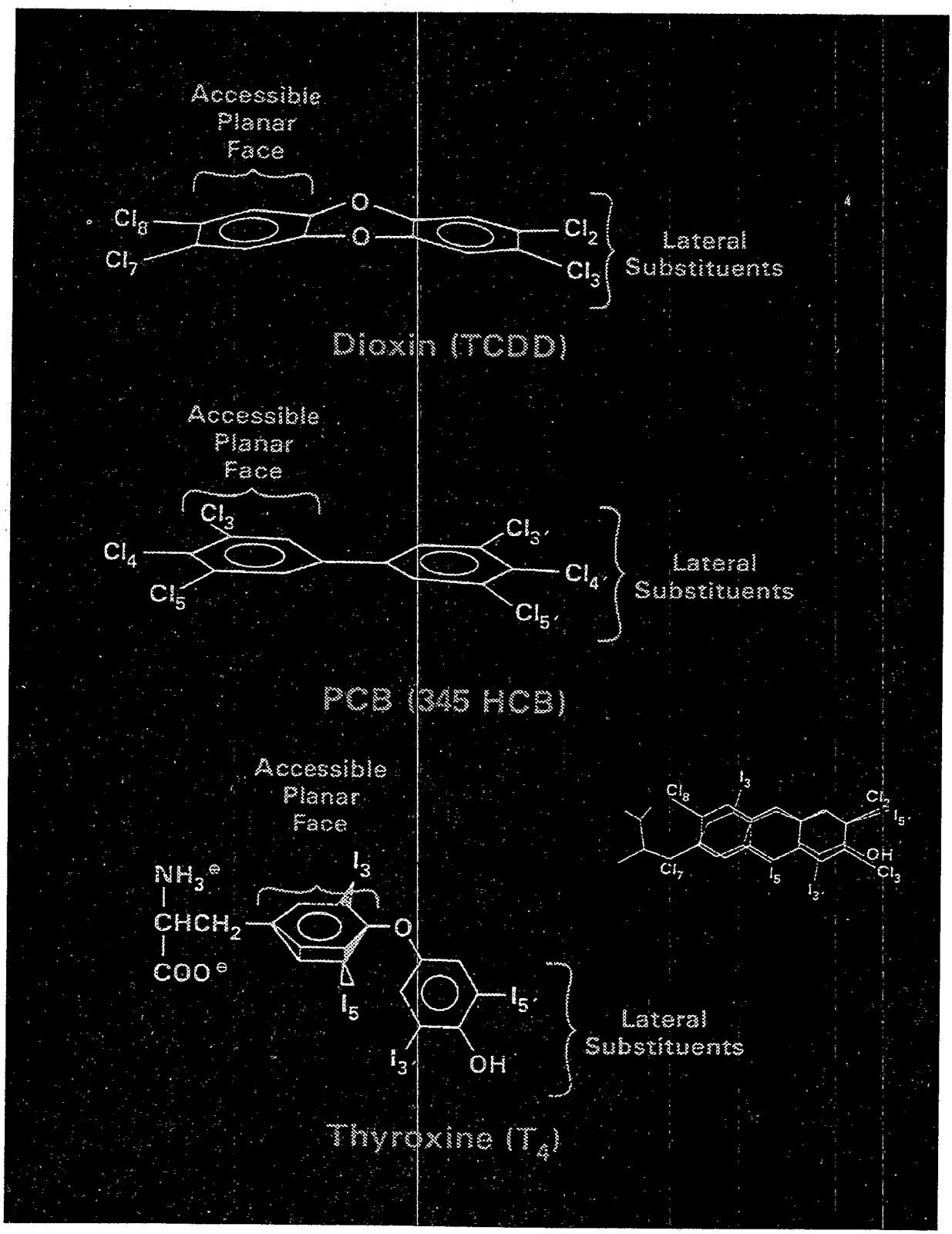
	Species	Effect	Exposure Duration	LOEL mg/kg/day
Reproductive	rat	estrus cycle, ↓ receptivity	1 mo	30
	mouse	↓ conception	4 mo	12.5
	monkey	menstrual cycle, ↓ conception	7 mo	0.1 - 0.2
	mink	↓ reproduction rates, ↓ litter size	9 mo	0.4

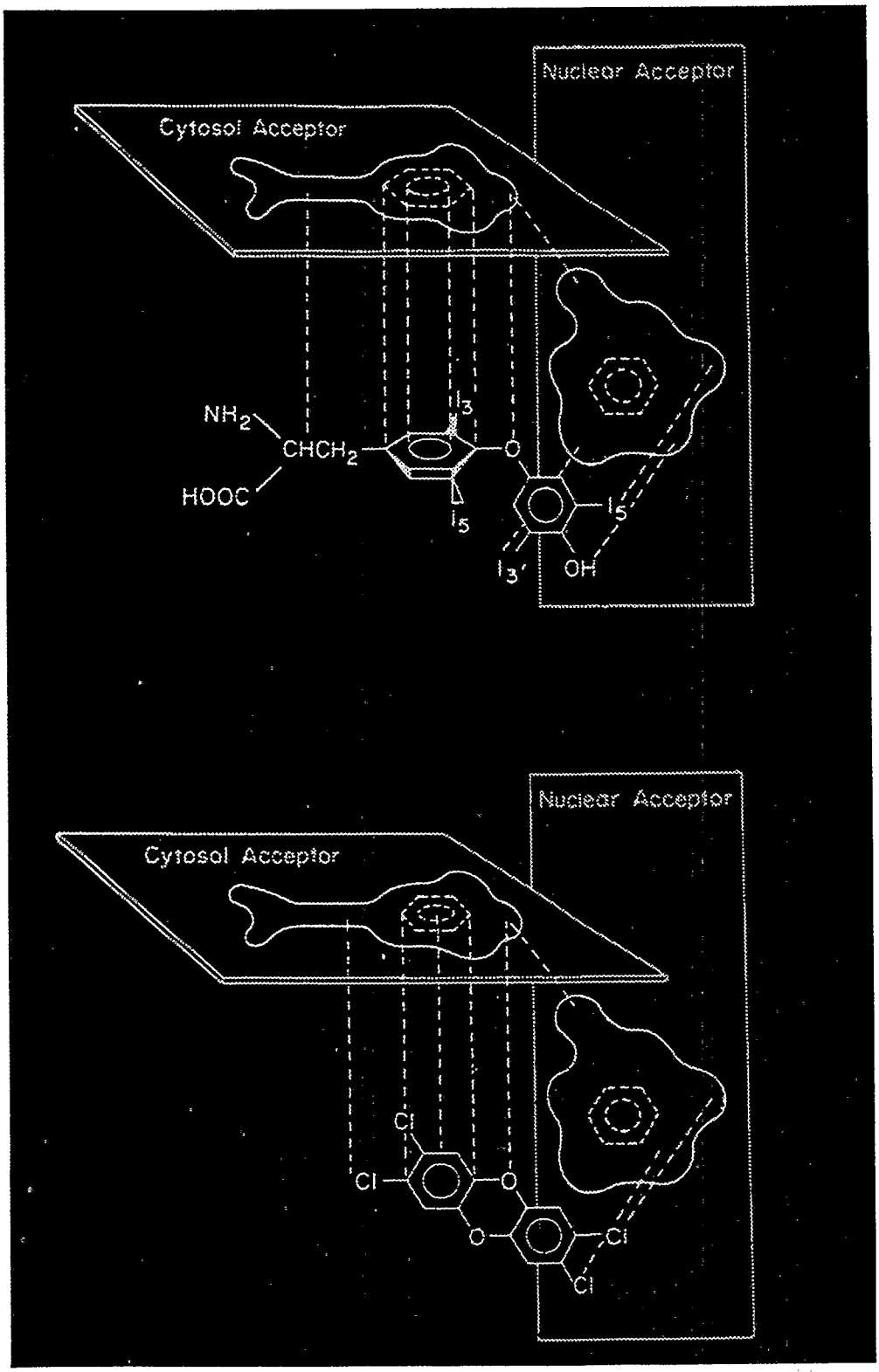
PCB TOXICITY

Chronic Exposure	Species	Effect	Exposure Duration	LOEL mg/kg/day
Death	rat	↓ survival	26 mo	2.5
Systemic	rat	dermal, ↓ BW gain	26 mo	1.25 - 2.5
	monkey	dermal, hepatic, thyroid, hematopoietic	12 mo	0.1 - 0.2
		GI, thyroid	28 mo	0.2
Immune	monkey	↓ antibody response	27 mo	0.005
Developmental	monkey	learning, memory, hyperactivity	16 mo	0.03 - 0.1
		↓ BW	12 mo	0.03
		↑ infant death	15 mo	0.1
Reproductive	monkey	↓ spermatogenesis	12 mo	0.1
Cancer	rat	liver	26 mo	1.25

COMPARATIVE TOXIC POTENCIES OF COPLANAR PCBs

Responses Subchronic toxicities	Target species/cell	ED_{50}/EC_{50} Values 3,3,4,4'-TetraCB	3,3',4,4',5-PentaCB	3,3'4,4'5,5'-HexaCB	2,3,7,8-TCDD
Body weight loss	Rat (umol/kg)	>500	3.3	15	0.05
Thymic Atrophy	Rat (umol/kg)	>500	0.95	8.9	0.09
Bursal lymphoid development	Chick embryo (ug/kg)	50	4	300	
Thymic lymphoid development	Mouse fetuses (M)	3×10^{-7}	2×10^{-9}	2×10^{-7}	2×10^{-10}
Immunotoxicity	Mice (umol/kg)				.0024
Tertatogenicity	Mice (umol/kg)			.055 - .110	.011


Accessible Planar Face
Cl8
Cl7
O
O
Cl2
Cl3
Lateral Substituents
Dioxin (TCDD)
Accessible Planar Face
Cl3
Cl4
Cl5
Cl3'
Cl4'
Cl5'
Lateral Substituents
PCB (345 HCB)
Accessible Planar Face
NH3⊕
CHCH2
COO⊖
I3
O
I5
I5'
I3'
OH
Lateral Substituents
Thyroxine (T4)
Cl8
I3
Cl2
I5'
OH
Cl3
Cl7
I5
I3'


Nuclear Acceptor
Cytosol Acceptor
NH2
CHCH2
HOOC
I3
O
I5
I5
I3'
OH
Nuclear Acceptor
Cytosol Acceptor
Cl
Cl
O
O
Cl
Cl

RECOMMENDED TEFs FOR VARIOUS CONGENERS AND CLASSES OF PCBs

Congener Class	*Relative Potency Range*	*Recommended TEFs*
3,3'4,4'5-PeCB	0.3 - 0.0006	0.1
3,3'4,4'5,5'-HCB	0.1 - 0.0012	0.05
3,3'4,4'-TeCB	0.02 - 0.000006	0.01
Mono-ortho Coplanar PCBs	< 0.005	0.001
Diortho Coplanar PCBs	~0.00002	0.00002
Others	-	?

Source: Safe, S. CRC Crit. Rev. Toxicol., 1990

1.6 PCB CRITERIA FOR WATER

Jennifer Orme Zavaleta, Drinking Water Health Assessment Section, Office of Science and Technology, Office of Water, U.S. EPA, Washington, DC

The Office of Science and Technology develops risk assessments for water contaminants. Within the Office of Science and Technology, there are several divisions, including the Engineering and Analysis Division, Health and Ecological Criteria Division, and the Standards and Applied Science Division. Within the Standards and Applied Science Division, the Risk Assessment and Management Branch evaluates risks associated with contaminated sediments and chemical contaminants in fish. Within the Health and Ecological Criteria Division, risk assessments for drinking water, ambient water, and sediment contaminants are developed. The Sludge Risk Assessment Branch, evaluates the disposal of municipal sewage sludge on land. In the Ecological Risk Assessment Branch, criteria, including those for PCBs, are being developed based on aquatic life and wildlife effects.

In the drinking water program, drinking water maximum contaminant level goals (MCLGs) and maximum contaminant levels (MCLs) are developed as well as some of the ambient water quality criteria (AWQC), specifically for the water and organisms and the organisms only. In developing the criteria, we regulate contaminants for drinking water that may have an adverse human health effect and that are known or anticipated to occur in water. This is done through a two-part process. The first part is developing an MCLG that represents a non-enforceable health assessment that would not be expected to have an adverse effect, and incorporates a margin of safety. This is similar to the ambient water quality criteria. The MCL, which represents the enforceable standard, is set as close to the MCLG as feasible, taking into consideration other aspects such as analytical methods, available treatment technologies, and costs. If a contaminant in water cannot be adequately monitored, then a treatment technique is established that would, more or less, remove the contaminant as much as possible from the water supply.

In comparison, AWQC are derived from an assessment that is based on the available scientific knowledge and reflects the identifiable health effects as well as the effects to ambient organisms found in water. In essence, this process involves an assessment of the entire ecosystem of which humans are considered a part of the system. The AWQC, like the MCLGs, are not federally enforceable, but unlike the drinking water program, the actual enforceable standard is developed by the states. They may adopt the AWQC values that EPA recommends, or they may develop their own criteria based on site-specific considerations. AWQCs that are developed as part of this program are developed for aquatic life and also for human health protection. In some of the comparisons with the surface water methodology for developing human health criteria, the process begins with a quantitative risk assessments for either the reference dose looking at non-cancer health effects or for the q_1^*, which represents a cancer potency factor looking at a quantitative estimate for excess cancer risk. These assessments, are then adjusted for a 70 kg adult and then divided by a number of other factors looking at water consumption, bioconcentration factor, and fish consumption.

In general, the water consumption rate used is 2 liters of water per day. This rate is used in the drinking water program in developing the MCLGs. One difference, though, is in looking at MCLGs, EPA assumes that water is being treated, which represents water that people actually drink. In the surface water program, the same value is used, but the 2-liter consumption rule may not be appropriate since people do not tend to drink 2 liters of untreated water per day. Thus, EPA will be reviewing the 2 liter water consumption factor for the AWQC.

EPA also will be looking at the bioconcentration factor, because currently, the bioconcentration factor only looks at the accumulation in a water medium. However, PCBs and other types of bioaccumulatives can accumulate in food materials. In addition, EPA also will be revisiting the assumed fish consumption rate of 6.5 grams per day, which is considered somewhat of a national average. However, in some areas, such as the Great Lakes or some of the coastal areas, people may have higher consumption, or there may be areas of the country where the consumption is actually lower. To give you an idea of where we might be going with some of these methodology changes, EPA recently sponsored a workshop last September (1992) and asked a number of experts to provide some indication of what the Agency should consider in revising these standards. One of the biggest changes focuses on the issue of how to allocate sources of exposure. In the drinking water program, sources are allocated to represent what stems from drinking water versus other sources. Similar in the surface water program, the bioaccumulation factor for drinking water will be reviewed. Specifically, EPA is developing what is called a reference residue concentration, which is a value that represents a reference dose, but subtracted or adjusted for sources of exposure other than fish consumption. Thus, the reference dose would be adjusted for the weight of the protected individual, generally considered to be an adult. However, for some contaminants, the protected individual also may be an infant or a child. Other sources of exposure would be subtracted such as dietary intake from foods other than fish. Inhalation may be a factor in some cases, particularly for volatile contaminants. In this general methodology, there are no established numbers yet, e.g., the standard weight and level of fish consumption have not been determined yet. Thus, EPA is looking into additional information. Other factors, such as the dietary intake and the water mass, will all be specific to the individual chemicals that will be reviewed. Once the residue concentration has been developed, the water quality criteria would be developed by dividing with a bioaccumulation factor.

For PCBs in drinking water, an MCLG of zero has been established. For both the surface water and drinking water program, there are clauses within the Clean Water Act or the Safe Drinking Water Act that indicate that, for contaminants that do not show a threshold of effect or that may be carcinogenic, the level is set at zero. Ideally, the public does not want carcinogenic substances in its drinking water, in fish, or in other materials that may be consumed. This, however, is a somewhat unrealistic goal, because it may not be possible to measure values that low or treat down that low. Thus, the MCL is set as close to zero as feasible and is usually restricted to analytical methods availability or achievability. In the case of PCBs, the MCL was set at 0.5 ug/L, and this was largely restricted to the analytical method capability. In this particular standard, it represents the whole mixture of 209 possible congeners. Again, this was restricted by available analytical methods, looking at somewhat of a fingerprint

assessment in monitoring PCBs in drinking water.

On the ambient water side, ideally, the criteria for human health would be set at zero. However, this would not be very helpful to the state standards program developing their standards. For that reason, the cancer potency factor was used in trying to determine the criteria for PCBs. Using the old 1980 methodology, the values that were derived for human health are specific to the Aroclors 1016, 1021, 1232, 42, 48, 54, and 60, resulting in a value of 0.000044 ug/L, which includes consumption of water and organisms. In the organisms only value, also based on the cancer potency factor, the value resulted in a slightly different value of 0.45 ug/L. The aquatic life criteria for PCBs were developed for both fresh water and marine water, although they were experimentally determined, the values have been reported for an acute response in fresh water as 2 ug/L and a value of 0.014 ug/L for a chronic value. In the marine systems, the risks do not appear to be quite as sensitive with an acute risk of 10 ug/L and a chronic risk of 0.03 ug/L.

Back in 1980 when the original human health criteria for PCBs was determined, EPA used a bioconcentration factor that was estimated from the log K_{OW}, which resulted in a value of 31,200. Since then, a bioaccumulation factor that focuses not just on water but also considers accumulation in food materials and has been normalized to represent a 5 percent lipid content in the trophic level remains to be determined. This will result in a considerable difference from what was used in 1980 and results in a BAF value of roughly 1,700,000. For the wildlife values, a slightly higher lipid content is used, and will result in a bioaccumulation value of 969,000 in trophic level 3 versus 2,800,000 in trophic level number 4. The Great Lakes initiative package was just released for public comment not too long ago, and these are some of the issues EPA will be accepting comments on to see how the Agency is going to change the criteria and whether this particular methodology makes sense for the future.

Some of the other criteria that have been developed include recommendations from the National Academy of Sciences. They were looking at water exposures only and developed what is called suggested-no-adverse-response levels, which focus on the non-cancer health effects. For a 1-day acute exposure for humans, they recommended that a value of 350 ug/L would not present an adverse health effect. A slightly lower value of 50 ug/L would be acceptable over a 7-day exposure. NIOSH and OSHA also have developed some short-term values looking at the inhalation route of exposure, again focusing on carcinogenicity as the main end point for the NIOSH value. These agencies arrived at a reliable exposure level of 0.001 mg/m^2. OSHA focused mainly on skin toxicity as their end point in determining their short-term effects and ended up with values of 1 mg/m^2 for chlorodiphenyls containing 42 percent chlorine, and for those containing 54 percent chlorine, recommended a value of 0.5 ug/m^2.

Human Health Methodology

- Current Surface Water Methodology

$$\frac{(\text{RfD}) \text{ or } (q_1^*) \times 70 \text{ kg}}{(2 \text{ L/d}) + \text{BCF}) \times (6.5 \text{ g fish})}$$

- Current Drinking Water Methodology

$$\text{MCLG} = \frac{\text{RfD} \times 70 \text{ kg}}{2 \text{ L/d}} \times \text{RSC}$$

$$= \text{zero for non-threshold contaminants}$$

Develop fish tissues residue and water column concentration criteria

$$\text{RCC} = \frac{(\text{RfD} \times \text{WT}) - (\text{DT} + \text{IN} + \text{WM})(\text{WT})}{\text{FC}}$$

where:

RRC	=	reference fish tissue residue concentration
RfD	=	reference dose
WT	=	average human body weight
DT	=	dietary intake other than fish
IN	=	inhalation
WM	=	water mass intake
FC	=	fish consumption

$$\text{WQC} = \frac{\text{RRC}}{\text{BAF}}$$

where:

WQC	=	water quality criteria
RRC	=	reference fish tissue concentration
BAF	=	bioaccumulation factor

Drinking Water Criteria

For PCBs, EPA set an MCLG of zero based on carcinogenicity in animals.

MCL of 0.0005 mg/l was set considering analytical methods.

10^{-4} to 10^{-6} excess cancer risk = 0.0005 to 0.000005 mg/l.

This regulation treats PCBs as a mixture of 209 possible congeners.

Ambient Water Quality Criteria (continued)

Aquatic Life Criteria for PCBs

Acute Fresh Water	2 ug/l
Chronic Fresh Water	0.014 ug/l
Acute Marine	10 ug/l
Chronic Marine	0.03 ug/l

Human Health Criteria

(Aroclor 1016, 1021, 1232, 1242, 1248, 1254, 1260)

Water and Organisms	0.000044 ug/l
Organisms	0.000045 ug/l

Bioconcentration/Bioaccumulation Factors for PCBs

Water Quality Criterion BCF for PCBs (U.S. EPA 1980)

Based on a predicted BCF estimated from a log K_{ow}

Human Health BCF: 31,200

Great Lakes Initiative BAF for PCBs (U.S. EPA 1993)

Based on a measured BAF derived from field data for "total PCBs"

Human Health BAF at 5% lipid for Trophic Level 4: 1,776,860

Wildlife BAF at 7.6% lipid for Trophic Level 3: 969,239
Trophic Level 4: 2,807,439

Other PCB Criteria

- National Academy of Sciences:

  One Day SNARL = 350 ug/l;
  Seven Day SNARL = 50 ug/l

- NIOSH RELs: Chlorodiphenyl = 0.001 mg/m^3 (carcinogenicity)

- OSHA PELs and ACGIH TLVs:

  Chlorodiphenyl (42% chlorine) = 1 mg/m^3
  (54% chlorine) = 0.5 mg/m^3
  (based on skin toxicity)

1.7 SUMMARY OF QUESTIONS AND RESPONSES[2]

1.7.1 Dan Thomas of the Great Lakes Sport Fishing Council commented on the release of a recent study that was conducted by the University of Wisconsin by Darr, Keneric, and Anderson. He questioned why some of the information in this study was not given by the presenters.

Dr. Bolger indicated that the report had just been released and that there was not enough time to incorporate the report into the slides. He described the study which observed the reproductive outcome in women who were consumers of Great Lakes' fish. Dr. Bolger stated that, contrary to the negative correlations that had been found in other studies, this study actually showed a positive correlation between women who had consumed Great Lakes' fish and their reproductive outcome. In other words, the study found that the higher the PCB body burden in the mother, the heavier the child was. Dr. Bolger stated that this finding is therefore, contrary to what has been reported in other epidemiological studies of populations in the Great Lakes.

Dave De Vault stated that he believed that the results were actually not contrary to what has been reported in other studies. He stated that in comparing the exposures in the recent study and in some of the earlier Michigan studies, the "high exposures" in the recent study are probably close to or perhaps even lower than the what was considered a "low exposure" dosage in the previous Michigan studies. Mr. De Vault referred to the tissue concentrations in the fish tissues.

Dr. Bolger responded that the way fish consumption was estimated for some studies (such as in the Jacobson study) made accurate correlations difficult. He stated that the most accurate method to develop correlations is to compare the PCB levels in the blood with the levels in maternal cord levels.

1.7.2 Dr. Heraline Hicks of the Agency for Toxic Substances and Disease Registry (ATSDR) in Atlanta, Georgia, asked Mr. De Vault whether he knew what source was contributing to the increase in PCB atmospheric deposition in the Great Lakes region.

Mr. De Vault stated that EPA does not know the source at this point. He stated that the apparent increase is in the southern Lake Michigan area. Since this is one of the most highly industrialized areas in the country, there are numerous potential sources. EPA is attempting to locate the source(s).

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[2] Ed. note: The question and response portion includes summaries derived from transcribed conversations. The summaries have been carefully edited to present the discussion as accurately as possible. However, these question and response summaries have not been reviewed by the speakers--unlike the proceeding abstracts.

1.7.3 Dr. Heraline Hicks of the Agency for Toxic Substances and Disease Registry (ATSDR) offered a comment to the panel and audience. She stated that ATSDR has recently initiated a research program, mandated by Congress under the Great Lakes Critical Programs Act of 1990, to look at human health impacts from pollutants in the Great Lakes area. For FY 92, ATSDR received $2 million for the research program. For FY 93, ATSDR received $3 million and it anticipated an additional $3 million in funding for FY 94. Thus far ATSDR has funded nine research proposals in the Great Lakes area, which examine human epidemiological effects from consumption of Great Lakes fish. She stated that seven of the eight Great Lakes States were involved in this research program; five of those seven states represent a consortium of Great Lakes State health departments. ATSDR studies encompass several issues (e.g., reproductive, developmental end points, immunological end points, neuro-behavioral, and also long-term health effects such as cancer). Dr. Hicks concluded by inviting other participants to see her for additional Great Lakes information.

1.7.4 Jennifer Orme Zavaleta of EPA asked Dr. Hicks whether the ATSDR-sponsored studies were measuring blood serum levels and adipose tissue in the subject cohorts.

Dr. Hicks confirmed that the studies would be examining adipose tissues as well as blood serum levels in the individuals. She stated that the studies will be looking both established and new population cohorts in the Great Lakes area.

1.7.5 Dr. Bolger asked Dr. Hicks if total PCBs or individual congeners will be studied in the ATSDR-sponsored studies.

Dr. Hicks stated that ten persistent toxic substances of concern in the Great Lakes had been identified. All nine grantees for FY 92 are examining PCBs as well as other persistent toxic substances (e.g., mercury, lead, dioxin, furans, mirex, and others). She stated that the grantees are looking at total PCBs as well as coplanar and non-coplanar PCBs.

1.7.6 Ram Tripathi from the Virginia Department of Health asked Jennifer Orme Zavaleta why there are such discrepancies between the drinking water maximum contaminant level (MCL) and the surface water ambient water quality criteria for PCBs.

Ms. Zavaleta stated that the difference can be attributed to the fish consumption factor and the bioconcentration factor that were used in deriving the surface water value. For the drinking water MCL value, although the goal for PCBs was set at zero, the standard was set after considering analytical methodology. Thus, she continued, the main difference is because of two different methodologies. For example, the surface water program incorporates bioconcentration and fish consumption factors, whereas in the drinking water program, only water consumption was examined and then adjusted for sources of exposure other than drinking water.

PART TWO
PCB TOXICITY AND HEALTH EFFECTS

2.1 REGULATORY UPDATE: HUMAN CARCINOGENICITY EFFECTS

Jim Cogliano, Chief, Carcinogen Assessment Statistics and Epidemiology Branch, Office of Research and Development, U.S. EPA*, Washington, DC

Studies on the potential carcinogenicity of PCBs are easier to describe than to interpret. Aroclor 1260 causes liver carcinomas in three strains of rats. Aroclor 1254 causes liver tumors in mice and rats; the tumor incidences appear to be lower than with Aroclor 1260. Less chlorinated mixtures have not, in general, been adequately tested. Worker exposure to mixtures with between 42 and 54 percent chlorine have been associated with some elevations in cancer, but there has been no consistent overall pattern.

At the root of the difference of opinion about the potential carcinogenicity of PCBs is a discussion of how to characterize the PCB mixtures that humans are exposed to. Alternative ways of characterizing PCBs include: total PCBs; characterizing mixtures as being similar to particular Aroclors; using percent chlorine as an index of toxicity; focusing on individual congeners; considering classes of congeners, using toxicity equivalence factors based on dioxin-like activity; or using toxicity equivalence factors based on other modes of action. Adequate toxicity information does not exist for any of these characterizations of PCB exposure; hence, substantial uncertainty will remain whatever measure is chosen.

In recent years new information is available to refine the cancer risk characterization of PCBs. The rat liver pathology was reviewed by a pathology working group; its findings have reduced the observed tumor incidences somewhat. A partial lifetime study in rats showed that lifetime exposure is not necessary for the induction of precancerous lesions. Initiation-promotion studies have been conducted for a few specific congeners; four congeners have shown promoting activity, and one of these has also shown weak initiating activity. New epidemiologic studies are available and have led to differing interpretations. EPA's Risk Assessment Forum considered the question of developing toxicity equivalence factors for PCB congeners, but concluded that there was more than one mechanism involved and that development of toxicity equivalence factors would be less straightforward for PCBs than for dioxins and furans.

In recent years there has been a greater realization that the transformation of PCBs in the environment is important to an accurate characterization of the risk to human health. The congeners are affected differently, depending on the number and the position of the chlorines

* The views expressed in this paper are those of the author and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency.

in a PCB molecule. The transformation of PCBs in the environment has the consequence of partitioning the original mixture so that substantially different fractions appear in air, water, soil, and sediment. These fractions may be more or less chlorinated than the original mixture, with a different distribution of congeners. Bioconcentration of PCBs in living organisms results in the retention of higher-chlorinated fractions.

Thus, the uncertainty in cancer risk characterizations is likely to remain in the foreseeable future. While toxicity information exists on some commercial PCB mixtures and on a few specific congeners, human exposure is not to these mixtures, but to residual mixtures that are weathered by years of environmental transformation and bioaccumulation.

Cancer Data on PCBs

- Aroclor 1260 causes liver carcinomas in 3 rat strains
- Aroclor 1254 causes liver tumors in mice and rats, apparently is less potent
- Clophen A30 (a 42% mixture) causes liver tumors in rats
- Worker exposure to 42-54% mixtures associated with some elevations in cancer, but no consistent pattern
- Carcinogenicity depends somehow on congeners

Current PCB Risk Assessment

- PCBs are classified as probable human carcinogens (Group B2) - available on IRIS
- 7.7 per mg/kg-d average lifetime exposure is a plausible upper bound for the increased cancer risk

Criticisms of the Current PCB Risk Assessment

- PCBs differ widely, but one assessment applies to all
- Common criticisms: choice of data set, inclusion of benign tumors, use of surface-area scaling, upper bounds, ...
- Some prefer a cancer assessment for each Aroclor
  - "Only 1260 is carcinogenic, others have no risk"
  - "Unit risk from less-chlorinated mixtures <7.7"
  - "All studies together show unit risk from 1260 <7.7"
- Some have advocated a TEF approach, based on congeners
- Some assessments are based on what had been released; others, on what is present now

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What New Carcinogenicity Data are Available?

- GE/IEHR review of rat liver pathology
  - Tumor incidences reduced slightly
  - Statistical significance for 60% mixtures only
- New initiation-promotion studies on specific congeners
  - Promoting activity with 2,2',4,5'-TCB, 3,3',4,4'-TCB, 2,3,4,4',5-PCB, and 2,2',4,4',5,5'-HCB
  - Weak initiating activity with 2,2',4,5'-TCB
- Partial-life study of Aroclor 1260 in rats
- New epidemiologic studies

Uncertainty in Quantitative Risk Estimates

- Toxicity data are on commercial PCBs and some congeners
  - Less-chlorinated mixtures appear to be less potent
  - Less-chlorinated congeners can be strong promoters
- Exposure is to residual PCBs weathered by years of environmental transformation and bioaccumulation
  - Not what had been released
  - Not what has been tested
  - Some congeners are enhanced 100-fold
- PCB risk are expected to vary, but we can't say by how much

2.2 REGULATORY UPDATE: NON-CARCINOGENIC EFFECTS

John L. Cicmanec, Veterinary Medical Officer, Systemic Toxicants Branch, Environmental Criteria Assessment Office, Office of Research and Development, U.S. EPA, Washington, DC

The health effects of Aroclors, commercial PCB mixtures that were produced in the United states, have been extensively tested in a wide variety of laboratory animals species. The evaluation of the health effects is complicated by the fact that each commercial mixture is made up of many congeners and ultimately the adverse health effects of a mixture depends upon the toxicity of the individual congeners of that mixture. To date, only limited information is available for toxicity studies of individual congeners. I have chosen to present this summary of the laboratory studies on the basis of individual target organs with some comparisons being made between species and between various commercial mixtures. More than 50 reports of animal studies of PCBs are added to the literature each year so this might provide an indication of the volume of material that is being summarized.

General Acute Toxicity

This information is presented only to give a comparative overview for different commercial PCB mixtures and for different animal species for which LD-50 data are available.

Rat	1,010 mg/kg	Aroclor 1254
Rat	4,250 mg/kg	Aroclor 1242
Mink	750-1,000 mg/kg	Aroclor 1221
Rhesus monkeys	4 mg/kg 60 days	Aroclor 1248

Gastrointestinal Effects

The ability of PCB mixtures to induce gastric ulcers is fairly well known. Studies in domestic swine by Hansen indicate that doses of 100 mg/kg-day of Aroclor 1254 caused gastric ulcers within 11 days of treatment. Studies with rhesus monkeys and pig-tailed macaques have shown that 4 mg/kg-day of Aroclor 1248 caused gastric ulcers within 2 months in four subjects and Becker reported induction of gastric ulcers with Aroclor 1242 at doses of 10 and 30 mg/kg-day. Studies with mink have shown consistent induction of gastric ulcers with Aroclor 1016, 1242, and 1254 within 90 days at doses lower than 50 mg/kg-day.

Hematopoietic Effects

Regarding adverse toxicological effects upon the blood-forming organs, consistent changes have been observed in macaques but not in rodents or mink. Anemia induced by Aroclor 1248 and

Aroclor 1254 is reported to occur at doses as low as 4 mg/kg-day and abnormal changes are observed as early as 60 days. These changes are characterized by up to 20% reduction in hemoglobin concentrations and packed cell volumes. Increases in reticulocyte counts are also observed. In a chronic study with rhesus monkeys, anemia was observed at a dose level of 0.2 mg/kg-day with Aroclor 1254. In this study, reported by Arnold, changes were first seen at this low dose 12 months into the study and these changes persisted to the end of the study at 28 months. In addition to anemia, hematologic changes that have been observed in long-term studies in rats and monkeys generally show an increase in total neutrophil counts and a decrease in lymphocyte counts.

Hepatic Effects

Perhaps the most consistent, and surely most thoroughly documented, toxic manifestations of PCB administration are for the liver. One of the most characteristic features of PCBs is their ability to induce hepatic microsomal enzymes (cytochrome P-450 of various groups) and it is likely that the development of more serious liver changes are an extension of this process. It has been postulated that the sequence of cellular change progresses from microsomal enzyme induction to hepatocellular damage to grossly observed hepatic enlargement to lipid deposition to fibrosis and finally focal hepatic necrosis. These microscopic changes are accompanied by changes in serum chemistry. Alterations in blood cholesterol levels (both increases and decreases) and vitamin A metabolism have been documented. Examples of significant liver changes involve both short-term and chronic studies. In a study reported by Buckner, Aroclor 1254 administered at the dose of 1 mg/kg-day induced elevated serum cholesterol levels within 4 days. When studies were extended to 3-8 weeks duration, an increase in total hepatic lipids with a decrease in hepatic cholesterol and a decrease in hepatic vitamin A concentration was observed. The lowest concentration that significant hepatic effects have been noted in rats for PCBs is 0.3 mg/kg. A similar pattern of microscopic liver lesions have been observed in rabbits dosed with Aroclor 1254 for 8 weeks at 2.1 mg/kg.

A pattern that will be emphasized throughout this presentation is that non-human primates are more sensitive to the toxic effects of PCBs that rodents and other conventional laboratory species. Effects upon the liver provide ample evidence of this. Perhaps most striking are the results reported by Allen and Barsotti in which two female rhesus monkeys that were dosed with Aroclor 1248 at 0.1 mg/kg died after 173 days and 310 days of the study. At necropsy, the most significant lesions noted were fatty accumulation within the liver and extensive focal necrosis. Similar hepatic effects were reported by Tryphonas in which rhesus monkeys showed fatty degeneration of the liver and focal necrosis as well as hypertrophic and hyperplastic changes.

Dermal and Ocular Effects

Changes noted in the skin and structures adjacent to the eye are among the most significant changes associated with PCBs. These lesions are of particular importance because the effects noted in animals, particularly non-human primates, have been directly associated with effects

directly attributable to PCBs noted in occupational exposures of humans. Studies with Aroclor 1248 and 1254 with rhesus monkeys provide the most detailed reports of the dermal changes. Specifically, facial edema most commonly observed in periorbital regions is accompanied by a purulent ocular discharge, swelling of the Meibomian glands, regional alopecia, and folliculitis of dermal sebaceous glands. If exposure persists, loss of fingernails occurs as well as gingival hyperplasia and dermal effects can progress to regional necrosis of the skin. These changes are consistently observed in Old World monkeys dosed with Aroclor 1248, 1242, and 1254 at levels as low as 0.1 mg/kg. The changes are observed as early as 2 months. Once dosing stops these effects are reversible.

Although dermal effects are not as thoroughly documented in rodent studies, erythema and altered sebaceous gland function has been observed in mice treated with Aroclor 1254 at doses of 26 mg/kg. Dermal and ocular effects observed in rats treated with Aroclor 1254 include alopecia, facial edema and exophthalmos.

Thyroid Effects

Initial reports of the effect of PCBs upon the rat thyroid were made by Byrne in which SD rats receiving 2.5 mg/kg (a relatively low "rodent" dose) of Aroclor 1254 exhibited reduced T-4 serum levels accompanied by enlargement of the thyroid, follicular cell hyperplasia, and the accumulation of colloid droplets. These changes were observed as early as 7 days of treatment and a subsequent study in rats noted similar changes at a dose of 0.09 mg/kg after 35 days of treatment. Similar changes have been noted for rhesus monkeys that received 0.2 mg/kg of Aroclor 1254 that were examined after 28 months of treatment. The authors believe that these effects may be reversible.

Adrenal Effects

The most extensive amount of data regarding the effects of PCBs upon the adrenal gland are available from studies with rats. Both Aroclor 1248 and 1254 cause an increase in corticosterone levels, the most biologically active adrenal steroid in rats. These changes were noted after 20 to 70 days at relatively low doses of 15 and 35 mg/kg. The effects upon the adrenal gland are felt to be particularly significant because chronic studies in which much lower doses (0.05 mg/kg) of two lesser chlorinated PCBs Aroclor 1242, and 1221 caused similar changes. No adrenal gland effects were observed in studies with rhesus monkeys that were dosed with Aroclor 1254 for periods exceeding 22 months. Adrenal gland histology was normal, and normal blood steroid levels were noted during the study.

Generalized Effects

A pronounced reduction in body weight for long term studies has been observed in rats, mink, pigs, and rhesus monkeys treated with PCBs. Some investigators have described the effect as a wasting syndrome in which for studies lasting more than 1 year the lack of body weight gain when compared to control animals ranged from 15 to 20%.

Immunologic Effects

The initial reports of immunologic effects of PCBs were made by Loose (in mice) and Thomas and Hinsdale (for mice and rhesus monkeys) in 1978. The reports by Loose described a reduction in immunoglobulins of BALB/c mice that had received 22 mg/kg of Aroclor 1242 for 3-6 weeks. Perhaps greater biological significance can be given to the results of increased mortality among PCB-treated mice that were challenged with Salmonella endotoxin and the malarial parasite, *Plasmodium berghei*. Earlier studies in rhesus monkeys showed a reduction in the antibody response to sheep RBCs when the monkeys had been treated with Aroclor 1248 (0.2 mg/kg) for 11 months. Interestingly, the response to tetanus toxoid was not altered by PCB treatment. A consistent response has been observed in all rat studies in which immunologic end points were observed. There is a significant reduction in the weight of the thymus gland when rats are treated with Aroclors 1248, 1254, or 1260 for 6 weeks. The most extensive study of the immunologic effects of Aroclor 1254 has been recently reported by Tryphonas, *et al.* For monkeys receiving 5 to 80 micrograms/kg after 23 to 55 weeks a reduction in IgG and Ig M specific for Sheep RBCs was noted as well as a reduction in T-helper lymphocytes. However, there was not a significant reduction in titers to pneumococcus vaccine in treated monkeys when compared to the control group and the monkeys did not show evidence of microbial infection at any time during the study. The authors describe these changes collectively as immunomodulation.

Neurologic Effects

Through quite important I will discuss only briefly the neurologic effects in monkeys described by Seegal's group in New York in which reduced concentrations of dopamine, an important neurotransmitter in selected regions of the cerebrum. It is quite interesting that these changes were associated with less-chlorinated congeners of PCBs and the changes were noted a long time after dosing had been completed.

Developmental Effects

Perhaps some of the most significant adverse effects of PCBs are developmental changes reported in rhesus monkeys. Barsotti, Allen, and others have reported the occurrence of reduced birth weights in infants born to dams treated with Aroclor 1248. In addition to the smaller body size, the infants also exhibited facial acne, swollen eyelids, the loss of eyelashes, and skin hyperpigmentation. Rhesus monkey dams that received Aroclor 1016, a lesser chlorinated PCB, also gave birth to smaller infants but the only clinical signs these infants exhibited was a skin discoloration at the hairline of the face. Once the infants were weaned, these clinical signs disappeared. The Lowest Observed Adverse Effect doses administered to the dams were 0.03 mg/kg-day of Ar 1016 and 0.1 mg/kg of Aroclor 1248. Some of the affected infants died at 44 to 329 days of age and lesions noted at post mortem examination were small spleens, rudimentary thymuses, and hypocellular bone marrow. To demonstrate the effect of residual PCBs in the tissue of rhesus monkey dams, the females were rebred 6 months after PCB dosing had ceased and the second group of infants also exhibited reduced birth weights and skin

discoloration as well as thymic and splenic atrophy and hyperplastic gastritis.

Realizing the significance of the general toxicity exhibited in the infants, investigators at the University of Wisconsin performed neurobehavioral tests upon the infants at the age of 14 months and 4 and 6 years. The infants from mothers treated with Aroclor 1248 showed decreased performance in discrimination learning tasks. These deficits are indicative of residual toxicity since tissue concentration of PCBs had returned to concentrations similar to control monkeys when the testing was performed. Infants from mothers treated with Aroclor 1016 showed normal performance on spatial learning and memory tasks but exhibited impaired learning of spatial discrimination tasks.

Developmental effects have also been reported for rats and mink.

Reproductive Effects

Effects of Aroclor 1254 upon male reproductive capacity in rats has been described by Sager in which young males exposed during lactation had a significant reduced ability to fertilize untreated female rats once they reached maturity. There was no detectable change noted in the sperm except the impaired ability to fertilize ova. One male rhesus monkey of 4 that received 4 mg/kg of Aroclor 1248 showed abnormal testicular histology, had hypoactive seminiferous tubules, and exhibited reduced libido.

The effects of PCBs upon female reproductive capacity have been more thoroughly documented. Studies in mink show that 0.4 mg/kg Aroclor 1254 and 0.9 mg/kg of Aroclor 1248 had a significant reduction on female reproductive performance. In rhesus monkeys 0.1 mg/kg of Ar 1248 cause increased menstrual duration and bleeding as well as reduced conception rates. The dose of 0.2 mg/kg of Aroclor 1254 caused erratic menstrual cycles and abortions in female rhesus monkeys.

Comparative Effects other Organs
Liver, Stomach, and Thyroid

Organ	Comparison	
Liver	Rat 0.3 mg/kg 2 mo	Rhesus monkey 0.1 mg/kg 7 m
Stomach ulcers	Pig 100 mg/kg	Rhesus monkey 4 mg/kg
Thyroid	Rat 2.5 mg/kg	Rhesus monkey 0.2 mg/kg

Salient Clinical Effects
Long Term Monkey Studies

Facial edema
Ocular discharge
Swelling Meibomian glands
Loss of fingernails
Gingival hyperplasia
Regional necrosis
Alopecia
Weight loss 15%

Comparative LOAELs for Reproductive Effects
Mink vs. Rhesus Monkeys

Mixture	Mink	Rhesus Monkeys
Aroclor 1016	0.9 mg/kg	0.03 mg/kg
Aroclor 1248	0.4 mg/kg	0.1 mg/kg
Aroclor 1254		0.025 mg/kg

Female Reproductive Alterations
Rhesus Monkeys Dosed with Aroclor 1248

Alterations	0.1 mg/kg	0.2 mg/kg
Anovulation	2/8	5/7
Decreased estrogen	5/8	3/7
Altered Function of Corpus Luteum	2/8	5/7
Altered Length of Menstrual Cycle	2/8	2/7
Altered Day of Ovulation	3/8	1/7

Summary
Effects of PCBs in Laboratory Animals

- PCBs produce a toxicity in many organ systems including reproductive, immunologic, integument, CNS, thyroid, adrenal, and liver
- Many species are affected with varying degrees of severity
- In general, more highly chlorinated PCB mixtures cause more severe toxicity
- Lesions in the CNS are associated with lesser chlorinated congeners

2.3 TOXICITY EQUIVALENTS FOR PCBS

Donald G. Barnes, Staff Director, Science Advisory Board, Washington, DC*

Over the past twenty years, analytical chemistry has provided toxicologists with a wealth of information about the molecular identity of compounds in the environment. The wealth of information has proved to be a significant interpretative challenge as toxicologists have tried to use this information to make better, more defensible decisions about the likely risks posed by these compounds—individually and as mixtures.

In the 1980s, an increasing number of laboratories were able to analyze environmental mixtures of chlorinated dibenzo-p-dioxins and chlorinated dibenzofurans (CCDs/CDFs) on a homologue-specific, isomer-specific, and, hence, congener-specific basis.[3] Environmental samples of CCD/CDF mixtures seemed to be popping up all over the place; e.g., residues in fish tissues, emissions from municipal waste incinerators, and smoke smudges from electrical equipment fires. At that time, considerable toxicological attention had been focused on the 2,3,7,8-TCDD congener.[4] However, relatively little was known about the toxic properties of the other 209 members of the structurally related CDD/CDF family.

Given this situation—congener-specific information about CDDs/CDFs in the environment—little toxicological information was left with two equally unappealing positions:

1. Ignore the toxic potential of all congeners in the CDDs/CDFs family other than 2,3,7,8-TCDD: the "Ignorance is Bliss" strategy, or

2. Assume that all of the congeners in the CDDs/CDFs family are equally toxic to 2,3,7,8-TCDD: The "It Could Be" strategy.

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* The views expressed in this paper are those of the author and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency.

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[3] Homologue: The group of CDDs (or CDFs) with the same level of chlorination. There are 8 homologous groups of CDDs (or CDFs), ranging from 1 chlorine substitution to 8 chlorine substitutions.

Isomer: The group compounds within a single homologous group (i.e., having the same degree of chlorination) that differ in the spacial distribution of those chlorines around the CDD (or CDF) three-ring structure of carbon and oxygen atoms. For example, there are 22 isomers in the homologous group of tetrachlorodibenzo-p-dioxins (TCDDs) and 27 isomers in the homologous group of tetrachlorodibenzofurans (TCDFs). The most (in) famous and most toxicologically potent of these is 2,3,7,8-TCDD.

Congener: A specific isomer of a specific homologous group. In all, there are 72 CDDs congeners; i.e., the sum of all the isomers of each of the 8 homologous groups.

[4] A Federal workgroup estimated that, by 1983, nearly $1 billion of research had been directed at the toxicology of 2,3,7,8-TCDD.

Dr. Judith Bellin, a toxicologist in the Office of Solid Waste at the time, and I tabled out the limited toxicity information on the CDDs/CDFs and saw arguably consistent patterns of relative toxicity, among the different congeners, across the different toxic endpoints. This observation—expanded (by the Risk Assessment Forum), critiqued (by everybody and his/her brother/sister), and peer reviewed (by the SAB)—led to the Agency's adopting the TEF (relative toxicity) scheme as an interim procedure[5] for assessing the risks of exposures to mixtures of CDDs/CDFs.

Two years after its initial adoption by the Agency, the TEF scheme was reassessed, and modest changes made. The new scheme was subsequently adopted by most of the Western nations through a workgroup of the North Atlantic Treaty Organization (NATO).[6]

The TEF scheme for CDDs/CDFs has been employed to good effect in a variety of situations over the past four years. While there is some interest is making additional modifications to the scheme, most of those involved in using TEFs in decisionmaking find greater benefit from a stable, widely accepted set of TEFs than in a marginally more "scientific" set of TEFs that are changing on an irregular, uncoordinated basis in different countries.

Criteria for TEFs

In the late 1980s, congener-specific analyses for PCBs became a viable possibility in a number of labs around the world. In addition, there was a growing body of toxicological information linking the toxicity of PCBs to molecular structure. Consequently, the stage seemed set for the appearance of another set of TEFs—this time for PCBs—to provide a rational interim procedure for assessing risks posed by another set of chemically related compounds.

Again, Dr. Judy Bellin was involved in the initial stages of the effort. But this time the data were even less complete than in the case of the CDDs/CDFs, and the story they told was less clear even to a sympathetic reader.

Before we launched into the nitty-gritty of trying to generate TEFs for PCBs we decided upon a set of criteria to guide our thinking and to keep us honest, especially for when our blood rushed hot from the thrill of the hunt. Those criteria are found in Table I. Based on that initial exploration of the issue, we decided that the PCBs fell short of meeting the requisite criteria.

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[5] The preferred approach was identified as a bioassay that would test the toxicity of the environmental mixture, or extract therefrom.

[6] It can now be disclosed that the TEFs for CDDs/CDFs were not the West's secret weapon that lead to the fall of the Berlin wall. However, it is true that OBM is seeking additional public comment on the TEF approach, in the context of some rules that EPA is planning to issue.

However, by December of 1990, additional data had been developed inside and outside of EPA laboratories that suggested revisiting the TEFs for PCBs issue. Consequently, the Risk Assessment Forum (RAF) sponsored a public workshop that drew participants from as far away as FDA (5 blocks), Canada, and Sweden. That group was more sanguine about the possibility of TEFs, particularly for the coplanar PCBs that exhibited "dioxin"-like toxicity, albeit at higher doses (RAF purple book; peer reviewed article in Quality Assurance); cf. Table II.

Current Status and the Future

The Agency is nearing the end of a multi-year effort to reassess the toxicity of 2,3,7,8-TCDD. This is a very complex and controversial project. It includes reassessing old endpoints (cancer and reproductive effects), and introducing new mathematical risk models. This stout stew will be further fortified by consideration of the toxicity of "dioxin"-like PCBs and the possibility of associated TEFs. New data—both health and ecological—are being generated in this enterprise, and new policies are likely to emerge as those data are examined. The data and the policy will be subjected to scrutiny by the public and to peer review by the SAB later this year.

In short, the use of TEFs for PCBs is not a "gimme". The concept will have to prove itself in the crucible of scientific review. In any event, the risk management implications are likely to be significant. 1993 should prove to be an interesting year.

TABLE I

Criteria for a TEF Scheme

1. A need (e.g., an interim regulatory need) for such an approach should be demonstrated.
2. The set of chemicals to which the scheme will be applied should be well defined.
3. A broad base of toxicity data should be available, covering many endpoints for many congeners.
4. Relative toxicity among the different congeners should be generally consistent across many different endpoints (*in vivo and in vitro*).
5. General additivity should be demonstrated in the response to simple mixtures of congeners.
6. A common mechanism should rationalize the observed SAR results.
7. A mechanism should be available for gaining widespread consensus on the TEF values.

TABLE II

TEFs for CDDs/CDFs and PCBs Evaluated by Applicability Criteria (as Defined in Text)

	CDDs/CDFs	PCBs
1. Need for TEFs	++	++
2. Well-defined group	+++	+++
3. Broad database	++, improving	+/-, improving
4. Consistency across toxic endpoints	++	++, for "dioxin"-like endpoints
5. Additivity of toxic response	+	+/-
6. Common mechanism	++	++, for "dioxin"-like congeners?,for other congeners
7. Mechanism for consensus	+	+ (potentially)

Note. +, generally meets criterion, based on available data; ++ meets criterion well, based on available data; - does not meet criterion, based on available data; ?, cannot evaluate, based on available data.

Source: *Quality Assurance*, 1(1991), 70-81, "TEFs for PCBs?," Barnes, D.G., *et al.*

2.4 EFFECTS OF OCCUPATIONAL EXPOSURE

John F. Brown, Jr., Manager of Health Research, General Electric Corporate Research and Development, Schenectady, NY[7]

During the period 1929-1978 about 1.3 billion pounds of PCBs were produced and used in the United States. Some 10-15 percent of this total is estimated to have reached the soils, sediments, and waters of the general environment, resulting in widespread, though low level, exposure of fish, other wildlife, and human populations. In addition, direct human exposure to undiluted PCBs occurred in many PCB-using operations. During the 1970s and 1980s about 20 different clinical or epidemiological studies of the dozen-odd more easily identified PCB-exposed worker populations, including our own longitudinal clinical study of GE capacitor workers [1], were undertaken. These studies have resulted in the publication of several dozen reports in the scientific literature, and several critical reviews [2]. The most recent, and most detailed, of these reviews is that by James *et al.* [2], which addressed, in turn, the questions of possible effects on the liver, lungs, skin, cardiovascular system, nervous system, certain endocrine systems, the blood/immune system, and the GI and urinary tracts. It was concluded, in line with the findings of previous reviews, that there was no evidence for adverse PCB effects on any organ system other than the skin, for which there was ambiguous evidence of possible effects at the highest exposure levels. (Parenthetically, we may note that the ambiguity arises because none of the original investigators who reported occasional observations of "chloracne" undertook histological or statistical examinations to distinguish the observed lesions from those of common acne. No cases of chloracne were observed in the GE capacitor worker population [1] that we studied, despite the presence of many individuals with serum PCB levels over 1000 μg/kg). The reports reviewed by James *et al.* [2] included ten mortality analyses, covering about 1000 different deaths, which generally showed no increased mortality due to cardiovascular disease, pulmonary disease, or cancer.

The extraordinary contrast between the absence of clinically- or epidemiologically-demonstrable health effects in heavily-exposed worker groups and the numerous reports of toxicological and carcinogenic effects in laboratory animals has been noted by several reviewers; however, there has remained some uncertainty as to whether these differences arise from interspecies differences in susceptibility to PCBs or to differences in dosage or accumulation [2]. Also unresolved has been the question of why statistical correlations between health abnormalities and PCB levels may exist even in population groups carrying PCBs at only background levels.

In hopes of shedding light on such issues, we have been examining PCB metabolism and pharmacokinetics in our capacitor worker study group, and will summarize some recent findings here.

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[7] Richard W. Lawton was a coauthor of this paper.

PCB Metabolism

The congener distribution in any partially metabolized PCB residue provides a highly characteristic indicator of the PCB-metabolizing system(s) present in the host organism or culture. The PCB residue in all occupational exposed workers thus far examined (>200) show only a congener distribution pattern like that produced by cytochrome P4502B (i.e., phenobarbital-induced) isozymes [3-4]. This is the pattern also exhibited by the chromatograms of PCB-dosed sheep and mice, as well as those of many wild birds, a few fish species, and some crustaceans.

Conversely, the pattern seen in the Yusho and Yucheng chloracne patients, who were poisoned by PCDF + PCB mixtures, indicates PCB metabolism by agents with selectivities like those of cytochrome P4501A (i.e., PCDF-induced) as well as by P4502B isozymes [3]. This is the pattern also seen in most PCB-dosed rats and probably in adult monkeys, as well as in many species of wild birds and fish. The rats and monkeys in which indications of P4501A activity appeared carried tissue PCB concentrations that were the same or lower than those of our capacitor workers, showing that the absence of a dioxin-like response to PCB in the human arises from a physiological difference in the species, not one of lower dose.

PCB Kinetics

Following the 1977 cessation of PCB use in capacitor manufacturing, serum PCB levels in our study group dropped rapidly. The decay in PCB levels occurred at rates that could be correlated with various physiological characteristics of the individuals involved, including age, sex, body fat, and serum iron, and followed approximately second order kinetics, indicating that the levels of the PCB-metabolizing P4502B-like isozymes must have declined roughly proportionally with those of the PCBs. Earlier indications of PCB-mediated induction of P4502B-like isozymes in capacitor workers were suggested by data on antipyrine clearance times. PCBs have also been observed to increase P4502B levels in rats, mice, and winter flounder, although apparently not in the rhesus monkey. Thus, the human would appear to be at least qualitatively similar to the rodents in this P4502B-induction response to PCBs.

In rodents, however, P4502B-inducing agents, such as the more heavily chlorinated PCBs, DDT, other chlorinated pesticides, and the barbiturate and hydantoin drugs, all appear to be either hepatotumorigenic or liver tumor promoters, whereas none of these agents have been found to be human carcinogens. Thus, there would appear to be a clear interspecies difference between rat and man in the sequelae of hepatic P4502B induction.

PCB Levels in Chronically Exposed Individuals

Most PCB congeners are so rapidly metabolized by human P4502B as to be undetectable in the serum. A few are scarcely metabolized at all, and hence can serve as permanent records of PCB exposure events [4]. In between are the dozen or so congeners that account for most of a measured human PCB level, and which have half-lives in the 1-15 year range [3]. In adults who have been exposed for several years to a single PCB source, whether environmental or occupational, body PCB levels of those dominant congeners will have approached a steady state level, where uptake is approximately balanced by metabolism. Simple calculation shows that in such individuals the serum PCB level will be as indicated by eq. (1)

$$[PCB]_s \cong [L]_s(D/EF)^{1/n} \quad (1)$$

where $[PCB]_s$ and $[L]_s$ respectively represent the levels of PCBs and neutral lipids in the blood serum; D the PCB intake rate; E, the inducibility of P4502B; F, the total level of neutral lipid (i.e., fat) in the body; and n, a number ranging between 1 (in the lightly exposed background population) and 2 (in heavily PCB-exposed and P4502B-induced individuals).

What this relationship shows is that among ordinary, background-exposed individuals, where $n \cong 1$, and D values are probably similar to those for everyone else in the same region, observable variations in serum PCB will arise primarily from variations in E, F, and $[L]_s$, and hence that serum PCB levels will be covariant with any health conditions that are covariant with P450 inducibility, body fat, or lipidemia. Early failures to recognize such relationships in occupationally exposed workers led to several reports that serum PCBs were causally associated with elevated serum lipids and the associated serum enzymes. The statistical associations disappeared, however, when the serum PCB levels were corrected for variations in $[L]_s$ [1,2]. More recently, much weaker statistical associations with fetal neurodevelopmental deficiencies have been reported for PCB levels in background-exposed promoters; however, no corrections of the PCB levels for variations in E, F, and $[L]_s$ have yet been carried out, so the hypothesis that the developing fetus may represent an organ system that is orders of magnitude more sensitive to PCBs than any other in the human body (which is clearly had not the case for the dioxin-like PCDFs) remains unproved.

Relative Risks of Different PCB Compositions

Long before the completion and review of clinical and epidemiological studies indicating absence of significant health effects in occupationally exposed human populations, it was recognized by the FDA that there existed no scientifically valid basis for the quantitative assessment of PCB health risks, and hence that any determination of tolerance levels would have to be made instead on the basis of administrative authority. This, however, leaves unresolved the question of how the relative "risks" (if any) of different PCB compositions should be assigned. Currently, the assessed risks of all PCB compositions are regarded as equal, a presumption widely regarded as scientifically implausible, albeit administratively convenient.

One briefly considered alternative, discussed elsewhere in this document has been to scale presumptions as to health risk on the basis of dioxin equivalency, a measure that may indeed be a plausible indicator of relative risk to some species of wildlife. As a measure of cancer risk to humans, however, it suffers the drawbacks (a) that PCBs do not seem to have appreciable dioxin-like activity in humans, as we have just seen, and (b), even if rats, where PCB compositions do have dioxin-like activity, that activity does not correlate with tumorigenic response.

An alternative suggested by the recent availability of metabolic rate data for the PCB congeners that are commonly detected in humans [3,4] would be to use the persistence, or accumulability, of the PCB composition as a measure of relative risk. This parameter, which is readily calculated from the rate data, does seem to track reported tumorigenicity in rats and immunotoxicity in mice, and probably also P4502B induction, which would currently appear to be the only demonstrable human response to elevated PCB loadings. Calculations show that the relative accumulations of the various commercial PCB compositions in a human exposed over a 70-year lifetime, would be: for Aroclor 1016, 0.026; for Aroclor 1242, 0.049; Aroclor 1248, 0.10; Aroclor 1254, 0.31; Aroclor 1260, 1.000; Aroclor 1262, 1.26; and Aroclor 1268, 2.32. Thus, if present regulatory presumptions as to the theoretical human health risk posed by Aroclor 1260 (which is calculated from the hepatocarcinogenicity of Aroclor 1260 in rats) were to remain unchanged, but those of the other Aroclors assessed on the basis of relative accumulation tendency, their measured levels would have to be multiplied by these factors in order to convert them to Aroclor 1260 equivalents. Application of such Aroclor 1260 equivalency factors for the various individual congeners or gas chromatographic peaks to available data on the PCB congener distributions in fish suggests that such an approach would often result in a two- or four-fold relaxation of PCB tolerance levels. Not so affected, however, would be fish those from sites contaminated with Aroclors 1260, 1262, or 1268, or those of species such as eels, lobsters, and blue crabs, where considerable metabolism of the PCB residues has already occurred.

Conclusion

The metabolic and pharmacokinetic behavior of PCBs in capacitor workers supports earlier conclusions that humans differ from rats and monkeys in their response to PCBs, just as various animal species differ from each other. At present, the only unequivocally demonstrable pharmacological response of humans to PCBs at levels produced by direct occupational exposure, which are 10-100 times greater than those produced by fish consumption, has been induction of metabolic enzymes having activity profiles like that of cytochrome P4502B. There is no evidence that such enzyme induction would occur at lower levels of exposure, nor is there any clinical or epidemiological data to indicate that this or any other pharmacological response has had deleterious effects on the health of the occupationally exposed individuals.

However, if concerns remain that there may still be real, though unmeasurable, health risks associated with any agent having a pharmacological activity in the human, then it would seem appropriate to regulate different PCB compositions according to their ability to accumulate to levels that would produce such a response. Institution of such an approach (e.g., regulation of fish on their content of "Aroclor 1260 equivalents" rather than that of "total PCBs") would not require any new analytical methods, but merely the incorporation of available kinetic data into the mathematical procedures used for computing a reportable parameters from the same raw data.

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TABLE 1
PCB Capacitor Plant Cohort Study Information

Cohort Size and Location	PCB Usage Interval	Study Authors and Year	Study Type	Number of Study Subjects
Indiana				
3 588 total workers	1959–1977	Smith et al. 1982[36]	Broad clinical survey	228
		Saiks et al. 1992[37]	Mortality analysis (192 deaths)	3 588
Massachusetts				
1 559 workers in PCB exposure jobs	1938–1977	Lawton et al. 1985[1]	Broad clinical survey	194
		Brown and Jones, 1981[38]	Mortality analysis (90 deaths)	1 599
		Brown, 1987[39]	Mortality analysis (179 deaths)	1 607
500 current workers	1941–1977	Acquavella et al. 1986[40]	Broad clinical survey	295
New York				
6,303 total workers at the two plant locations; 2,588 w/ PCB-exposure jobs	Plant 1 1951–1977	Alvares et al. 1977[41]	Liver function survey	5
	Plant 2. 1946–1977	Fischbein et al. 1979[42]	Broad clinical survey	326
		Warshaw et al. 1979[43]	Lung function survey	326
		Brown and Jones, 1981[38]	Mortality analysis (73 deaths)	968
		Fischbein et al. 1982,[27a] 1985[28a]	Dermal/ocular effect survey	181–289
		Fischbein, 1985[28]	Liver function survey	261
		Lawton et al. 1985[1]	Lung function survey	194
		Nicholson et al. 1987[30]	Mortality analysis (188 deaths)	788
		Brown, 1987[39]	Mortality analysis (116 deaths)	881
		Taylor, 1988[31]	Mortality analysis (510 deaths)	6,303
Australia				
34 PCB-exposed workers	1951–1974	Ouw et al. 1976[13]	Dermal effects/liver function	34
Italy				
1,310–2,100 total workers	1946–1980	Maroni et al. 1981b[15]	Dermal effects/liver function	80
		Maroni et al. 1984[16]	Enzyme induction/porphyria	51
		Bertazzi et al. 1987[20]	Mortality analysis (64 deaths)	2,100
Japan				
155 possibly exposed workers	1948–1972	Hara, 1985[18]	Limited clinical survey	155
Sweden				
145 exposed workers	1965–1978	Gustavsson et al. 1986[17]	Mortality analysis (21 deaths)	142

ORGAN SYSTEMS REVIEWED FOR CLINICAL SYMPTOMS

Blood/immune	Gastrointestinal	Pulmonary
Cardiovascular	Liver	Skin
Endocrine	Neurological	Urinary

MORTALITY DATA REVIEWED

Cancer	Cardiovascular	Pulmonary

James et al., 1993

UNRESOLVED PCB HEALTH EFFECTS ISSUES

In occupationally-exposed workers (serum PCB 100-1000 ppb)
- No clinical symptoms
- No increased mortality

In background-exposed populations (serum PCB 1-10 ppb)
- Some statistical correlations with health effects
- Widespread popular concern over risk

In laboratory animals (serum PCB 10-10,000+ ppb)
- Many examples of toxic responses

Why the differences in response?
- Higher doses in animal tests?
- Animal-human differences?
- Unrecognized covariances in statistical correlations?
- Bad data?

Table 1. Geometric Mean Gross Serum PCB Levels in Capacitor Workers and Contemporary Controls[a]

Group	Year	ppb Aro. 1242	ppb Aro. 1254
Off-site (Connecticut) controls	1976	6.7	~10
All plant employed >5yrs.[b]	1976	~291	~19
Longitudinal (GE) study group	1976	1471	84
	1979	277	55
	1983	116	34
	1988	90	32

a. Reported Aroclor levels in serum as calculated by sum of selected peak heights procedure. The "Aroclor 1242" and "Aroclor 1254" values generated by this procedure have been estimated to overstate the actual levels of lower PCBs and higher PCBs by factors of about 4 and 1.5, respectively [8].

b. Recalculated from data of Wolff [9] to permit expression on a common basis.

METABOLISM OF PCB CONGENERS BY CYTOCHROME P450s

P4502B

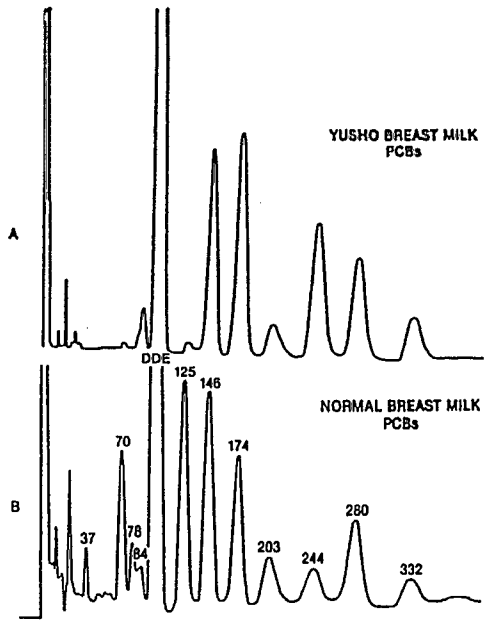
- Rapidly removes congeners with open 3,4- (or 4,5-) positions
- Slowly removes congeners with open 3- (or 5-) positions

P4501A (AHH)

- Ditto, but only when <2 ortho chlorines present

Recognition feature for P4501A induction

- Accelerated loss of otherwise recalcitrant mono-ortho's
- E.g., decrease in: 24-4, 245-4, 245-34, 234-34
  Relative to: 24-24, 245-24, 234-24



from Masuda, Kagawa and Kuratsune, 1974

METABOLIC PATTERNS SEEN IN BLOOD OR TISSUE PCB RESIDUES

Like P4502B

- Background-exposed humans
- PCB-exposed workers
- PCB-dosed mice; lightly dosed rats
- Eels, cunner, lobster, blue crabs

Like P4502B + P4501A

- PCDF-exposed chloracne patients
- PCB-dosed rats, monkeys (?), mink (?)
- Dogs, polar bears, some birds

Like P4501A

- Some porpoises
- Many species of fish

PCB ACCUMULATION AND CLEARANCE

1. Monkey Aro 1254 steady state accumulation 1st order in PCB
   - P4502B activity ~ $[PCB]^0$
2. Human Aro 1242 clearance 2nd order in PCB
   - P4502B activity ~ $[PCB]^1$
3. Human variables that may affect clearance rate:
   - Age
   - Sex
   - Body fat
   - Serum iron
   - Serum albumin
   - Drugs, smoking
4. Relative rates of PCB congener metabolism estimated for:
   - 55 congeners from human data
   - 67 congeners from biochemical or animal data
   - 68 congeners by structure-activity relationships

   146 different congeners in total
   - Data permits calculating accumulability for any PCB mixture

SUMMARY OF EVIDENCE FOR INDUCTION (+) OR NON-INDUCTION (–) OF CYTOCHROME P450 ACTIVITIES BY PCBs IN HUMANS OR ANIMALS

Species	(ref.)	Aroclor/exposure	Max. lipid PCB, ppm	P450 Induc'd, 1A	2B
Man	(2,10)	1254, 1242, 1016 occup., 2-35 yr.	17-597	–	+
Man	(11)	1260, occupational, obs. yr. 25	~ 200	–	+
Man	(10,13)	1248 + PCQ + PCDF, yusho	<50	+	±
Rat	(14)	1016, 100 ppm/diet, 8 mo.	236	–	±
Rat	(14)	1242, 100 ppm/diet, 8 mo.	143	+	+
Rat	(18)	1254, 489 mg/kg, obs. da. 4	~2000	+	+
Mouse	(12)	1254, 500 mg/kg, obs. wk. 4-55	~2000	–	+
Monkey	(15)	1016+?[a], 1 ppm/diet, 18 wk.	3	±	?
Monkey	(19)	1254, 5-80 µg/kg/da, 37 mo.	4-51	±	–

a. Published chromatograms (15) indicate exposure to other agents besides Aroclor 1016, probably Aroclor 1248

DEPENDENCY OF STEADY STATE SERUM PCB LEVELS, $[PCB]_S$, ON DOSE RATE, D, SERUM NEUTRAL LIPID, L, BODY FAT, F, AND P450 INDUCTION

1. At low PCB levels:

$$[PCB]_S = [L]_S \left(\frac{D}{x \cdot F}\right)$$

Where:
x = constitutive P450 activity

2. At high PCB levels

$$[PCB]_S = [L]_S \left(\frac{D}{r \cdot F}\right)^{1/2}$$

Where:
r = responsiveness of P450 to $[PCB]_{SL}$

3. Approximate general relationship

$$[PCB]_S \simeq [L]_S \left(\frac{D}{E \cdot F}\right)^{1/n}$$

Where:
E = overall P450 inducibility
$1 \leq n \leq 2$

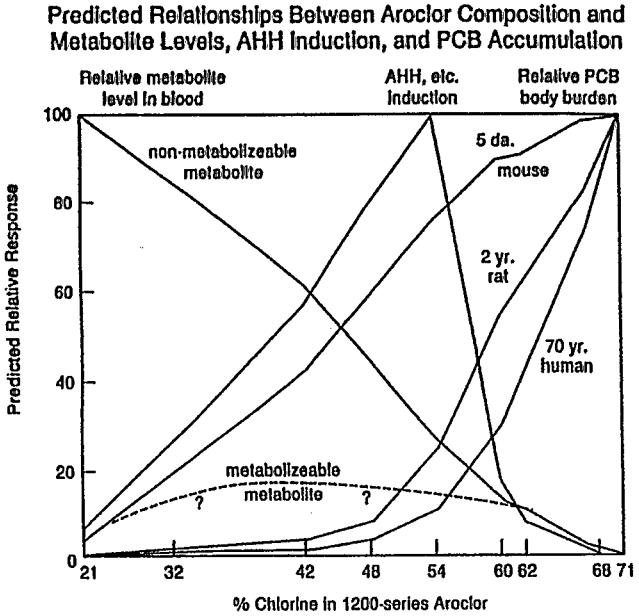
EXACT RISK/TOLERANCE LEVEL OF A PCB COMPOSITION CAN ONLY BE DETERMINED BY ADMINISTRATIVE AUTHORITY

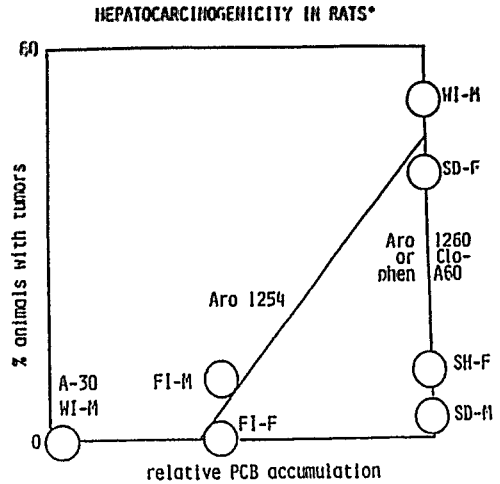
RELATIVE RISKS OF DIFFERENT COMPOSITIONS BEING QUESTIONED

- Treat all as equal?
- Assess on basis of dioxin equivalency (TEQ)?
- Assess on basis of relative accumulability?

THE TOXIC EQUIVALENCY DEBATE

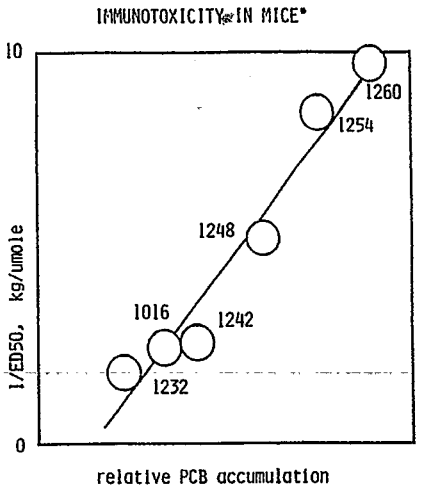
- Currently, environmental PCDF/PCDD mixtures being assessed for total dioxin-like toxic equivalency (TEQ) by use of individual toxic equivalency factor (TEF) for each PCDF/PCDD congener
- Some minor PCB congeners also have measurable dioxin-like activities; could be assigned TEF's
- Total TEF may correlate with some indicators of wildlife toxicity
- Proposal: co-regulate dioxins, PCDFs, PCBs as a group via suitably determined TEF Values
- Problem: Arcolor TEQ's don't correlate with carcinogenicity





* as measured by increase in % animals with hepatocellular carcinoma after 2 yr. continuous dosing at 100 ppm in diet. Key: WI-Wistar, SD-Sprague-Dawley; SH-Sherman; FI, Fischer rats; M-males, F-females; from 1991 panel rescoring of original slides.

Moore, 1991



* as measured by 1/ED50 for inhibition of murine splenic plaque-forming cell response to sheep red blood cells 5 da. after single dose of Aroclor

from Davis and Safe, 1989

CONCLUSIONS

1. PCB effects on humans, rats, mice, monkeys all different.
2. P4502B induction only identified pharmacological response to occupational PCB exposures 10-100 times greater than those resulting from fish consumption.
3. Critical reviews of *ca.* 20 different clinical or epidemiological studies of occupationally exposed workers have shown no measureable health effects.
4. If concerns remain that there must be some real, though unmeasureable, health risk posed by PCB accumulations in the body, the appropriate measure of relative risk is relative accumulability, or persistence.

2.5 ANIMAL/HEALTH CONNECTION

Theo Colborn, Senior Fellow, W. Alton Jones Foundation, World Wildlife Fund, Washington, DC

PCBs are reported in fish tissue from the equator to the Arctic. They are persistent, hydrophobic, and vaporize readily, atmospherically transported long distances. Recent studies demonstrate that PCBs are deposited at the same rate in the Arctic as they are in the Great Lakes. Atmospheric deposition contributes 90 percent of the PCBs to Lake Superior, a lake with little industrial activity on its shoreline. By comparison, Lake Ontario, with a highly industrialized shoreline, receives 6 percent of its PCBs from the atmosphere.

Effects Reported in Wildlife Dependent Upon Fish

A comprehensive examination of the literature about wildlife from the Northern Hemisphere reveals that many species dependent upon fish are having difficulty maintaining stable populations. Population instability is associated with effects in offspring leading to embryo or early mortality while the animals directly affected, the adults, exhibit little or no overt effects. The transgenerational problems in embryos, fetuses, and newborn animals have been associated with PCB concentrations and dioxin toxicity equivalents in their tissue. The endocrine and reproductive systems of the progeny are affected, measured in terms of thyroid and other endocrine tissue malfunction, or sex reversal, and/or reduced fertility in birds, fishes, and marine mammals; less quantitative and observational evidence has been reported on behavioral changes in birds; and more recently, emerging evidence suggests that the immune system is involved in premature mortality in birds and marine mammals.

Some of the anomalies reported in Great Lakes wildlife that are associated with endocrine disruption include:

- Female herring gulls sharing a nest and males in the same population forming "fraternities" and not carrying out their parental responsibilities
- All double-crested cormorant chicks with crossed bills have been female
- One hundred percent of fish examined by a team of wildlife biologists from Guelph University have hypertrophic and hyperplastic thyroids and recently the thyroids of Lake Erie fish are rupturing because of their extremely large size
- Herring gulls also have enlarged thyroids
- Fish and herring gull thyroid hormone ratios are skewed (T3:T4)
- Top predator male fish are precocially developing sexually but never achieving full sexual maturity

- Most top predator fish species and other bottom fish exhibit various stages of hermaphroditism

A case study is provided to demonstrate that the endpoints (measurable health effects) as a result of exposure to PCBs and other contaminants may be very sensitive and easy to miss. The endpoints shift over time, differ among species, and are dependent upon timing of exposure and dose. In 1983 an association was made between total PCB concentration and delay in incubation time, poor hatchability, poor chick weight gain and loss of weight leading to early mortality ("wasting"), decreased fledging success, and overall mortality in a breeding population of Forster's terns on an island in Green Bay. In addition to chemical assay to measure the concentration of total PCBs in the chicks and abandoned eggs, the HII4E rat liver hepatoma assay was used to determine toxicity. By day 17, almost all the chicks were dead and the parents had abandoned the area. The study was repeated 5 years later in 1988 after remedial action for PCBs in the Green Bay area. Although everything appeared normal throughout incubation, hatching, and among the offspring up to day 17, on day 18 the chicks began to "waste" and by day 31, the same mortality was recorded as in 1983. If the biologists had returned to their laboratories on day 18 instead of staying in the field, it would have been assumed that the PCB concentrations reported in the offspring in 1988 were "safe".

The importance of congener specific analyses in order to make cause and effect associations is borne out by a study comparing lake trout egg mortality with PCB #77 (3,4,3',4'-tetrachlorobiphenyl) and total PCBs. Eggs were stripped from ripe females from 5 locations around the Great Lakes. No association was found between egg mortality and total PCB concentration in the eggs. However, a correlation of 99.9 was discovered with congener #77.

Almost no large-scale marine mammal die-offs occurred before 1987. Since then animals have been found beached and dying from new strains of viruses specific for seals, dolphins, and porpoises. In each event, elevated concentrations of PCBs and other organochlorine chemicals were found in the tissues of these animals and the animals' immune systems appeared to be compromised. It is yet to be determined whether immune suppression was the result of chemical exposure or the result of the viral infections. These events took place only among toothed mammals dependent upon fish. Baleen whales have not been affected similarly.

Effects in Laboratory Animals Fed Contaminated Fish

Rats fed a 30 percent diet of Lake Ontario salmon for 20 days no longer respond well to stressful events, such as a change of scenery in their cage, a mild shock, or a reduction in food pellets. The same effect is reported after a 10 percent diet for 60 days. The offspring of females fed Lake Ontario salmon from the day they were bred and during the first seven days of lactation cannot cope with stress either. These fish were contaminated with approximately 8 ppm PCB and a number of other organochlorine chemicals.

The Wildlife/Human Parallel

A number of models have been generated to assign a biomagnification or bioaccumulation factor to PCBs when determining risk to humans. However, the unpredictability of these models is borne out by tracing the course of PCBs in the Arctic food web from the arctic cod to the ringed seal, and ultimately to the polar bear. The cod hold primarily the tri- and tetra-chlorinated PCBs; the seals, the tetra- and penta-; and the polar bears the hexa- and hepta-chlorinated PCBs. The anomalous enrichment of the higher chlorinated PCBs in the animals in this simple food chain is reflected in the pattern of PCB congeners found in the tissue of native Americans dependent upon marine and freshwater fish and mammals. Breast milk of native Americans from eastern Arctic Canada holds 3 to 5 times more PCBs than breast milk from women in temperate zones and the congener composition is quite different. This raises questions concerning the reliability of models when dealing with chemicals that are comprised of multiple compounds (PCBs are comprised of 209 different compounds called congeners) in which each congener appears to have a distinct toxicity pattern; and which have become distributed worldwide and whose fate, therefore, is almost impossible to determine.

Thirty two of the 43 areas of concern around the Great Lakes designated by the Canada and US International Joint Commission and EPA were chosen because of elevated PCB concentrations in abiotic and biotic samples from the areas. Advisories are currently issued in these areas warning people not to eat certain species and sizes of fish depending upon the consumer's age and sex. These advisories are based on a cancer model using data that are over 20 years old. Despite health advisories people are still fishing and eating their catch.

A number of studies suggest that PCBs when present in the womb have the potential to affect the developing nervous system of the embryo, fetus, and newborn. Neurotoxic effects have been reported in offspring at birth and later at age four of mothers who ate Lake Michigan fish two to three times a month for at least six years preceding their pregnancies. Effects were seen in children whose mothers' breast milk fat PCB concentrations exceeded 1 ppm. Similar effects were reported at birth in a cohort of children borne of women from North Carolina. However, no effects were detected later in follow-up examinations of these children. The median PCB concentration in the women from North Carolina was higher than those from Michigan who had consumed Lake Michigan fish. Both studies suggest that the neurotoxic effects in the children were of prenatal origin, not from breast feeding. A study involving the cross-fostering of Chlophen-A30-exposed and unexposed rat pups (a German analog of PCB), confirmed that the neurotoxicological effect was initiated in the womb, not postnatally. It is important to note, that when the children whose mothers ate Lake Michigan fish were tested at age four, 17 of the children refused to cooperate and take some or all of the tests. These were children whose mothers had the highest PCB breast milk concentrations in the study.

A close examination of the literature on laboratory animal and human neurotoxic effects as a result of exposure to PCBs reveals that the human is 10,000 times more sensitive to PCBs than the rat, using the traditional rat endpoint for neurotoxicity.

An examination of the literature on PCBs and male fertility revealed that the:

- Sperm of mature male rats exposed postnatally to PCBs through their mothers' breast milk were unable to penetrate the ova in healthy, PCB-free females

- Male pups of female rats fed one low-dose meal (0.064, 0.160, 0.4, and 1.0 ug/kg/body weight) of dioxin (2,3,7,8-TCDD) on day 15 of gestation (the approximate day sexual differentiation commences in rats) were demasculinized and feminized as they matured and their sperm count was reduced by 75 percent

- Motility of sperm from men visiting a fertility clinic was inversely related to the concentration of three PCB congeners, one of which is 2,4,5,2',4',5'-hexachlorobiphenyl which comprises about 20 percent of total PCBs in humans in temperate zones and 40 percent to 45 percent of total PCBs in humans in the Arctic

- Male sperm count declined worldwide by 45 percent between 1938 and 1991. Taking ejaculate volume into consideration, which decreased over the same time period by 25 percent, the decrease in sperm count is equivalent to a 50 percent reduction

- Reproductive biologists, endocrinologists, and toxicologists agree that exposure in the womb to PCB and other estrogen-like substances in the womb can irreversibly affect sperm production in adult males

Human health assessments can no longer be based on the probability of developing cancer alone. Multigenerational loss of function must become a part of the human health assessment process. Parallels in wildlife, laboratory animals, and humans in response to exposure by PCBs and other chemicals found in fish tissue cannot be ignored. To date it appears that the exposed adults are not overtly affected. Instead effects result from parental transfer of the chemical to the offspring. In human offspring the effects may not be manifested as clinically relevant endpoints and may not be recognized at birth. In humans and wildlife the effects could be easily missed and not expressed until adulthood—making a causal link almost impossible.

Species	Population Decline	Reproductive Effect	Eggshell Thinning	Metabolic Changes	Deformities	"Wasting"	Target Organ Damage	Behavioral Changes	Hormonal Changes	Immune Suppression	Generational Effects	Tumors
Bald Eagle	X	X	X	X	X		X			X		
Beluga Whale	X	X	N/A		X	X		X	X	X	X	
Black-Crowned NH	X	X	X		X							
Caspian Tern	X	X		X	X		X			X		
Chinook/Coho Salmon	N/A	X	N/A			X		X		N/A	X	
Common Tern	X	X		X		X	X		X			
D.C. Cormorant	X	X	X	X	X	X	X			X		
Forster's Tern	X	X		X	X	X	X			X		
Herring Gull	X	X	X	X	X	X	X	X	X	X		
Lake Trout	X	X	N/A	X		X	X			X		
Mink	X	X	N/A	X		X				X		
Osprey	X	X	X									
Otter	X		N/A									
Ring-Billed Gull		X		X	X				X			
Snapping Turtle	X	X		X	X	X				X		

Observed effects that have been reported in the literature.

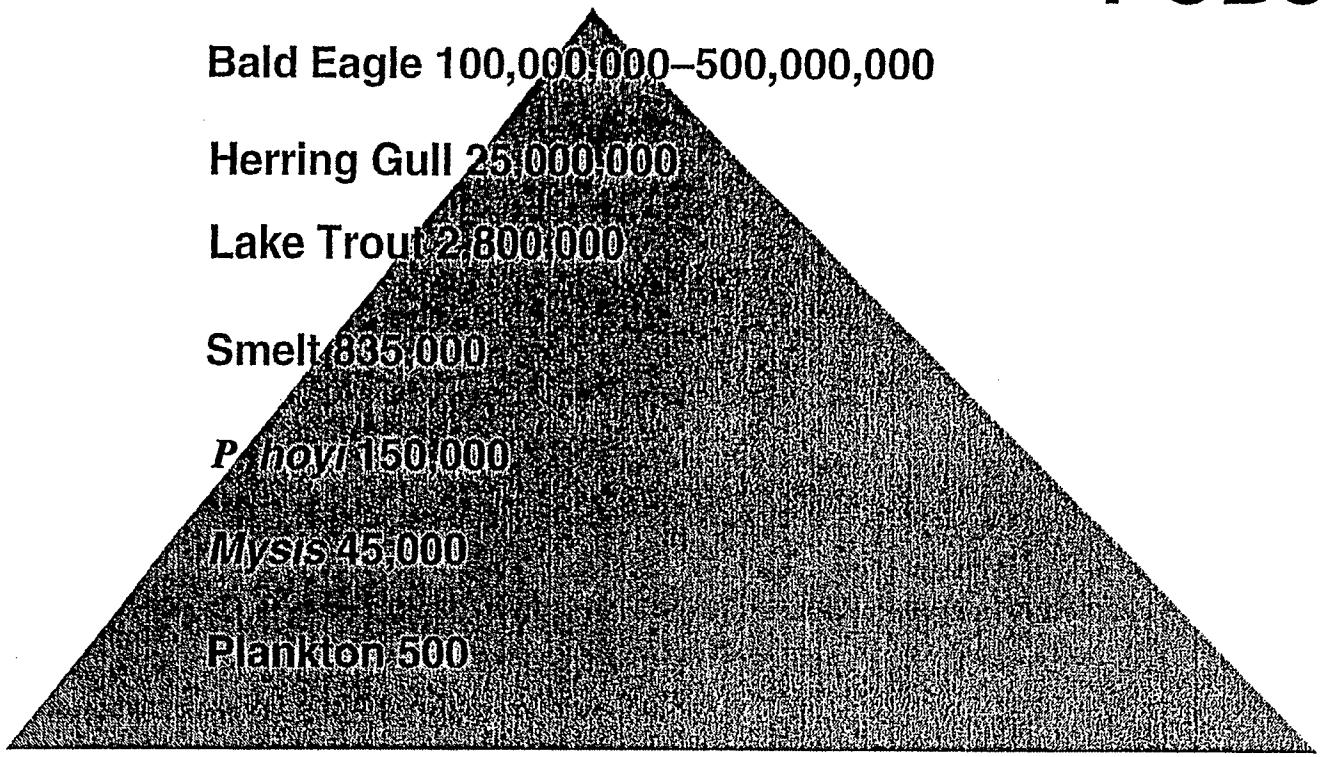
OBSERVED EFFECTS IN MARINE MAMMALS

MARINE MAMMAL		HEALTH EFFECT					
		Population Decline; Strandings	Reproduction & Endocrine Impairment	Immmune System Compromise	Organ Damage	Infection & Health Decline	Tumors
Dolphin	bottlenose	X	X	X	X	X	
	striped	X		X	X	X	
Porpoise	Dall's		X				
Sea Lion	California	X	X		X	X	
Seal	Baikal	X		X		X	
	grey	X	X			X	X
	harbor	X	X	X	X	X	
	ringed	X	X		X	X	
Whale	beluga	X	X	X	X	X	X
	sperm	X				X	

LOCATION OF MARINE MAMMAL STUDIES

LOCATION		MAMMAL	YEAR	REPORT
Canada	Newfoundland	pilot whale	1980	organohalogens
	St. Lawrence Estuary	beluga whale	1979-1989	population decline
	Bay of Fundy	right whale	1988-1989	endangered
Europe	Baltic Sea	ringed,grey,harbor seals	1987-1991	dieoff
	North Sea	ringed,grey,harbor seals	1987-1991	dieoff
	Wadden Sea	ringed,grey,harbor seals	1987-1991	dieoff
	Mediterranean Sea	striped dolphin	1990-1991	dieoff
	European & Norwegian coasts	sperm whale	1988-1989	strandings
Russia	Lake Baikal	Baikal seal	1987-1988	dieoff
US	North Atlantic	bottlenose dolphin	1987-1988	dieoff
	Gulf of Mexico	bottlenose dolphin	1990	dieoff
Japan	North Pacific	killer whale	1982	organohalogens
	"	striped dolphin	1981	organohalogens
	"	white-beaked dolphin	1980	organohalogens
	"	white-sided dolphin	1981	organohalogens
	"	finless porpoise	1985	organohalogens
	"	Baird's-beaked whale	1985,1988	organohalogens

PCBs



Adapted from Canadian Fish & Wildlife Service, 1988 and Norstrom *et al.*, 1978.

Table V. Biomagnification Factors for the Food Chain Arctic Cod/Ringed Seal/Polar Bear[a]

compound	fish to seal		seal to bear		
	male seals	female seals	male seals	female seals	fish to bear
S-PCB	8.8	3.7	7.4	13.9	49.2
PCB homologue					
Cl_4	2.5	1.2	<0.2	<0.4	<0.5
Cl_5	11.3	5.1	1.9	3.1	13.9
Cl_6	23.0	9.7	9.3	18.3	170.6
Cl_7	17.0	6.9	19.8	38.6	263.4
Cl_8	>3	>1.4	24.6	47.2	>67
Cl_9	*b*	>109	*b*	>109	*b*
S-DDT	20.2	8.2	0.3	0.5	3.6
S-CHLOR	7.3	4.7	6.6	9.5	44.2
S-HCH	1.5	1.6	9.3	1.7	2.7
S-CBz	0.2	0.2	15.55	17.4	3.4
dieldrin	2.4	2.2	4.88	5.5	11.4
p,p'-DDE	62.2	17.6	0.3	0.7	10.7

[a] Ratio of tissue concentrations on a lipid weight basis. [b] Cl_9 PCBs not detected in fish muscle (<2 μg/kg of lipid wt) or seal blubber (<0.5 μg/kg of lipid wt).

Source: Muir et al., 1988. Environmental Science and Technology, pp. 1071-1079.

2.6 SUMMARY OF QUESTIONS AND RESPONSES[8]

2.6.1 Gordon Blaylock of the Oak Ridge National Laboratory questioned Dr. Cogliano regarding the uncertainty that should be attached to the carcinogenic potency ("slope factor") for PCBs.

Dr. Cogliano stated that when applying the slope factor to an Aroclor 1260 mixture, the uncertainty factor should probably be no more than half an order of magnitude, a factor of 2 or 3 at most. He stated that when applying the slope factor to other mixtures, one to two orders of magnitude is acceptable, although the uncertainty increases for dissimilar mixtures. He noted that for mixtures that do produce cancer, one of the striking features is that the toxicity values are fairly close.

2.6.2 Brian Toal of the Connecticut Health Department asked Dr. Cogliano whether the contamination of PCB mixtures by furans is still considered an issue, as it was in some of the older studies.

Dr. Cogliano stated that he did not believe that furans were an issue with the mixtures that were tested on animals. He noted that one of the studies reported that their mixtures were free of furans. Dr. Cogliano stated that a sensitivity analysis was conducted in 1989 (based on the toxic equivalency factors of some of the dibenzofuran contaminants of the PCB mixtures). He noted that based upon this analysis, it was found that the furans would have contributed less than approximately ten or twenty percent of the carcinogenicity seen in animals. However, he stated, when evaluating actual human exposures to PCB mixtures, this may not be the case. He noted that, in the Yusho incident for example, the rice oil was heated, which facilitates the transformation of PCBs into dibenzofurans; therefore, he concluded, there may have been higher concentrations of furans in those mixtures than in any commercial mixture.

2.6.3 Mitch Erickson from the Argonne National Lab asked Dr. Cogliano whether there were any documented human cancers as a result of PCB exposure.

Dr. Cogliano stated that there are several epidemiological studies that increased cancer rates. Other studies do not show an elevation in cancer. He stated that some of the elevations are statistically significant. However, EPA considers the human data inconclusive. He stated that the assessment on PCBs, as with most environmental chemicals, is currently based on animal studies.

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[8] Ed. note: The question and response portion includes summaries derived from transcribed conversations. The summaries have been carefully edited to present the discussion as accurately as possible. However, these question and response summaries have not been reviewed by the speakers--unlike the proceeding abstracts.

2.6.4 Peter Somani of Columbus, Ohio, asked Dr. Cicmanec whether the doses used in non-cancer studies were comparable to those used in cancer studies. Did the dosages differ between the monkey studies and the rodent studies? Also, how is the information derived from rodent and monkey studies used to develop coherent policy involving PCBs in humans.

Dr. Cicmanec did not recall carcinogenicity studies in monkeys where comparisons could be made. He stated that in the rodent studies, doses of 100 ppm were generally used, although doses as low as 50 ppm were sometimes used. In rodents, the effects were generally seen at 100 ppm. However, the Rhesus monkey studies sometimes showed effects at dosages 100-fold lower than the 100 ppm dose.

Concerning the question on applying animal data to humans, he stated that although a wide range of studies for the non-cancer effects are available for EPA to choose from, the Agency has focused on Rhesus monkey studies, because of physiological and other similarities.

Mr. Cicmanec also noted that, in the case for non-cancer effects, his group had chosen to use a number of commercial mixtures. He acknowledged that these may not be exactly the same as the Aroclor mixtures found in the environment, but they are currently the best we have available.

2.6.5 Dr. Bolger commented that although there is a vast body of information on PCBs, regulatory agencies tend to focus on a key study (or studies) and the associated dose level. As a result, he stated, other data may be discussed, but not used quantitatively.

Dr. Cicmanec agreed and added that the other studies may be used to characterize the uncertainties associated with a risk assessment, although this information may not receive enough attention. He stated that risk managers who make crucial decisions would have better information upon which to base their decisions, rather than just using a single number.

2.6.6 Gerald Pollock of the California EPA questioned Dr. Barnes about whether it might be appropriate to develop a Toxicity Equivalent for dioxin-like PCB congeners and add that to the total TEQ for dioxin, thus deriving an overall Toxicity Equivalency calculation for dioxins in fish tissues.

Dr. Barnes agreed that this was a reasonable goal but there was no official EPA position at present. He noted that this was discussed at an earlier PCB workshop.

2.6.7 Jack Moore of IEHR commented that he believed it was going to be several years before TEQs for PCBs are likely to be established. He cited two examples to illustrate the difficulties. One was a study by Nickels and Peterson (who conducted a study last year using fish fry

mortality with PCB congeners). The study indicated that the numerical toxicity values that had been historically assigned to particular congeners seemed to be in error. Mr. Moore also cited another study which examined results of PCB rat tests, assigned TEQs on a congener-specific basis, and then used the TEQs to predict what the results of a two-year bioassay might be. The predicted results were the opposite to what had actually been observed.

Dr. Barnes acknowledged that the interpretation can be complex. He noted that Steve Safe has demonstrated antagonism within Aroclor mixtures in which non-dioxin like PCBs can reduce the apparent toxicity of the mixture, despite the presence of other highly toxic congeners.

2.6.8 David Pierce of the Massachusetts Division of Marine Fisheries commented that, from his review of recent literature in scientific journals, it appears that many areas of the country have already begun to use the TEFs for PCBs. He stated that this suggests that the carcinogenic potency factor (CPF) for dioxin could become a very significant factor in evaluating PCB toxicities. Pierce asked if any work was being conducted within EPA or elsewhere to verify the CPF for dioxin.

Dr. Barnes responded that EPA's reassessment of dioxin is looking at the current CPF. He stated that the Agency is seriously considering a different model for deriving the cancer potency factor. This could in turn affect the CPF for PCBs.

2.6.9 Brian Toal asked that, if TEFs are adopted for PCBs, whether the TEFs would likely be based on dioxin carcinogenicity or on the most carcinogenic PCB congener(s).

Dr. Barnes responded that it is unclear at this point. TEFs could be kept within the sphere of PCBs. However because the current focus is on the coplanar, dioxin-like PCBs, the TEFs will probably be related to 2,3,7,8-TCDD.

2.6.10 Peter Somani from Columbus, Ohio, asked Dr. Brown whether there was information about the type of PCBs that workers in his longitudinal studies were exposed to. And, based upon these studies, Mr. Somani asked if problems had been noted with the liver enzymes or with incidences of cancers or tumors.

Dr. Brown responded that the workers in his studies were exposed initially to Aroclor 1254 in the 1940s and 1950s, to Aroclor 1242 in the 1960s, and to Aroclor 1016 in the last few years of PCB usage. He noted that in G.E.'s studies, they tracked individual congeners. They had pharmacokinetics data for approximately 40 individual congeners for the workers study. Dr. Brown also responded to Mr. Somani by noting that there were no indications of liver disease in those individuals studies; he added that it was the absence of such clinical findings that led to an examination of the correlation between PCB levels and serum lipid levels where the covariance was identified. Dr. Brown stated that he did not conduct a study on cancer

epidemiology. However, he noted that two other groups had: one study was conducted by NIOSH, and the other was conducted by New York State. The conclusions from these studies were that there were no elevations of cancer in that study group.

2.6.11 Dr. Bolger of the FDA questioned Dr. Brown regarding the population of those studied.

Dr. Brown responded that the longitudinal study started with 194 workers in 1976. He stated that the workers had been reexamined in 1979, 1983, and 1988. He noted that for the last examination, 138 of the subjects participated. He added that, although many had left the company, his research team completed health questionnaires from 30 additional persons. He stated that the epidemiological studies have been based on all 6,300 people who have ever worked in that plant.

Dr. Bolger pointed out that those numbers represent a fairly small population, and that to see an effect in that sized population would have been unusual.

Dr. Brown responded that one would not expect to see a one in a million effect. However, he noted that for a cancer mortality effect, 6,000 people comprised a substantial group.

2.6.12 Dr. Bolger asked Dr. Brown to verify a previous remark during his presentation regarding the toxicity difference observed in humans and in mammals.

Dr. Brown stated that the different animals responded differently to the PCBs in terms of measurable parameters, such as enzyme induction or toxic manifestations. He stated that there were some commonalities among the animals, but that a total commonality was not seen.

2.6.13 Dr. Heraline Hicks of ATSDR asked Dr. Brown how many female workers were in the study cohort, and whether any of the females were observed to experience any unusual medical effects.

Dr. Brown responded that approximately 25 percent of the cohort was female and that no unusual effects were seen. He stated that metabolic clearance is slightly slower in the females, but it had little effect.

He also mentioned one of the parallel studies that was conducted by Bill Taylor (who was then with the New York State Department of Health). That study observed reproductive outcome in the plant population as a whole; Dr. Taylor observed approximately 200 pregnancies in the more-heavily-exposed women versus 200 less-heavily-exposed women. The study showed that in the more-heavily-exposed women there was a small shortening of gestation time and a slight reduction in average birth weight. However, there were fewer below-normal birth weights

recorded. Dr. Brown stated that he did not have a comparable study for this group of very heavily exposed people.

2.6.14 Peter Somani of the Ohio Department of Health described a policy dilemma that faces agencies that issue fish advisories. He explained that it is difficult to convince people to reduce their fish consumption when they are also being told that the chemical concentrations in the tissues are generally declining and that the water quality is improving.

Dr. Colborn agreed that fish are part of the protein food base that we need desperately, and until we can definitely show that all the dietary inputs come from one food source, we will continue to have a difficult time setting standards. In the interim a continued emphasis must be placed on the prevention of these problems, through increased testing and other ways to prevent the release of harmful chemicals. She emphasized the need for more developmental testing, including transgenerational effects.

Dr. Southerland stated that one of the main reasons for the workshop was to assist the states with fish consumption advisories. EPA recognized that the conference would not give participants an explicit "cookbook" approach for handling PCBs in their fish advisory program. However, the conference should give participants different information about PCBs that can be used if states adopt a risk assessment approach to fish consumption advisories.

2.6.15 Mr. Schwartz asked Dr. Brown if the participants are missing important data by not analyzing for neutral lipids; also, Mr. Schwartz asked whether testing for "neutral lipids" would clear up certain ambiguities associated with the total lipid measurement (as it relates to organic compounds).

Dr. Brown defined neutral lipids as "the sum of cholesterol, cholesterol esters, and triglycerides with the exclusion of polar lipids, meaning phospholipids." He stated that neutral lipid testing is conducted because lipophilic organic compounds are distributed among body compartments in proportion to their content of fat. A possible exception, however, is the lipids that are prominent in brain tissue, which does not pick up PCBs and DDT (unlike ordinary body fat).

2.6.16 Dr. Gerald Pollock returned to the policy problem raised earlier by Mr. Somani. Dr. Pollock did not regard the setting of revised exposure limits as a major policy dilemma, even if a new, lower value is needed. If a new, more sensitive end point is recognized, they will be begin using the new information. A problem that may arise, however, is how to balance the risks of eating fish against the benefits and how to communicate that.

Dr. Southerland noted that people may question the validity of exposure assumptions that are frequently used in risk assessments, particularly for cancer assessments (e.g., assuming maximum exposure for an entire 70-year life span). Because of this question, people are becoming more interested in effects that manifest themselves after shorter exposure periods.

2.6.17 Mr. Thomas Fikslin of the Delaware River Basin Commission then asked if the Agency was planning to move toward congener-specific risk assessments. He also wanted to know the implications for state monitoring programs that currently monitor Aroclors, and level-of-chlorination, rather than specific congeners.

Dr. Cogliano stated that he believed it was unrealistic to expect a congener-specific PCB assessment in the next several years, because the toxicity data for individual congeners is lacking and because of the difficulty establishing toxicity equivalency factors for most of the congeners. Therefore, Dr. Cogliano stated that he anticipated the use of total mixture basis in the meantime.

Dr. Barnes added that his personal belief is that the EPA is moving toward congener-specific analysis, and that it is basically a question of time.

Mr. Fikslin stated that there is a need for a long-range plan as to what to implement in the interim (while waiting for the congener data). He stated that there appears to be a long lead time in terms of getting laboratories capable of conducting a proper analysis.

Mr. Hoffmann stated that he believed that different parts of EPA were monitoring different congeners (e.g., the EMAP program). He noted that certain programs within the EPA are confronting the same issues that states are regarding analytical methods and interpretation of the data.

2.6.18 Ms. Amy Owen of the Inter-Tribal Fisheries & Assessment Program then stated that she was concerned about the absence of proof for developmental effects in humans. She stated that lifestyle habits (e.g., smoking, drinking) had an effect on development rather than the fish consumption in the study.

Dr. Colborn noted that she was aware of this factor, and stated that the Jacobson studies had adjusted for lifestyle habits.

Ms. Owen stated that another study (Dr. Hovinga's) had not accounted for lifestyle habits. Dr. Colborn stated that she would have to look at the study.

Dr. Colborn also noted that in regards to the study where women who had consumed contaminated fish and who had delivered higher weight babies, the women had actually consumed white fish, which is a far less fatty fish. These women also had consumed less fish than the cohort of women in the earlier study. She also explained that the changes noted in the

Jacobson study were very slight in regards to breast milk fat and PCB level of the mother. She noted that in a small cohort, changes would be difficult to observe.

Ms. Owen then questioned Dr. Colborn about the population decline and adverse effects that Dr. Colborn had described for various wildlife species. Specifically, she wished to know if the population decline could have been caused by factors other than PCBs.

Dr. Colborn responded that the population declines were not necessarily the result of PCBs; rather, the declines were reported in populations that were exposed to higher concentrations of organochlorine-type chemicals in the Great Lakes system since the 1950s. Factors other than PCBs could be responsible. She reiterated the need to prevent the release of detrimental chemicals and to test for developmental endpoints.

2.6.19 Mr. David Pierce questioned Dr. Southerland regarding whether the EPA will continue to provide advice to the states regarding fish consumption, specifically regarding the level of acceptable risk as 10^{-6} (as it was provided in the past), or the newer level of 10^{-5}.

Dr. Southerland answered that the Agency would provide technical guidance, when requested by a state, regarding fish consumption. She emphasized that the guidance is strictly non-regulatory. She noted that all 50 states have the Agency's current draft of how to sample and analyze fish to support state fish consumption advisories. The Agency is also working on its next guidance document for risk assessment. The risk assessment guidance will recommend procedures for assessing cancer risks, estimating exposures, IRIS information, etc. It also will include reproductive toxicity data, including appropriate end points, exposure information, etc.

Dr. Southerland stated that, following risk assessment, states have to make risk management decisions about whether to issue fish consumption advisories; EPA has no regulatory authority for fish consumption advisories. She also noted the difficulties that bordering states would experience in attempting to reach a consensus (individual states may reach different decisions with regards to the same body of water).

2.6.20 Dr. John Brown then returned to Dr. Colborn's earlier topic about multigenerational effects in the children of PCB-exposed workers. He reiterated that his study group had identified populations of pregnant women who had PCB levels above the background level. Therefore, if he could obtain specific research questions and could identify quantitative indicators related multigenerational effects, his group would be willing to explore them.

Dr. Colborn felt that Dr. Brown's cohort of women aged 15 to 35 years of age was a perfect cohort to find out whether such effects are taking place. She cited the case of DES-exposed women as an example of a subpopulation in which chemically induced alterations in sexual development resulted in transgenerational effects.

Dr. Southerland asked for clarification on Dr. Brown's statement, specifically, regarding whether it was the cohort with the high blood serum levels or the 6,000 that had the more variable exposures just slightly above background levels. Dr. Brown stated that it was the roughly 400 women who had varying levels of PCB exposure while pregnant (400 out of the 6,000). Dr. Brown stated that 200 were in a higher exposure group versus 200 in a lower exposure group.

2.6.21 Mr. Roy Martin of the National Fisheries Institute made two comments relating to how exposures to chemical contaminants are addressed in fish advisories. He recommended that, when states issue fish advisories, they explain to the public that research is often based on whole tissues and organs, not necessarily the fish fillets that people actually eat. Specific recommendations on how to reduce fat levels using different cooking methods is also useful information in an advisory.

Dr. Southerland agreed. She noted that these were two of the suggestions that the Agency would cover in its upcoming guidance. She also described how some states incorporate fish size limits into their fish advisories. This approach can allow a state to minimize exposure without depriving people of a valuable source of protein. It also helps avoid the banning of whole fisheries because of PCBs, which are ubiquitous.

2.6.22 Mr. Daniel Thomas of the Great Lakes Fishing Council then asked Dr. Brown when his reports were conducted and when the reports were made available to the scientific community.

Dr. Brown answered that the study was initiated in 1976 and is still continuing. He stated that the major results appeared after the first two series of examinations, and that his group had several major papers out in the 1985-86 period, and even smaller papers after that time.

Mr. Thomas then brought up a point regarding an earlier slide that Dr. Colborn had shown regarding animals that were at risk, specifically, the lake trout. Mr. Thomas wanted to clarify that the lake trout had never been placed at risk or extirpated because of chemicals. Instead, he noted, the lake trout was extirpated in the 1950s due primarily to habitat losses, over-commercialization and the sea lamprey. He noted that since that time, 60 million lake trout have been planted in the Great Lakes by the Fish and Wildlife Service, and overall, the population has not been re-established. He attributed this to the different genetic strains, degraded habitat, etc. He also discussed factors that affected the Coho.

Dr. Colborn responded that several other species disappeared (the bald eagle, osprey, other species) at the same time the lake trout disappeared during the 1950s. She noted that there are toxicologists that would disagree with Mr. Thomas; they believe that by now, if the lakes had been cleaned properly, the fish would have come back. Dr. Colborn acknowledged that she is presenting the issue from a toxicological perspective, particularly since the parallels are quite

convincing. She agreed that the lakes have been devastated for many years; however, in many areas the habitat has been restored and the fish are not coming back.

Mr. Thomas commented that Dr. Terry Bills conducted extensive studies on the lampreycide that is used for the control of lamprey, TMF, which show little or no effect on other species.

2.6.23 Dr. Gerald Pollock addressed Dr. Southerland's earlier comments regarding the fish consumption advisory and the fish size relationship. He agreed the Great Lakes states are a good source of information with regards to fish size, body burdens, age, etc. However, he explained that these size relationship principles may not hold true for ocean fish. In a limited study of selected fish populations, he found that the contaminant levels did not necessarily go up as the fish size increased. He speculated that as ocean and/or estuarine fish grow, they may move to different, less-contaminated niches and reduce their body burden. Thus, although the general principal is valid, site specific information may be necessary.

PART THREE
ANALYTICAL METHODS

3.1 PCB ANALYSES—AN OVERVIEW

Mitchell Erickson, Group Leader, Environmental Research Division, Argonne National Laboratory

Communication with the laboratory is key to good data quality. It is necessary to understand what the laboratory is doing to ensure there is sufficient information concerning the sample request. Often there is insufficient communication resulting in that are not appropriate for the data quality objectives.

Every analytical method basically consists of a flow scheme that starts with the laboratory receipt of the sample and includes steps for sample preparation, instrumental determination, and ultimately, data generation. Although there are various ways of conducting the analysis, the important thing to understand is that there needs to be sufficient information concerning the laboratory's requirements to ensure that they have a proper sample, conduct the appropriate procedures, and provide appropriate documentation.

Although the defensibility and documentation issue sounds like contract laboratory program legalities, even a scientific study for peer review publication needs to have its methods defended and documented.

Method 8080 (a GC/ECD method) is a method found in SW-846, which is the RCRA bible. This method is used by thousands of laboratories conducting tens, maybe hundreds of thousands of analyses. A verbatim quote from the method on how to conduct qualitative analysis is: "A choice must be made as to which Aroclor or mixtures of Aroclors will produce a chromatogram most similar to that of the residue." This suggests that there is a lot of latitude in analyst's decisions. Another quote is: "This may involve a judgment about what proportions of different Aroclors to combine to produce the appropriate reference material." It says nothing about non-Aroclor PCBs, i.e., weathered samples that no longer look like an Aroclor.

Quantitative analyses often are not much better: "Measure the total area or the height response from a common baseline." Analysts who have seen chromatograms know the difficulty in defining what is a "common baseline." This is the entire set of instructions on how to quantitate the results.

Descriptive methods are traditionally what are found in the scientific journals. This is the text description in the experimental section that describes how the person conducted the analysis, and to adapt it in your laboratory, you have to take certain liberties. This is the traditional professorial type of an approach to analytical methods.

There has been considerable evolution over the years to *prescriptive methods*, such as those found in the AOAC manual, the ASTM manual, and many EPA methods. This approach prescribes the steps that must be taken. The premise is that if all of the steps are followed precisely, the correct answer will be achieved. There are limitations to this approach. Quality control is not integrated into the methodology. Inflexible methods discourage adaptations to fit circumstances, local laboratory preferences, or professional judgement.

Performance-based methods, which have become increasingly popular over the last several years, involve a strong attempt on the part of the methodology to provide some flexibility while providing a measure of the method's performance on each individual sample. The premise is that it is not as important how one arrives at the answer provided the correct answer is obtained. This is where isotope dilution, addition of surrogates, internal standards, and other similar actions will indicate on every sample whether or not decent recoveries were obtained and whether or not interfering compounds or other factors that may have given a wrong answer were present.

PCB analysis is a complex and challenging area. Despite more than two decades of development, methods are still lacking in several aspects as discussed above. The challenges of providing routine methods that can provide good data to customers in a timely fashion at a reasonable cost continue to face analytical chemists and research is ongoing on several fronts as discussed elsewhere in this document.

3.2 RECENT PCB RESEARCH

Ted R. Schwartz, Chief Chemist, National Fisheries Contaminant Research Center, U.S. FWS, Columbia, MO

Polychlorinated biphenyls (PCBs) constitute a complex heterogeneous group having 209 possible isomers distributed among Cl_{1-10} homologues. In spite of the concern about contamination with PCBs since their discovery as environmental pollutants, much remains to be determined about their ultimate effects and fates in the environment. This lack of knowledge is due in part to the complexity of the chromatographic profile and the associated problems that must be overcome in data reduction and interpretation.

The interpretation of analytical results from PCB residue analyses is challenging from several perspectives: (1) data obtained from a single analysis are numerous (e.g., 100-150 PCB congeners are often encountered in a single environmental sample), (2) source profiles of PCB input into the environment are poorly characterized, (3) PCB congeners in polluting materials mix with congeners from other sources, and (4) a PCB mixture can undergo alteration due to metabolism and become partitioned into multiple environmental compartments that may be further changed by weathering or degradation. A thorough understanding of these processes and correlation of residue profiles with specific toxic responses requires congener specific methods of analysis and increased use of multivariate statistical tools.

Development of an congener specific method that can provide detailed information on environmental samples has been a goal of many scientists. However, after data acquisition and quantitation, a most important step remains, data must be examined for quality control and information content. The U.S. Fish and Wildlife Service (FWS) approached the problem of data reduction and interpretation from a chemometric perspective. The SIMCA (Soft Independent Modeling of Class Analogy) pattern recognition technique developed by Albano, Wold, and their coworkers is based on derivation of disjoint principal component models. These models can be used for graphical representation and classification of new samples. In the chemometric evaluation of complex profiles, data from a single analysis are viewed as a point in multi-dimensional space. Data from the analysis of many samples form a data cluster that may have structure related to such factors as exposure or distance from discharge. A distinct advantage of principal components modeling of multivariate data, such as those encountered in Aroclors and PCB residues, is that data is presented graphically rather than in a tabular format which is difficult to visually interpret. Provided that the data generated can be reduced and interpreted the most common question asked of PCB residue analyses is, what is the toxicological significance of the data? The approach FWS took to answering this question is to evaluate PCB residues in terms of "dioxin equivalents." The analysis and interpretation of PCB residues in fish provide a good example of using a chemometrics approach to data analysis by pattern recognition.

NATIONAL CONTAMINANT BIOMONITORING PROGRAM (NCBP)

Since 1967, the FWS's NCBP has measured and reported PCB levels in freshwater fish as mixtures of four common Aroclors. These measurements indicate that PCB residues in fish continue to decline in those areas of the U.S. where levels have historically been the highest. An inherent assumption in these measurements is that the PCBs in fish closely resemble Aroclors with respect to their congener compositions and toxicity(s). To determine if PCB congener residue distributions are compositionally similar to commercial Aroclors, individual PCB congeners were measured in a subset of the NCBP fish collected in 1988. Principal component analysis[9] was used to compare PCB congener distributions in fish to the PCB congener distributions of four reference Aroclors.

Lake Michigan Lake Trout

In efforts to describe the role of persistent organic contaminants in the failure of hatchery-planted lake trout (*Salvelinus namaycush*) to become self-sustaining throughout the Great Lakes, a series of studies were conducted between 1979 and 1988 to evaluate the quality of eggs taken from spawning adults. During this same period, observations were made on a number of other species found in the Great Lakes basin that suffered reproductive impairment due to the presence of organic contaminants. Some of these observations were detailed in a Workshop on Cause-Effect Linkages (1991). Based on the observations presented in that workshop and the growing laboratory evidence that PCBs, particularly the dioxin-like PCB congeners, interfere with reproduction, archived egg samples were analyzed for PCB congeners. The composition of congeners present in eggs and some adult tissue were examined to see how this composition changes over time, among lakes and from adult to egg. Eggs from southeastern Lake Michigan comprised the majority of samples tested, but eggs from other sites were used for comparisons.

Methods

Twenty-eight composite fish samples from the 1988 NCBP collection, representing 26 monitoring stations (Tables 1 and 2), were ground whole and analyzed for 115 congeners. Lake trout (LKT) eggs and sperm were taken from spawning adults gill-netted in Lake Michigan near Saugatuck, MI in the falls of 1979, 1981, 1983, 1985, 1986, 1987, and 1988 and near Sturgeon Bay, WI in the fall of 1987. Collections made from 1979 through 1984 were pooled samples of eggs from several females while eggs collected from 1985 through 1988 were from individual females. In addition, pooled samples of lake trout eggs were collected from Lake Superior near Marquette, MI in 1987 and 1988 and from Lake Huron near Alpena, MI and Lake Ontario off Yorkshire Bar in 1988.

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[9] Principal component models are bilinear projection models obtained by decomposing a class data matrix **X** into a score matrix **T** (n x F), a loading matrix **P** (F x p), and a residual matrix **E**:

$$\mathbf{X} = \mathbf{I}o\mathbf{x} + \mathbf{T} \circ \mathbf{P} + \mathbf{E} \qquad \text{[Eq. 1]}$$

Carbon column fractionation and high resolution mass spectrometry was used in the analysis of those PCB congeners in LKT and LKT eggs that induce a number of enzymes through the Ah receptor. These are referred to as AHH-active, referring to one of these enzymes, aryl hydrocarbon hydroxylase. A column (1.0 x 23 cm) was prepared with a mixture of 350 mg carbon (sized 2-10 μm) and 4.5 g of Whatman GF/D filter material. The column was characterized with analytical standards to determine elution profiles for AHH-active PCB congeners, then the samples and control materials were processed with tissue samples to assure quality control. After the chromatographic analysis, the data were arranged into a matrix suitable for pattern recognition.

RESULTS

National Contaminant Biomonitoring Program

Total PCBs were lowest at NCBP station 46 (Columbia R.) and highest at station 109 (L. Ontario). Relationships between technical Aroclors and PCB residues in fish are displayed in PC-plots (Figure 2). The dominant feature in Figure 2 are the Aroclor samples, however, Lake Superior (sample numbers 22, 37, 41 and, 62) and Columbia River (number 25) samples are clearly grouped together, apart from the main cluster, farthest from the Aroclor standards. Removal of Aroclors 1242 and 1248 (Figure 3) and then removal of 1254 and 1260 (Figure 4) from the PC-model emphasizes the relationship between groups of samples. In Figure 3, all samples lie above the line defined by a linear mixture of Aroclors 1254 and 1260. Fish samples from Lakes Michigan (14, 43, 47 and 61), Lake Huron (49), and Lake Ontario (52) group together and are separated from Lake Erie samples (12 and 51) and Lake Superior samples (22, 37, 41 and, 62). The distinction between samples from different lakes was difficult to quantitatively assess because sample sizes are limited. However, it appears that qualitative differences in the PCB profiles exist between fish from Lake Superior, Lake Erie and fish from the other Great Lakes (Figure 3). It also appears that fish from the east coast sampling stations have remarkably different residue patterns (Figure 4). These data suggests that fish populations are exposed to different sources of PCBs.

These data indicate that clustering of Aroclor samples 1242, 1248, 1254 and 1260, showed little similarity to tissue residue profiles. To report data from these fish as combinations of technical Aroclors would misrepresent the true composition of the environmental residues. The PCB residue profiles were examined further to determine the relevance of modeling a reduced data set containing 18 PCB congeners which are measured in EPA's EMAP program (PCB IUPAC numbers 8, 18, 28, 44, 52, 66, 101, 105, 118, 128, 138, 153, 170, 180, 187, 195, 206 and, 209). After normalization and extraction of principal components as described above, plots analogous to those presented in Figures 2-4 were generated. The first plot shows the relationship between the fish samples and the technical Aroclor samples, which dominate the explained variance in the data set (Figure 5). Reduction of the number of variables did not alter the conclusion that the fish samples are not similar to Aroclors 1242 and 1248. However, the EMAP data set suggests most of the fish samples lie along a line described by a linear combination of 1254 and 1260. Removal of Aroclors 1242 and 1248 from the PC-model fails

to emphasize the relationship between groups of samples (Figure 6). Most samples appear to lie on the line defined by a linear mixture of Aroclors 1254 and 1260 with the exceptions of sample 28 (Merrimack River) and 5 (Hudson River). The distinction between Great Lakes fish samples are much less clear (or lost) with the EMAP 18 measured data set even after removal of Aroclors 1254 and 1260 (Figures 7). These data suggests that the fish populations were exposed to similar sources of PCBs, which is contradictory to the 115 congener data set. The information loss resulting from the reduction in measured variables is potentially very large. This loss of information must be considered, if comparisons of sample composition are an important objective of the problem under study.

Lake Michigan Lake Trout

Chemical concentration profiles in tissue and eggs from Lake Michigan, Lake Huron, and Lake Ontario form a distinct cluster which differ from Lake Superior samples and the commercial Aroclor mixtures (Figure 8). The cluster representing samples from Lake Michigan indicate no significant change in PCB composition over the 9-year sampling period for LKT eggs and the 2-year period for adult female LKT. The distinction between samples from different lakes was difficult to quantitatively assess because sample sizes were limited. However it appeared that qualitative differences in the PCB profiles existed between LKT eggs from Lake Superior and LKT eggs from the other Great Lakes, which suggests that the two populations were exposed to different sources of PCBs. Also, the clustering of Aroclor samples 1242, 1248, and 1260, showed little similarity to tissue and egg residue profiles. A second PCA was restricted to s subset of the samples (Figure 9) which included adult tissue samples for which we had corresponding egg samples and Aroclor 1254 as a reference point due to its close proximity to the tissue and egg cluster in Figure 8. Projections of the samples for the first two PC indicated markedly different clusters for adult LKT and their eggs, and Aroclor 1254 (Figure 9). These two figures indicate that the chemical profile in adult LKT tissue and their corresponding eggs is different, and is unlike any technical mixtures of Aroclors. The difference in chemical residue profile suggests some selective deposition of PCB congeners from adult to egg. Examination of gas chromatographs revealed a greater abundance of lower chlorinated PCB congeners in the LKT eggs.

Examination of AHH-active PCB residues were unable to distinguish between adult fish and the LKT egg groups of samples. This indicates that, even though there is a greater concentration of AHH- congeners in the adult LKT, the composition is the same as in the LKT eggs. It appears from the concentration data and TCDD-EQ data in Table 3 that there is no relative enrichment of these PCB congeners from adult fish to egg. Even after lipid normalization (Table 4) no clear indication of enrichment of AHH-active PCB congeners is apparent.

CONCLUSION

The PCB congener distributions in all NCBP samples analyzed are significantly different from those of common Aroclor mixtures. Samples from stations 24 and 111 have PCB congener distribution that are most similar to those of common Aroclors. PCB congener distributions for samples from station 3 (Hudson River) appear to be similar to those of Aroclors only when samples and Aroclors are analyzed together.

Samples from Lake Superior stations 22, 102, 103, and the Columbia River station 46 are the least similar to Aroclors. Others have suggested that Lake Superior fish receive PCB contamination mostly from atmospheric sources to the lake.

Application of pattern recognition by SIMCA characterized the profiles of PCBs in a typical environmental situation and statistically showed that residues in LKT tissue and LKT eggs from various locations differ in PCB congener composition. No difference in congener composition in eggs over time were observed, indicating that the more toxic AHH-active congeners are not being selectively accumulated or enriched in lake trout. Differences in the composition of all 115 congeners between females and their eggs were observed. Egg deposition appears to select for lower chlorinated congeners, but does not influence composition of AHH-active congeners. Because the residue profiles cannot accurately be represented as Aroclors, and total PCBs was the best correlate of biological effects in eggs, PCBs should be expressed in terms of total PCB concentration and calculated by summing all individual congeners.

Table 1. Total PCB Concentrations in Selected NCBP Fish Samples Collected in 1988.

Station[1]	Species[2]	River or Lake	Locations	Total PCB [3](ng/g)
2	CHC	Connecticut R.	Windsor Locks, CT	1170
3	WSU	Hudson R.	Poughkeepsie, NY	2669
4	CHC	Delaware R.	Trenton, NJ	1166
8	CHC	Cape Fear R.	Elizabethtown, NC	480
18	WSU	L. Ontario	Port Ontario, NY	1292
19	WSU	L. Erie	Erie, PA	444
20	C	Saginaw Bay	Bay Port, MI	743
21	LT	L. Michigan	Sheboygan, WI	2263
22	LT	L. Superior	Bayfield, WI	300
23	CHC	Kanawha R.	Winfield, WV	2119
24	C	Ohio R.	Marietta, OH	3577
46	BRB	Columbia R.	Cascade Lock, OR	37
52	WSU	L. Champlain	Burlington, VT	69
52	NP	L. Champlain	Burlington, VT	174
53	WSU	Merrimack R.	Lowell, MA	608
54	WSU	Raritan R.	Highland Park, NJ	1458
66	WSU	St. Lawrence R.	Massena, NY	212
68	C	Wabash R.	New Harmony, IN	623
69	C	Ohio R.	Cincinnati, OH	2545
70	C	Ohio R.	Metropolis, IL	1342
70	CHC	Ohio R.	Metropolis, IL	1547
102	LT	L. Superior	Keeweenaw, MI	3696
103	LT	L. Superior	Whitefish Point, MI	546
104	LT	L. Michigan	Beaver Island, MI	1103
105	LT	L. Michigan	Saugatuck, MI	2174
106	LT	L. Huron	Alpena, MI	1720
107	C	L. St. Clair	Mt. Clemens, MI	3939
108	C	L. Erie	Port Clinton, OH	624
109	LT	L. Ontario	Roosevelt Beach, NY	4624
111	C	Mississippi R.	Lake City, MN	1969

1. Stations as designated by NCBP and shown in Figure 1.
2. CHC, Channel catfish; WSU, white sucker; C, Common carp; LT, lake trout; BRB, brown bullhead; NP, northern pike.
3. The sum of individual PCB congener concentrations.

Table 2. List of selected 1988 NCBP fish samples and Aroclors used for Principal Components Analysis.

Object No.	Station No.	Description	Object No.	Station No.	Deccription
1-4	2	Connecticut R.	49	106	L. Huron
5-8	3	Hudson R.	50	107	L. St. Clair
9	4	Delaware R.	51	108	L. Erie
10	8	Cape Fear R	52-53	109	L. Ontario
11	18	L. Ontario	54	111	Mississippi R.
12	19	L.Erie	55	52	L. Camplain
13	20	Saginaw Bay	56-57	69	Ohio R.
14-21	21	L. Michigan	58-61	---	L. Mich. Composit
22	22	L. Superior	62-65	---	L. Superior Composit
23	23	Kanawha R.	66-69	---	A1111 (0.1)
24	24	Ohio R.	70-73	---	A1111 (0.25)
25-26	46	Columbia R.	74-77	---	A1111 (0.5)
27	52	L Champlain	78-82	---	A1111 (1.0)
28	53	Merrimack R.	83-86	---	A1111 (2.0)
29	54	Raritan R.	87-90	---	A1111 (5.0)
30	66	St. Lawrence R.	91-92	---	1242 (0.8)
31	68	Wabash R.	93-95	---	1242 Matrix Spike
32	70	Ohio R.	96-97	---	1248 (0.8)
33-36	70	Ohio R.	98-100	---	1248 Matrix Spike
37-40	102	L. Superior	101-102	---	1254 (0.8)
41-42	103	L. Superior	103-105	---	1254 Matrix Spike
43-46	104	L. Michigan	106-107	---	1260 (0.8)
47-48	105	L. Michigan	108-110	---	1260 Matrix Spike

Figure 2. NCBP 1988 Fish, 115 PCB Variables

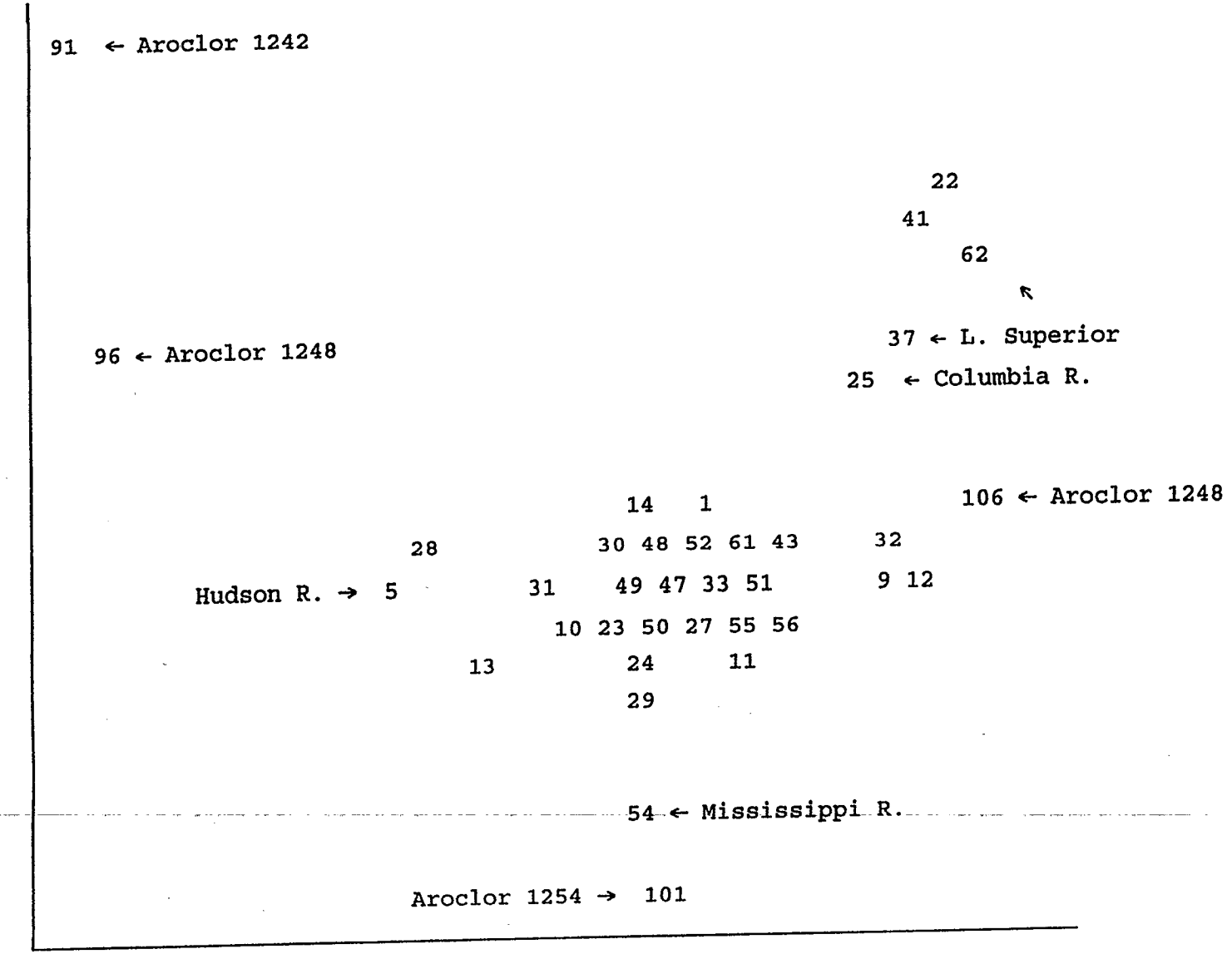


Figure 3. NCBP 1988 Fish, 115 PCB Variables

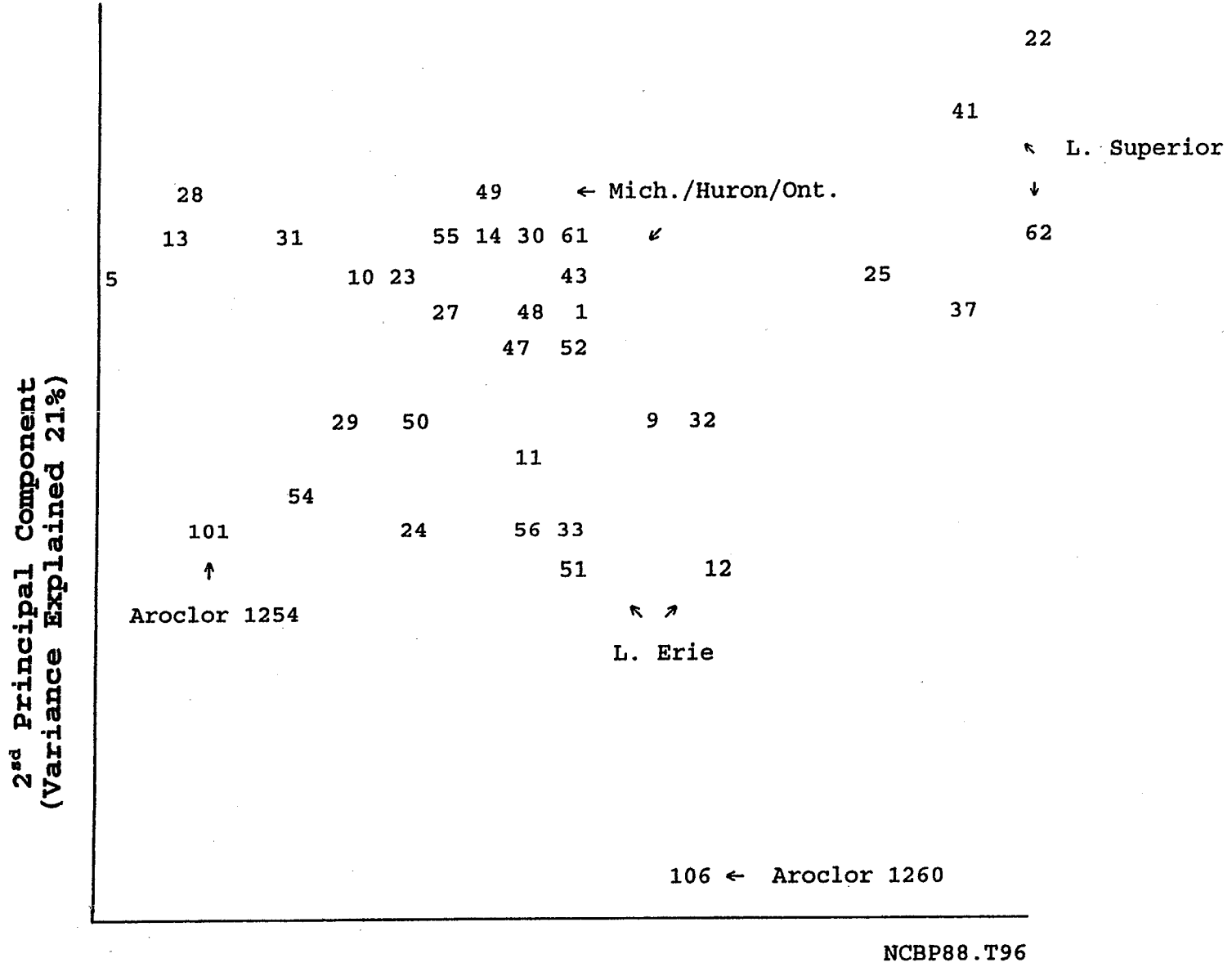


Figure 4. 1988 NCBP Fish, 115 PCB Variables

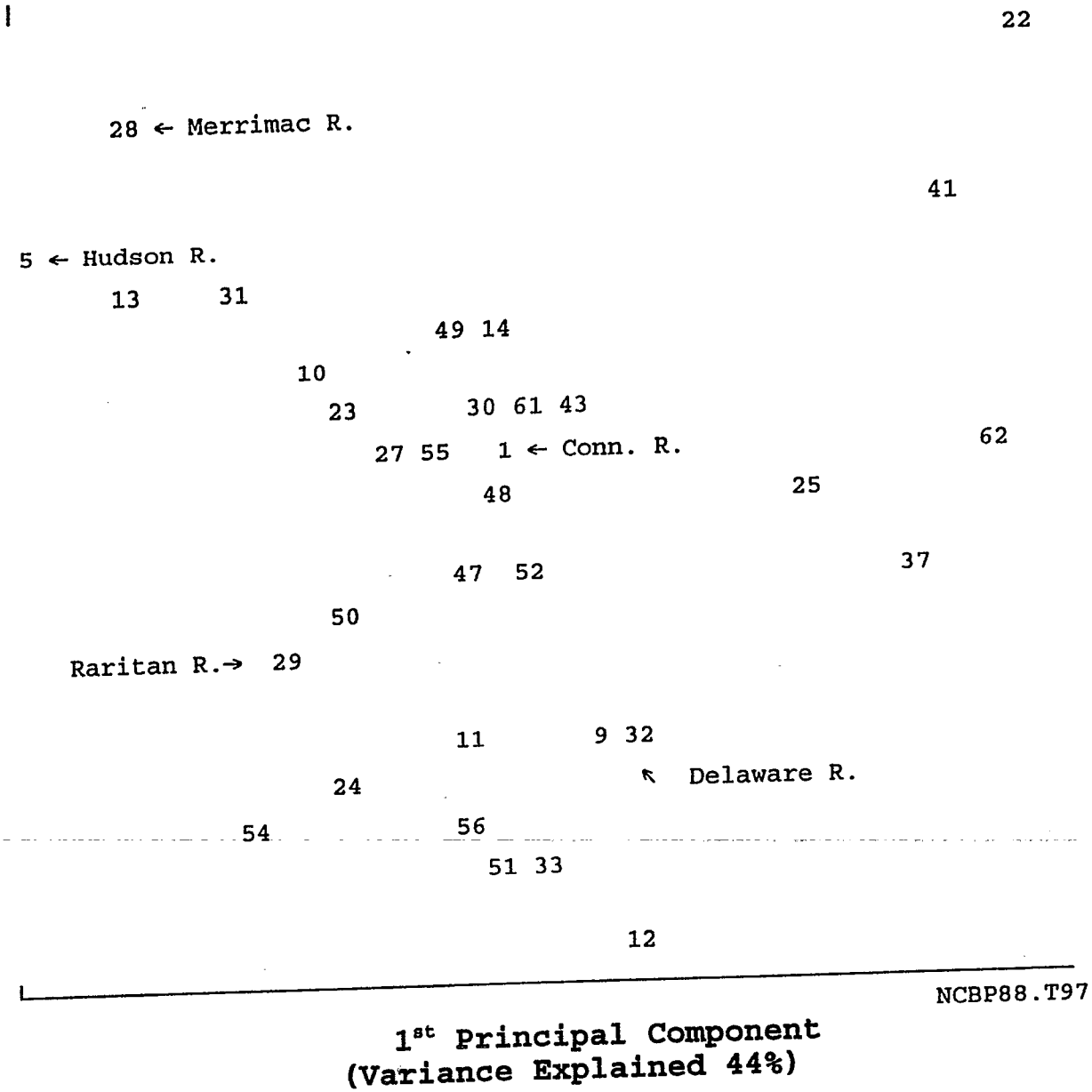


Figure 5. NCBP 1988 Fish, PCB Variables Reduced From 115 To EMAP's 18 Variables

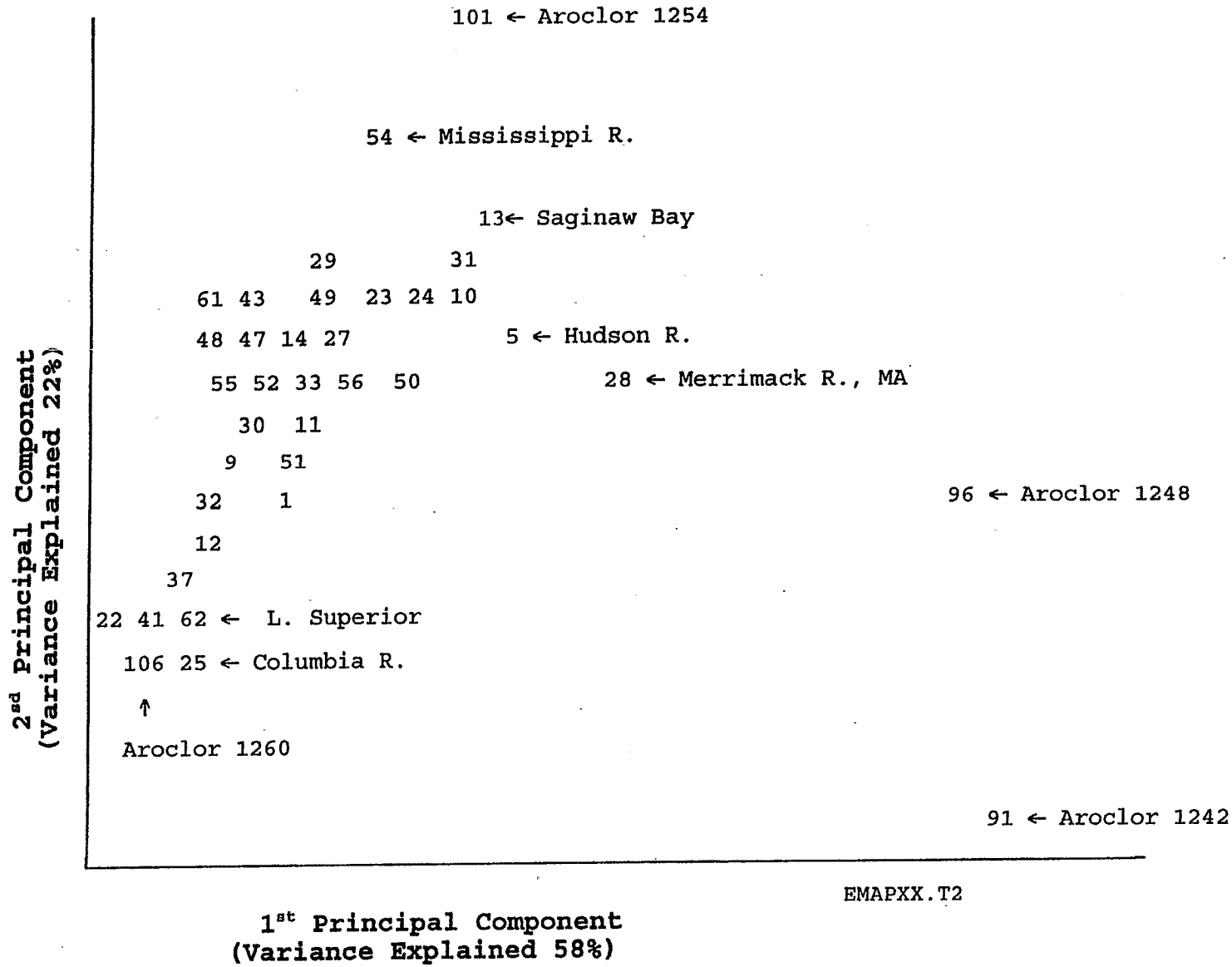


Figure 6. NCBP 1988 Fish, PCB Variables Reduced From 115 To EMAP's 18 Variables

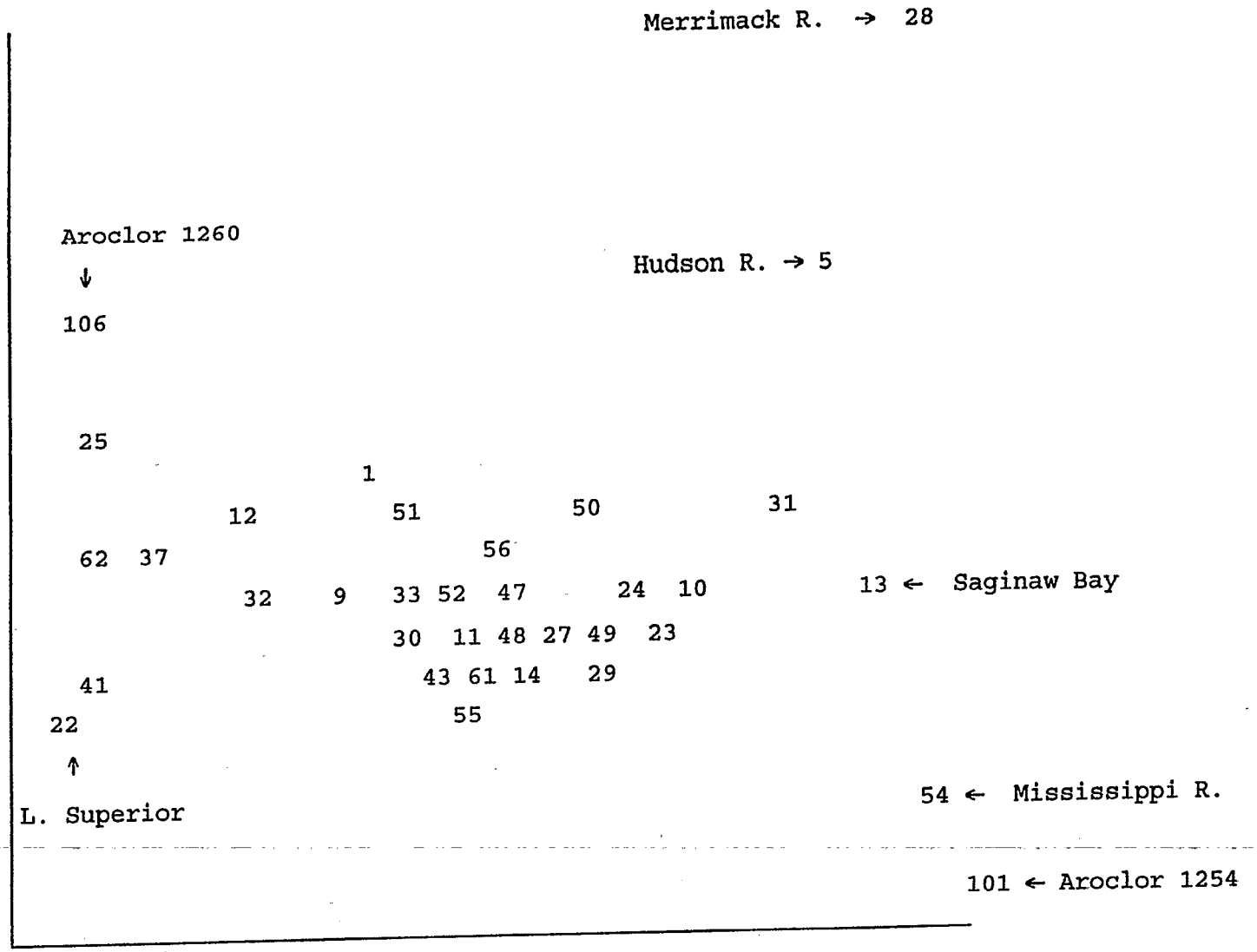


Figure 7. NCBP 1988 Fish, PCB Variables Reduced From 115 To EMAP's 18 Variables

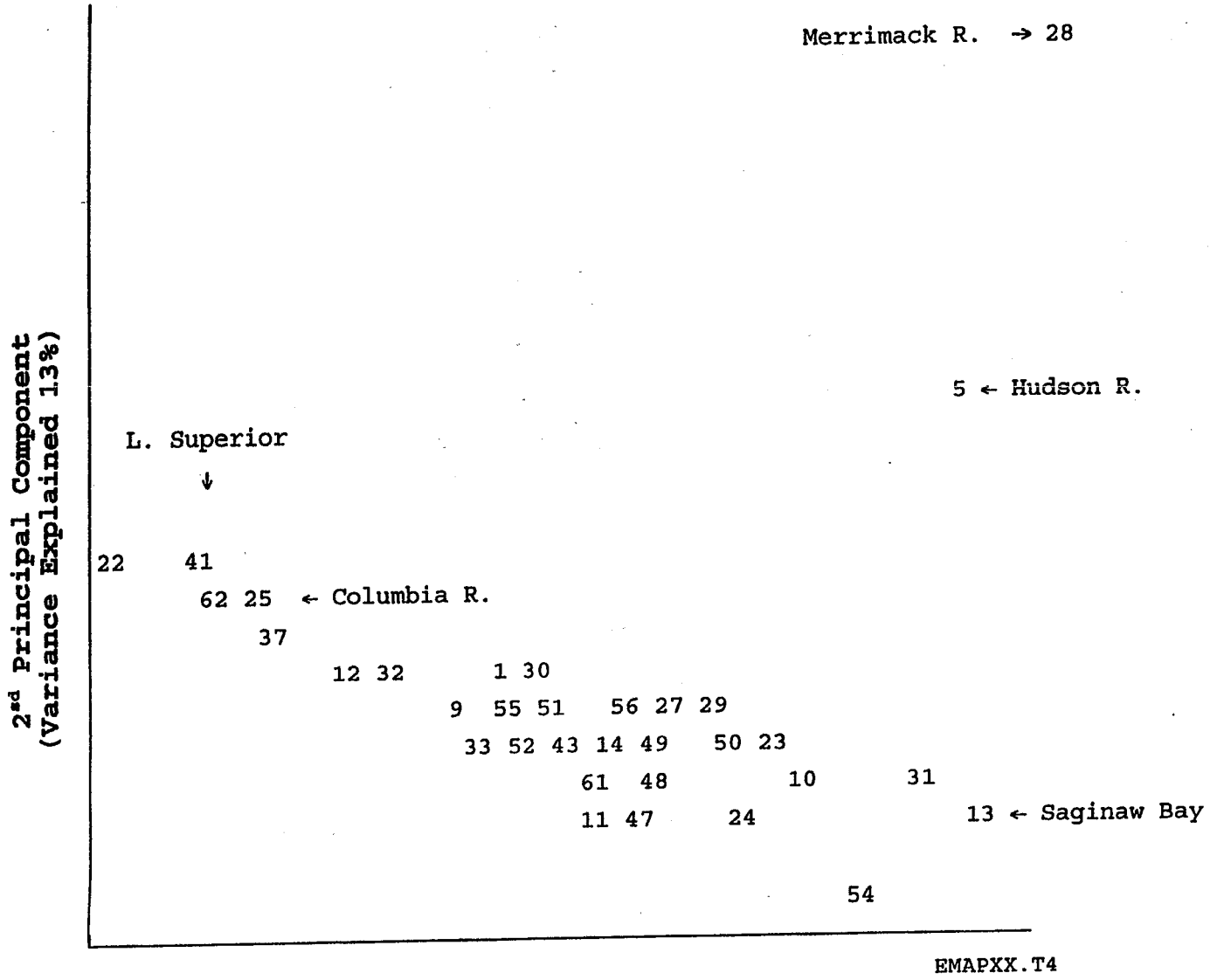
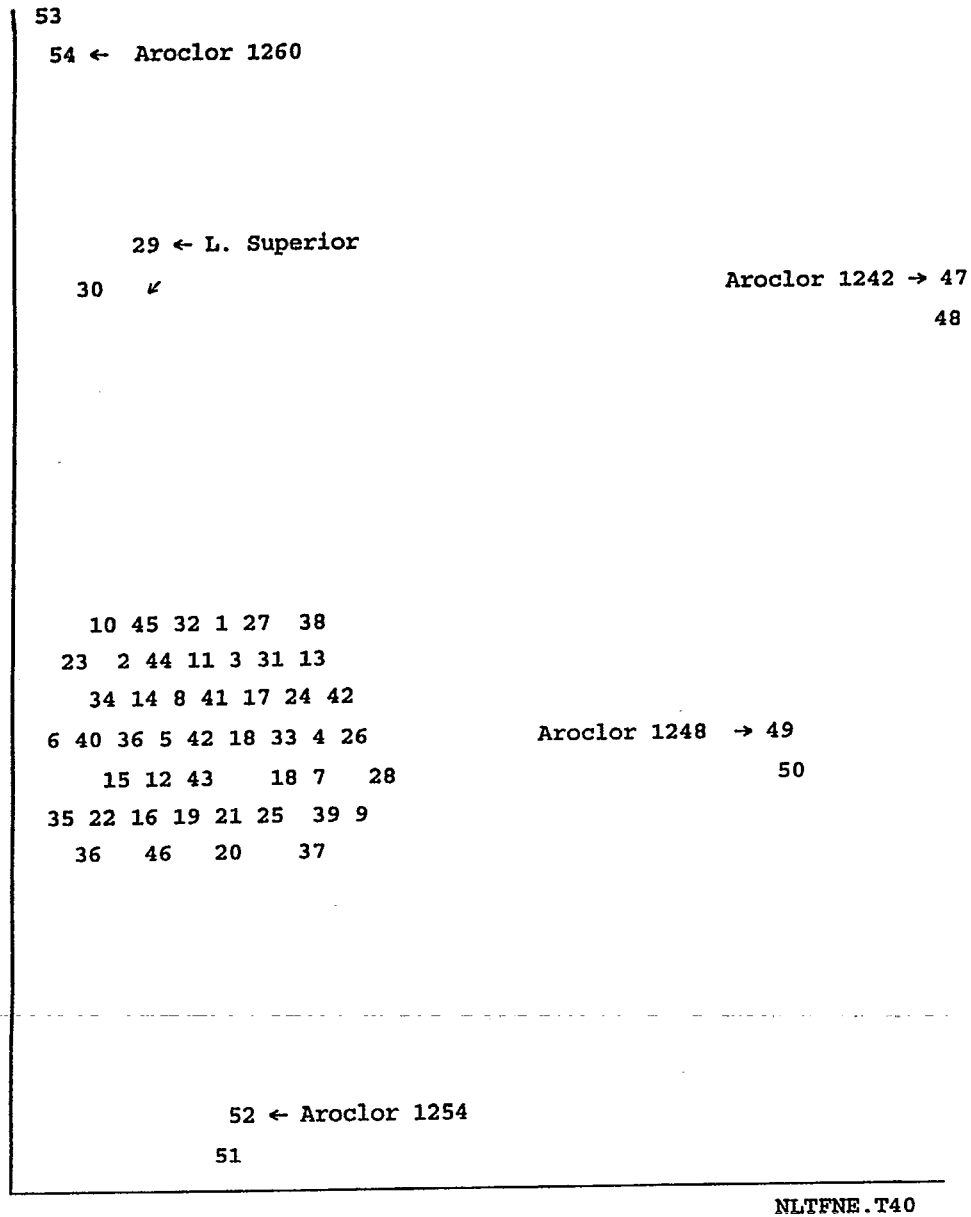


Figure 8. Principal Components Model of PCB Residues in Lake Trout Fish and Eggs.

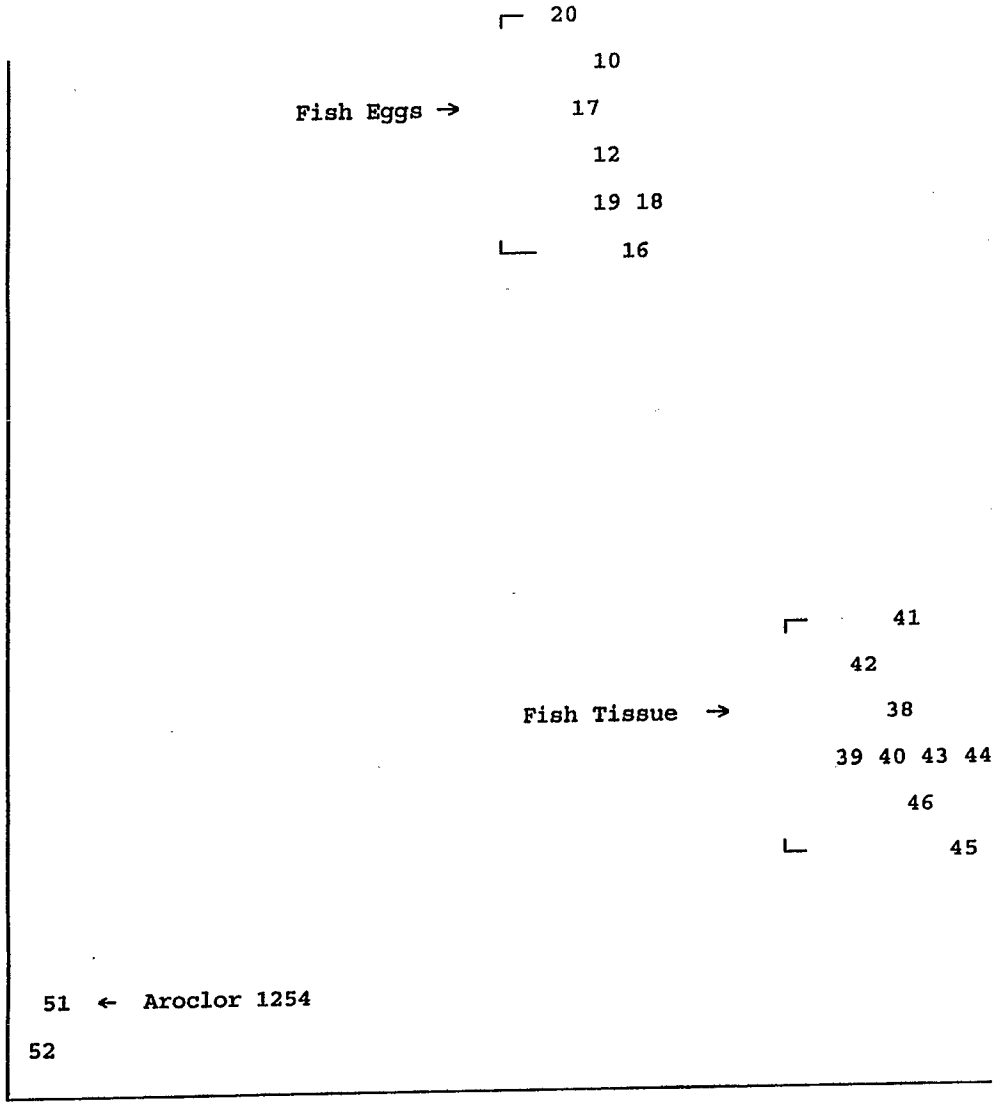


2nd Principal Component (Variance Explained 19%)

1st Principal Component (Variance Explained 50%)

	Fish Eggs		FISH	
1	Saug. (R1) 79	33	Saug. #1(R1) 85
2	Saug. (R2) 79	34	Saug. #1(R1) 85
3	Saug. (R3) 79	35	Saug. #3 85
4	Saug. (R1) 81	36	Saug. #4 85
5	Saug. (R2) 81	37	Saug. #5 85
6	Saug. 83	38	Saug. #4 86
7	Saug. #1 86	39	Saug. #7 86
8	Saug. #2 86	40	Saug. #1 87
9	Saug. #3 86	41	Saug. #2(R1) 87
10	Saug. #4 86	42	Saug. #2(R2) 87
11	Saug. #5 86	43	Saug. #2(R3) 87
12	Saug. #7 86	44	Saug. #3 87
13	Saug. #8 86	45	Saug. #4 87
14	Saug. #9 86	46	Saug. #5 87
15	Saug. #10 86		
16	Saug. #1 87		Aroclors
17	Saug. #2 87	47	Aroclor 1242
18	Saug. #3 87	48	Aroclor 1242
19	Saug. #4 87	49	Aroclor 1248
20	Saug. #5 87	50	Aroclor 1248
21	Saug. #1 88	51	Aroclor 1254
22	Saug. #2 88	52	Aroclor 1254
23	Saug. #3 88	53	Aroclor 1260
24	Saug. #12 88	54	Aroclor 1260
25	S.Bay #1 87		
26	S.Bay #2 87		
27	S.Bay #4 87		
28	S.Bay #5 87		
29	L.Superior 87		
30	L.Superior 88		
31	L.Huron 88		
32	L.Ontario 88		

Figure 9. Principal Components Model of PCB Residues in Adult Lake Trout and Their Eggs.



2nd Principal Component
(Variance Explained 25%)

1st Principal Component
(Variance Explained 62%)

Fish Eggs

10 Saug. #4 86
12 Saug. #7 86
16 Saug. #1 87
17 Saug. #2 87
18 Saug. #3 87
19 Saug. #4 87
20 Saug. #5(R1) 87

Fish

38 Saug. #4 86
39 Saug. #7 86
40 Saug. #1 87
41 Saug. #2(R1) 87
42 Saug. #2(R2) 87
43 Saug. #2(R3) 87
44 Saug. #3 87
45 Saug. #4 87
46 Saug. #5 87

Aroclor

51 Aroclor 1254
52 Aroclor 1254

Table 3. Concentration of AHH-active PCB Congeners (ng/g - wet weight) in Lake Trout and thier eggs.

Lab ID	338C-1	6057	338C-9	6058	338C-3	6059	338C-8	6060	338C-2	6051	338C-7	6053
SIMCA #	40	16	41,42,43	17	44	18	45	19	38	10	39	12
	Fish	Egg	Fish[a]	Egg	Fish	Egg	Fish	Egg	Fish	Egg	Fish	Egg
Cl4 -PCBs:												
81	1.3	0.3	1.7	0.52	1.6	0.32	0.5	0.09	2.2	0.72	1.3	1.0
77	4.1	0.71	9.7	2.1	4.5	0.88	3.0	0.43	6.2	1.6	5.1	1.7
Cl5 -PCBs:												
105	76	12	300	50	110	23	60	7.2	120	28	140	42
114	6.0	0.8	23	2.9	7.7	1.5	4.1	0.4	8.6	2.3	10	3.0
118	180	31	670	120	240	51	130	16	260	66	310	97
123	3.2	0.5	11	1.5	3.8	0.4	1.9	0.2	4.6	1.0	4.9	1.5
126	1.8	0.17	4.0	0.65	1.6	0.2	0.9	0.07	2.0	0.38	2.3	0.51
Cl6 -PCBs:												
128	63	19	340	92	96	36	78	11	120	52	120	72
138	320	45	1300	220	470	75	270	25	480	82	600	140
156	10	2.8	42	8.9	14	2.8	17	0.96	15	3.1	19	5.1
157	6.1	0.69	24	3.1	8.2	0.86	4.5	0.34	8.5	0.67	11	1.5
158	21	3.1	94	16	29	5.6	17	1.7	29	5.3	37	8.5
166	0.7	< 0.12	4.3	0.5	0.8	0.5	1.0	< 0.12	1.1	0.6	1.9	0.3
167	9.3	2.6	42	7.7	13	2.7	7.3	0.84	15	3.5	19	4.9
169	< 0.4	< 0.4	< 0.4	< 0.4	< 0.4	< 0.4	< 0.4	< 0.4	< 0.4	< 0.4	< 0.4	< 0.4
Cl7 -PCBs:												
170	31	4.4	120	21	40	7.3	26	2.4	39	7.9	54	12
189	1.3	0.22	4.8	0.67	1.5	0.23	0.9	0.07	1.7	0.22	2.1	0.34
Total PCB (ug/g)[b]	4.26	0.68	13.8	2.78	5.28	1.31	3.48	0.37	6.11	1.5	6.9	2.0
TCDD-EQ (pg/g)[c]	918	101	2220	374	891	131	511	47	1104	227	1220	298
TCDD-EQ/PCB	215	149	161	135	169	100	147	127	181	151	178	146

a Average value (n = 3) for Saugatuck fish sample.
b Congener-specific quantitative methods needed to determine total PCB residue values were used as described by Schwartz and Stalling 1991.
c TCDD equivalents calculated from several references summarized in Smith et al. 1990.

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Table 4. Lipid Normalized Concentration of AHH-active PCB Congeners (ng/g) in Lake Trout and thier eggs.

% Lipid	22	4	24	3	16	4	17	2	16	5	12	5
Lab ID	338C-1	6057	338C-9	6058	338C-3	6059	338C-8	6060	338C-2	6051	338C-7	6053
SIMCA #	40	16	41,42,43	17	44	18	45	19	38	10	39	12
	Fish	Egg	Fisha	Egg	Fish	Egg	Fish	Egg	Fish	Egg	Fish	Egg
Cl4 -PCBs:												
81	6	8	7	16	10	7	3	5	14	15	11	19
77	19	18	41	66	28	20	17	22	38	33	43	35
Cl5 -PCBs:												
105	345	308	1271	1563	683	523	347	360	741	583	1176	857
114	27	21	97	91	48	34	24	20	53	48	84	61
118	818	795	2839	3750	1491	1159	751	800	1605	1375	2605	1980
123	15	13	47	47	24	9	11	10	28	21	41	31
126	8	4	17	20	10	5	5	4	12	8	19	10
Cl6 -PCBs:												
128	286	487	1441	2875	596	818	451	550	741	1083	1008	1469
138	1455	1154	5508	6875	2919	1705	1561	1250	2963	1708	5042	2857
156	45	72	178	278	87	64	98	48	93	65	160	104
157	28	18	102	97	51	20	26	17	52	14	92	31
158	95	79	398	500	180	127	98	85	179	110	311	173
166	3	< 0.12	18	16	5	11	6	< 0.12	7	13	16	6
167	42	67	178	241	81	61	42	42	93	73	160	100
169	< 0.4	< 0.4	< 0.4	< 0.4	< 0.4	< 0.4	< 0.4	< 0.4	< 0.4	< 0.4	< 0.4	< 0.4
Cl7 -PCBs:												
170	141	113	508	656	248	166	150	120	241	165	454	245
189	6	6	20	21	9	5	5	4	10	5	18	7
Total PCB (ug/g)b	19	17	58	87	33	30	20	19	38	31	58	42
TCDD-EQ (pg/g)c	918	101	2220	374	891	131	511	47	1104	227	1220	298
TCDD-EQ/PCB	47	6	38	4	27	4	25	3	29	7	21	7

a Average value (n=3) for Saugatuck fish sample.
b Congener-specific quantitative methods needed to determine total PCB residue values were used as described by Schwartz and Stalling 1991.
c TCDD equivalents calculated from several references summarized in Smith et al. 1990.

Mac; Schwartz; et al. J. Great Lakes Research (in press) 1993

3.3 FDA PCB ANALYSIS

Leon Sawyer, Branch Chief, Methods Research Branch, Division of Pesticides and Industrial Chemicals, Center for Food Safety and Applied Nutrition, U.S. FDA, Washington, DC

The Food & Drug Administration (FDA) monitors for pesticides and PCB residues in food and feeds for food-producing animals in approximately 15-20,000 samples a year. In FY'92, this included 1148 samples of seafood, the commodity in which the highest incidence of PCB finding occur. In addition to the monitoring activities, FDA conducts a total diet study program, where food is collected from around the country, prepared "table-ready" and analyzed for pesticides and PCBs. Historically, the FDA determinative step for PCB analysis is the packed column gas chromatography using halogen-specific electrolytic conductivity detectors or the selective electron capture detectors. Results are reported as "total PCBs" by pattern matching with specific lots of Aroclor(s) as reference standard materials. The quantitative procedures used have gone through rigorous interlaboratory testing by the AOAC.

The AOAC has had four PCB collaborative studies related to quantitative procedure. The first study in 1973 was conducted to show that PCBs could be accurately quantitated by "pattern matching" with Aroclors and to show that PCB/DDT combinations could be dealt with. The second collaborative study in 1974 addressed both the extraction and quantitation of PCB residues in paperboard. The third collaborative study demonstrated that "highly altered" residues could be analyzed by packed column chromatography using a Webb & McCall approach that uses individual peaks and calibrated Aroclor standards. The last study in 1989 was conducted to demonstrate that PCBs could be accurately analyzed in blood serum using a variation of the Web & McCall approach.

Commonalities of all the quantitation methods in the AOAC are they all use packed methyl silicone columns, electron capture detection, and some method summing the "total" areas or peak heights measured from the residue against similar responses with matching retention times obtained with specific lots of Aroclor reference materials. In the Webb & McCall procedure, "total" PCB is arrived at by summing individually calculated ppm values.

Demonstration of differing toxicity among congeners and development of high resolution capillary chromatography procedures that can establish congener identity, provided a legitimate rationale for monitoring PCBs on an individual congener basis. FDA has not done so and has been criticized for not using this advanced technology. FDA rationale for following "archaic" procedures is: (1) FDA is a regulatory agency and all published tolerances are on "total" PCBs. (2) "Official" methods are available which, for regulatory purposes, is very important. (3) The "Official" methods are compatible with FDA's commonly used pesticide monitoring procedures. (4) Resource considerations do not deem it practical to equip several laboratories throughout the country to conduct individual congener analysis when most residues that are encountered, mainly in fish, actually have a chromatographic profile similar to some type Aroclor(s). The exceptions would be a residue extracted from an internal organ such as lobster tomalley or a residue isolated from a product like milk that has been altered by the digestive pathway. (5) From a

public safety viewpoint, it seems prudent to report "total" PCBs than individual congener concentrations since the question remains on which congeners are of concern—all observed toxicological endpoints cannot be attributed to those that demonstrate AHH activity.

A point that should be clarified about FDA PCB findings is that "total" PCBs are reported, contrary to an existing perception that results are "Aroclor" findings. Aroclors are used for reference standards and the identity of the reference standard(s) is/are reported to provide information that may be useful in either; (1) tracking the source of the contamination, or (2) providing some hint if higher or lower chlorinated congeners are predominant in the residue. Aroclor reference materials are used for analyses of PCB residues when it is known an Aroclor was not the source of contamination, *e.g.*, residues isolated from samples of foreign origin.

Many approaches to individual congener analysis are being used and several have been published. However, most of them target just a select few congeners and do not attempt to measure or identify them all. In fact, some laboratories use as few as 2 congeners to report quantitative results. Use of these various procedures leads to confusion when comparing interlaboratory results from identical or similar samples. As an illustration, in a laboratory comparison study of identical lobster tissues, results varied almost by a factor of 2 when different methods of quantitation were used.

Criticism of using archaic methodology and generating poor risk assessment numbers for PCBs, prompted FDA to initiate an individual congener analytical study. The method chosen to study was that described by Dr. Mike Mullin of EPA's Large Lakes Research Station in Grosse Ile, MI. Dr. Mullin, along with Dr. Stephen Safe, synthesized all 209 possible PCB congeners and then used them to characterize the congener content of several Aroclors. The Aroclors, once characterized, could be used individually or in mixtures to serve as secondary standards for determining congener identity and content from real world samples.

Interest in obtaining comparative "total PCB" values using the Mullin approach and traditional packed column procedures was not limited to FDA. Laura Maack and William Sonzogni, published comparative PCB results for 18 Wisconsin fish samples calculated by both procedures. The overall grand averages of the 18 samples were 1.18 ppm by summing the individual congener values and 1.05 ppm by the traditional packed column procedure. The authors' found the 2 data sets were correlated within a linear coefficient of 0.9854. FDA confirmed the close agreement between the 2 procedures with fish samples that had been previously analyzed in the field and reanalyzed at headquarters. The FDA headquarters study was limited to 6 samples and the overall grand averages were 1.58 ppm by individual congener summation and 1.50 ppm by packed column.

In conclusion, the Mullin procedure for individual congener analysis appears to be both a good qualitative and quantitative analytical approach that could be used for "regulatory" purposes where "total" PCBs are a concern, and for future risk calculations where specific congeners may be of concern. However, considering the resources involved and the declining

numbers and levels of PCB residues, FDA is encountering in its pesticide monitoring and total diet programs, there does not appear to be a justifiable reason to change current procedures. This does not rule out the possibility of doing limited congener investigations in cases where "high" residues are found or, resources permitting, doing limited surveys.

FDA — FY'92 Seafood PCB Findings

Total Samples	**1148**
No. Positive	**209 (18.2%)**
Violations	**5**
Range*	**< 0.1 to 3.6 ppm**

***21.3 ppm in one lobster tomalley/0.76 ppm in flesh.**

AOAC/PCB Collaborative Studies

- *Collaborative Study of the Recovery and GC Quantitation of PCBs in Chicken Fat and PCB–DDT Combinations in Fish*

  JAOAC 56, (1973) 1015-1023

- *Collaborative Study of the Determination of PCBs in Paperboard*

  JAOAC 57, (1974) 518-520

- *Quantitation of PCB Residues by Electron Capture Gas-Liquid Chromatography: Collaborative Study*

  JAOAC 61, (1978) 272-281

- *Gas Chromatographic Determination of PCBs (as Aroclor 1254) in Serum: Collaborative Study*

  JAOAC 72, (1989) 649-659

AOAC/PCB Quantitation Methods

- **Packed methyl silicone columns**
- **Electron capture detection**
- **Select reference Aroclor(s) by "pattern matching"**
- **Comparisons for quantitation - sample residue against Aroclor(s)**
  - **total area, total peak height, individual areas - summed, and relative responses vs. DCB**
- **Measure "Total PCB"**

FDA Rationale for Method Choice

- Tolerances are on total PCBs
- "Official" methods are available
- Compatible with pesticide methods
- Resources
- Most residues similar to Aroclor(s)
- Aroclors are references—*not findings!*
- Safety

PCBs (ppm) in Lobster

[Aroclor 1254 Reference]

Laboratory	1	2	3
Tissue	1.9	1.2	1.2
	2.2	1.0	1.2
	2.0	1.1	1.2
Tomalley	11.6	5.7	7.1
	10.2	5.7	7.4
	8.0	4.6	-.-

Lab 1 Capillary GC; 2 congeners compared

Lab 2 Packed column; AOAC "total area"

Lab 3 Packed column; 4 major peaks compared

Comprehensive Congener Analysis

- Synthesis of all 209 congeners (primary stds)
- Determine congener content of Aroclors
- Aroclor(s) used as secondary stds
- Internal stds for response factors
- Compare response factors for quantitation
- Results: "Individual" or "Total" basis

Analysis of Aroclor 1254

EPA Reference Aroclors: 1221:1016:1254:1262 (20:10:7:6)

Internal Standards: PCB congeners 30 & 204

Results:

EPA 1254	97% of formulation
FDA 1254	106% of formulation

60 m x 0.25 SPB-1 temperature programmed: 3 hr. chromatographic run

PCBs (ppm) in Wisconsin Fish

		Capillary	Packed
L. Michigan	Whitefish	0.52	0.52
L. Michigan	Chub	0.66	0.48
	Chub	0.78	0.59
	Chub	0.92	0.70
	Chub	0.95	0.80
	Chub	0.96	0.70
	Chub	1.1	0.83
	Chub	1.1	0.70
	Chub	1.2	0.83
	Chub	1.2	1.0
	Chub	1.4	1.2
	Chub	1.4	1.3
Wisc. River	Sturgeon	0.57	0.67
	Sturgeon	1.0	1.2
	Sturgeon	1.1	1.2
	Sturgeon	1.4	1.7
	Sturgeon	1.7	1.9
	Sturgeon	2.4	2.5
	Average (18)	1.13	1.05

Reference: Maack, L., Sonzogni, W.C. (1988) "Analysis of Polychlorobiphenyl Congeners in Wisconsin Fish" *Arch. Environ. Contam. Toxicol.* 17, 711-719.

"In general, good agreement was found between the two methods (the data were linearly correlated with a correlation coefficient of 0.9854)"

"These data suggest that total PCBs obtained by summing the individual congener concentrations in fish may be comparable to values obtained by traditional packed column techniques."

FDA Comparative Analysis

(ppm)

	Packed		Capillary	
	Field	CFSAN	SPB-1	SB-Octyl 50
Bluefish	0.19	0.16	0.17	0.23
Chin. Salmon	0.77*	0.57	0.63	0.65
Coho Salmon	0.89*	0.84	0.92	0.96
Coho Salmon	1.0*	0.92	0.94	0.75
Chin. Salmon	1.3*	1.3	1.3	1.5
L. Tomalley	5.5	5.2	5.5	-.-
Average (6)	1.61	1.50	1.58	

* Widebore capillary operated in "packed" mode by total area.

3.4 PERFORMANCE-BASED METHODS

Margaret M. Krahn, Sin-Lam Chan, and Usha Varanasi, Environmental Conservation Division, Environmental Chemistry Program, Northwest Fisheries Science Center, National Marine Fisheries Service, NOAA, Seattle, WA

This presentation discusses the methods used by the Environmental Conservation Division of NMFS/NOAA to analyze for PCBs in fish tissue. In addition, the reasons these methods were selected for use in many of NOAA's research and monitoring programs are outlined.

Before an analytical method can be selected, the particular analytes to be determined must be established, as well as the end-use for the analytical data. For example, two of the major uses for PCB analytical data are for regulatory and research purposes. The regulatory category is used in a general sense to include seafood safety. Several federal agencies require PCB analyses for a variety of end uses. For example, the EPA uses PCB data to regulate environmental quality and the FDA and NOAA to regulate seafood safety. NOAA also uses contaminant data to assess damages to natural resources and to support litigation for subsequent restoration of marine habitats. In addition, a number of groups conducting research study the relationships between concentrations of PCBs in fish and shellfish and environmental quality (NOAA, EPA), the health of marine organisms (NOAA), seafood safety (FDA, NOAA) and human health (various agencies).

The regulatory agencies often have different needs for data than do the research groups. For example, some questions that may be of interest to the regulators are: (1) Which Aroclors are being released into aquatic environment? and (2) Can a source of contamination be determined from the Aroclor patterns in fish or shellfish? To answer these questions, PCB concentrations are determined and Aroclor patterns are identified in water, sediment, or fish. These data can then provide information necessary to identify for regulatory agencies the amounts and the sources of the Aroclors and possibly those responsible for the contamination.

Researchers may ask different sorts of questions: (1) Are particular congeners preferentially bioavailable to fish? or (2) Which individual PCB congeners accumulate in the largest concentrations in fish? These question may be answered by analyzing for individual congeners in fish for comparisons to sediment concentrations or to indices of human or animal health. With the data obtained, links between PCB contaminants and various deleterious biological effects may be pursued.

NOAA established the National Status and Trends Program (NS&T) in 1984 to assess and document the status of and the long-term changes in the environmental quality of the Nation's coastal and estuarine waters. Two major projects were included: Mussel Watch, which is conducted by contractors outside NOAA, and the National Benthic Surveillance Project (NBSP) which is conducted by NMFS. The original objectives of the NBSP were to measure organic and heavy metal contaminants in sediments and in tissues of bottom-dwelling species at selected sites in US coastal waters and to determine the

prevalences of diseases as related to chemical contaminants in these fish.

In 1984, at the inception of NS&T, methods that analyzed for PCBs and other contaminants in tissue samples were excessively laborious and time consuming. Gravity-flow columns used large quantities of solvent and other materials. As a result, we soon launched an effort to develop rapid, automated methods to replace these laborious methods (Figure 1). Procedures for tissue extraction and instrumental analyses were modified only slightly. In contrast, two gravity-flow columns that separated analytes from biogenic interferences were replaced by HPLC using preparatory size-exclusion columns. As a result, the cleanup time was reduced by 75 percent, solvent consumption was cut 50-70 percent, and the cleanup was automated. This advance in methodology allowed us to increase our sample throughput substantially without an increase in staff. Furthermore, this automated cleanup has been adopted of use by government, academic, and private laboratories.

Without assuring and documenting the quality of the data from measuring contaminants, the data obtained are of little value. For example, those who assess and manage risks need to base their risk calculations on data of known quality. We use a performance-based quality assurance program in which a laboratory documents analytical methods and quality assurance/quality control (QA/QC) practices. The QA manager for the project (e.g., NS&T) selects the performance evaluation materials to be analyzed by the laboratories participating in the intercomparison exercises. The manager then evaluates the performance of the laboratories on the intercomparison exercises and accepts into the program those laboratories that have demonstrated comparability (within certain set limits) with the other laboratories. To continue in the program, laboratories must maintain performance-based QA standards.

In monitoring for NBSP, several species of bottom-dwelling fish were collected yearly at 45 sites along the Atlantic, Gulf, and Pacific Coasts. The fish were necropsied and samples of the internal organs were collected for chemical and histopathological analyses (Figure 2). Chemical analyses for PCBs, PAHs, pesticides and metals were conducted on sediments, fish livers, and fish stomach contents. In addition, bile of the fish was analyzed for PAH metabolites because these contaminants, unlike PCBs, are metabolized in the liver and excreted in bile for elimination. Several organs were analyzed for diseases by histopathology. The original analytes chosen for NBSP were those on the EPA "priority pollutant" list, which included PCBs (Figure 3). First, concentrations of all the isomers of a given chlorination level were summed and reported, and the sum of all these levels was then reported as "total PCBs." In addition, 8 individual congeners were determined initially, but that number was increased to 18 for the QA intercomparison exercises.

In the NBSP, results of the chemical and histopathological analyses were examined statistically to find any correlations that would link contaminants to diseases in the fish (Figure 4). Toxicologists then examined the data in terms of assessing the risk of the contaminants for causing health problems, such as liver and kidney lesions, in individual fish or the fish population. These analyses of the data showed correlations between

concentrations of PCBs in sediments and in fish livers, establishing the bioavailability of the PCBs and bioaccumulation of these contaminants by fish. In addition, correlations were found between concentrations of PCBs and lesions in fish livers, but because many groups of chemicals tend to co-occur (PAHs, PCBs, and pesticides), the relative contribution of each type is difficult to determine. Regional differences also were found in PCB patterns in sediments, possibly because of differences in the input sources. Furthermore, PCB patterns in the fish did not match any particular Aroclor or mixture of Aroclors, possibly due to differential bioavailability/bioaccumulation of the PCBs or to metabolism.

As a result of this research, questions have been raised: (1) Should we be measuring toxicologically important compounds, e.g., the coplanar PCBs? (2) How do the proportions of certain toxic contaminants (e.g., coplanar PCBs) found in marine species change as they are transferred up the food chain to predators at the top? and (3) Are the most important toxic endpoints being measured, i.e., should there be a change from the emphasis of cancer/tumors/disease to looking at reproductive, immune, and developmental disorders? The objectives of the NBSP program have been altered and other projects, such as the Coastal Ocean Program, have been initiated to attempt to answer these questions by evaluating links between tissue concentrations of contaminants and bioeffects, such as reproductive or immune system disorders.

The well-established NBSP continues in 1993 and last year, NMFS added a research effort in analytical methods development to its existing Seafood Product Quality and Safety (PQ&S) Program (Figure 5). Two other projects have been initiated recently: habitat research for NOAA's Coastal Ocean Program (COP) and research on contaminant levels and sources for the Marine Mammal Health and Stranding Response Program. These programs demonstrate how research objectives have changed since the inception of NBSP in 1984. For example, the NBSP has broadened its definitions of analytes and of effects—investigating those analytes with toxicological importance for inclusion in the list of analytes. In addition, the endpoints used to define effects in NBSP and COP have been expanded to include reproductive, immune, biochemical, and other disorders. The PQ&S Program includes research into developing better analytical methods for determining those contaminants (1) postulated by toxicologists as potentially harmful to human health and (2) that can be transferred to the human consumer of seafood products. For the first time, toxicology is driving which chemical and biological parameters are to be measured, as evidenced by inclusion of toxicologically important analytes and biologically significant endpoints in our contaminant programs (Figure 6). The results of the chemical and biological analyses are examined statistically to find any links between contaminants in the fish and endpoints that determine effects. Toxicologists can then evaluate the data in terms of assessing the risk of contaminants for producing health problems in the human or fish populations.

Currently, detailed analytical methods available for determining coplanar PCBs are time-consuming and laborious (Figure 7). The fish tissue is extracted and the extract must is cleaned up to eliminate lipids and some interfering analytes (PAHs). However, the coplanar PCBs are only a small fraction of the total PCBs and several coplanars coelute with other

PCBs in GC analyses. Thus, an initial separation on a gravity-flow carbon column is necessary to isolate the coplanar PCBs and improve the accuracy of the determination. Finally, the analytes are quantitated by HRGC/HRMS. Therefore, in programs requiring large numbers of analyses, e.g., monitoring or seafood safety, cost-efficiency can be increased through the initial screening of samples, i.e., rapidly identifying those samples with high concentrations of the coplanar PCBs that require further analysis by detailed methods.

We have developed a screening method for rapidly identifying and quantitating coplanar PCBs (Figure 8). PCBs in the tissue extract are separated from lipid and interfering contaminants (PAHs) on a small-size gravity-flow column of acidic silica gel. The cleaned-up extract is then chromatographed on HPLC (Cosmosil PYE column) and the PCBs are detected by photodiode array (ultraviolet) (Figure 9). The retention times and integrated areas can be calculated at any ultraviolet wavelength in the range selected for analysis. In addition, ultraviolet spectra are taken twice each second and a software algorithm compares the spectra to each other to determine peak purity and to the spectra of standard in a library to determine peak identity. Finally, PCB concentrations can be confirmed in selected samples by HRGC/HRMS or other methods.

The HPLC/PDA method provides excellent quantitative results for many of the PCBs and DDTs. A comparison of coplanar PCB concentrations obtained for NIST SRM 1588 (cod liver oil) by HPLC/PDA, NIST, and GC/ECD showed good agreement (Figure 10). Advantages of the HPLC/PDA method are low cost, the ability to confirm compound identity and purity, and the ability to select samples for detailed analyses by HRGC/HRMS. In addition, the method provides semiquantitative concentrations for those PCB congeners that coelute with other analytes and is nearly as sensitive as some of the detailed methods.

In conclusion, the objectives and methods for determining PCBs and other contaminants have evolved over the past 10 years in a number of ways. Labor-intensive procedures have been replaced by automated, cost-effective methods. The use of initial screening analyses, followed by confirmation of selected samples by detailed analyses, has lowered analytical costs and provided for rapid dissemination of results. Furthermore, toxicologically and environmentally important analytes and endpoints of effects have been chosen.

Figure 1

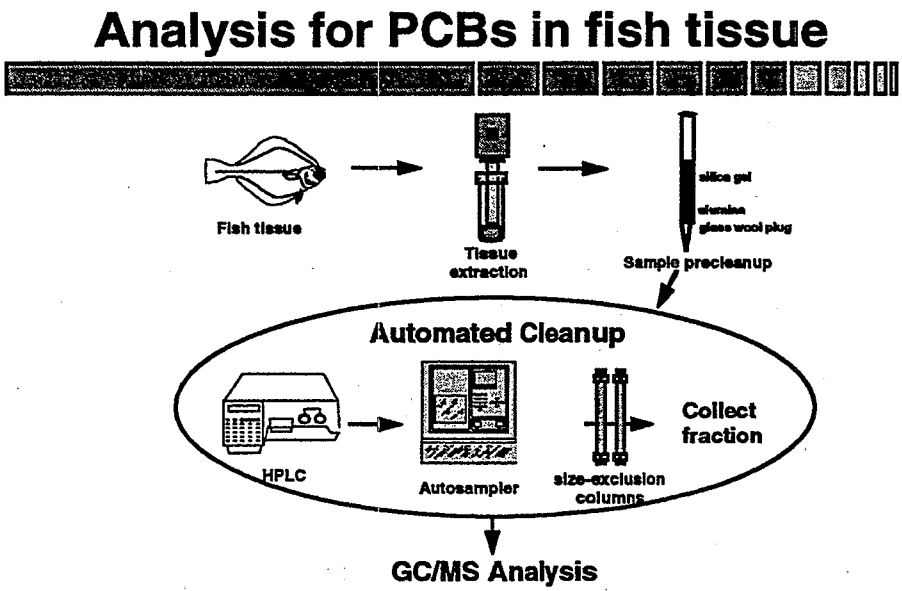


Figure 2

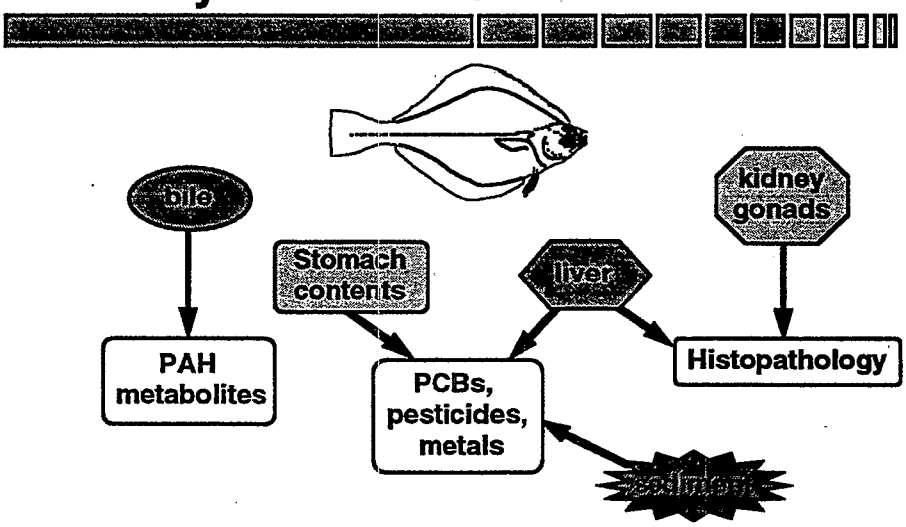


Figure 3

Original PCB analytes (NBSP)

Chlorination level	Individual PCBs (congener number)	
trichlorobiphenyls	8	18
tetrachlorobiphenyls	28	44
pentachlorobiphenyls	52	66
hexachlorobiphenyls	101	105
heptachlorobiphenyls	118	128
octachlorobiphenyls	138	153
nonachlorobiphenyls	170	180
decachlorobiphenyls	187	195
$\sum$ levels = total PCBs	206	209

Figure 4

Original objectives of NBSP Field Studies

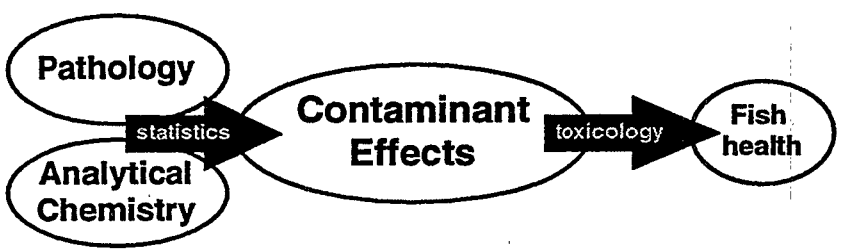


Figure 5

NMFS's Contaminant Programs—1993

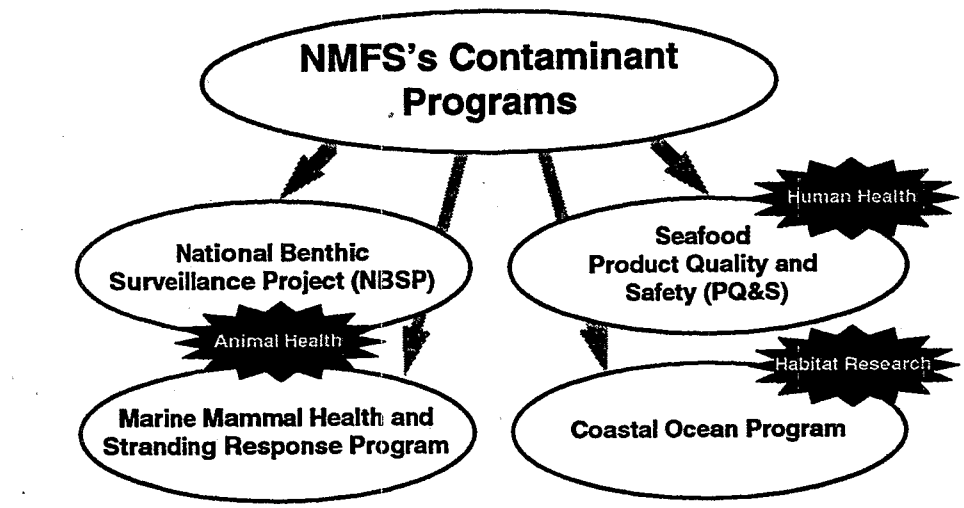


Figure 6

Objectives of the NMFS Contaminant Programs—1993

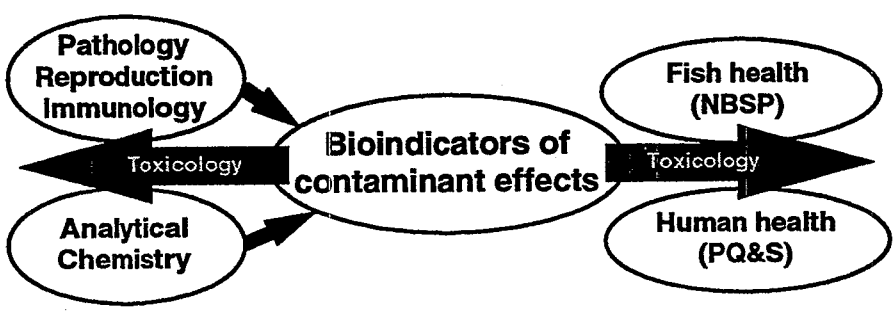


Figure 7

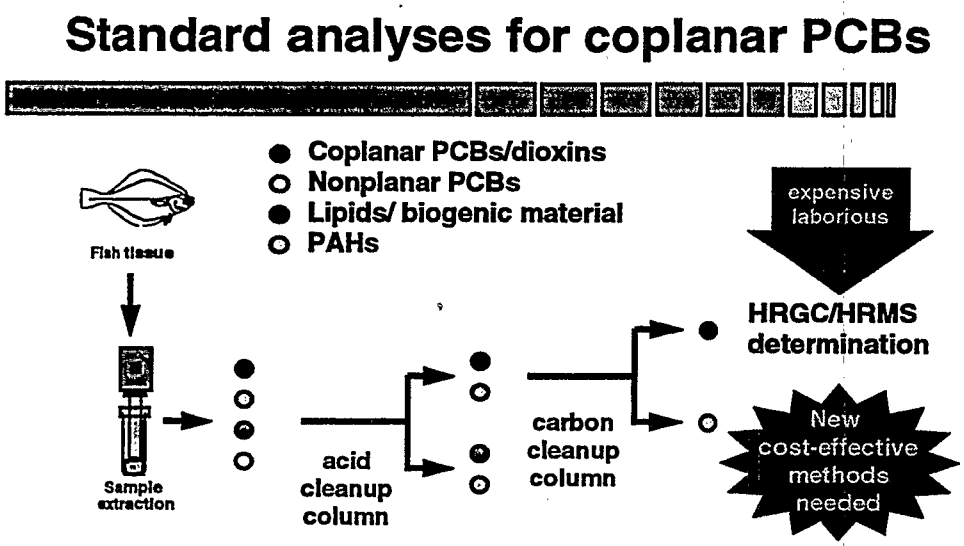


Figure 8

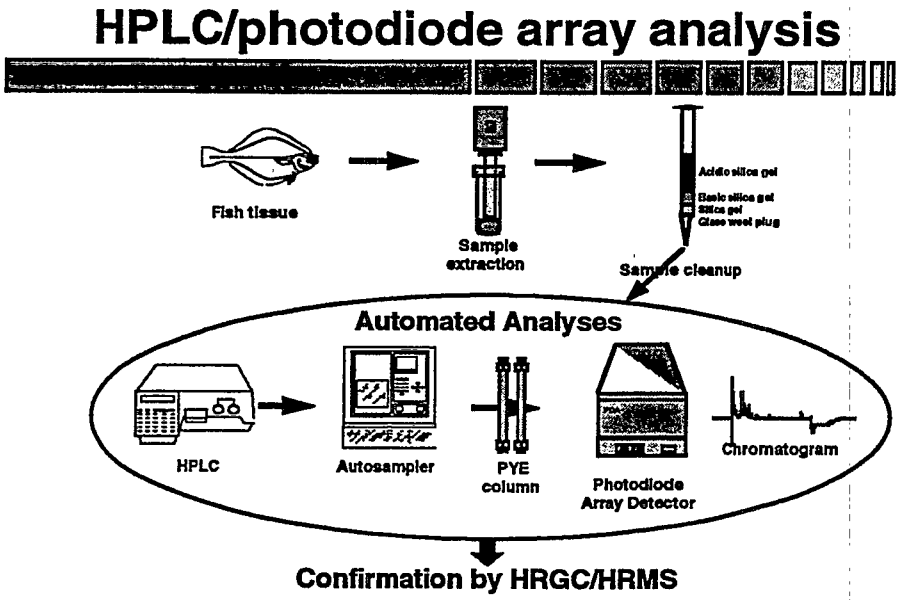


Figure 9

HPLC/PDA Chromatogram

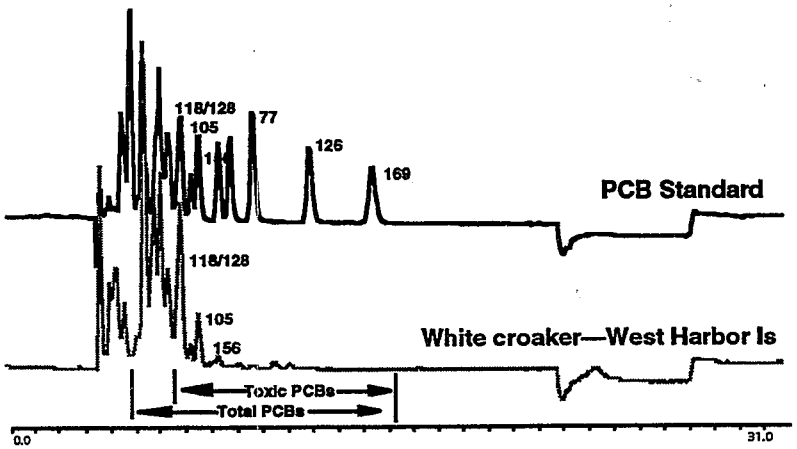


Figure 10

Method comparison—NIST SRM 1588

Coplanar PCBs (congener#)	Concentrations (ng/g) HPLC/PDA n=6	NIST certified	GC/ECD n=1
118	190±3	177±3	170
105	68±7	61±3	44
156	19±2	28±1	13
77	<1.4	ND	1.4
126	<1.2	ND	1.9
169	<1.2	ND	0.5

ND = not determined

3.5 EPA'S GREEN BAY PCB STUDY—CONGENER ANALYSIS

Deborah L. Swackhamer, Associate Professor, University of Minnesota

This presentation reviews a study conducted by the U.S. EPA Great Lakes National Program Office (Chicago, IL) that involved conducting a monitoring-level study using research-level technologies, both for sample collection and analysis. The Green Bay Mass Balance Study (GBMBS) (De Vault and Harris, 1989) was a pilot study to determine the feasibility of using a mass balance modeling approach to make management decisions regarding regulatory, remediation, and source reduction strategies. The goal was to construct a state-of-the-art fate and exposure assessment model coupled to a state-of-the-art foodchain model to be able to predict contaminant levels in fish with a low uncertainty. The need for such a model arises from lake-wide management plans of the Great Lakes and the Water Quality Agreement of 1987 between Canada and the United States. This seven-year study is in its finishing stages. One of the contaminants of interest was polychlorinated biphenyls (PCBs). To calibrate and test the validity of the Green Bay Mass Balance Model, a calibration data set of PCBs was needed for all relevant media and of sufficient temporal and spatial complexity. Green Bay, a major bay of Lake Michigan, has received PCBs historically from industries along the Fox River, which flows north through Wisconsin and empties into the southern end of Green Bay. The lower 65 miles of the Fox River at one time had 15 pulp and paper mills, 4 paper recycling plants, and 6 sewage treatment plants all contributing PCBs to the river in the form of Aroclor 1242. The interest in implementing remediation strategies in the Fox River or in the Bay made this site an ideal pilot study choice for model development and calibration.

We chose to collect a PCB calibration data set that was congener specific for a number of reasons. The primary reason was that a data set containing 80-90 congeners would provide the greatest flexibility for the model, compared to 3-4 Aroclors or simply total PCBs. A state-of-the-art model deserved state-of-the-art data. It was clear that such data would be useful to the research community far beyond the modeling effort. Having data for a wide range of compounds would also permit correlation of distribution and fate processes to compound physical-chemical properties that could be used to predict the behavior of other chemicals.

The complexity and scale of study is underscored by the number of investigators and support staff who participated in the study, and the number of analyses undertaken. Four federal agencies, two state agencies, and 14 academic institutions were involved in the study. Overall, several thousand PCB analyses were done by 8 different laboratories, including 2 federal contract laboratories, 1 federal laboratory, 1 state laboratory, and 14 academic research laboratories. Media included air (vapor and particulate), precipitation, bay water and tributary waters (dissolved and particulate), sediments, phytoplankton, zooplankton, and fish.

A study of this size required an immense planning effort. As part of this planning, a rigorous quality assurance (QA) program was designed at the onset to ensure that the data generated in the study were of sufficient and comparable quality to be used in the model

(Swackhamer, 1988). The number of sample analyses for PCBs required the participation of eight laboratories. While analytical procedures for sample handling, extraction, and cleanup were performance-based, the instrumental quantitation of PCBs was done by a specified method. The method used was an adaption of one by Mullin (1985), who characterized the weight-percent composition of each peak of a 25:18:18 mixture of Aroclors 1332, 1248, 1262 for both DB-5 and DB-1 columns by capillary column gas chromatography and electron capture detection. Investigators were provided the Aroclors needed to make this standard mixture and the weight-percent information, thus allowing the generation of congener-specific response factors. Laboratories reported data in terms of 85 components by the internal standard method using congeners #30 and #204. All data were corrected to the recoveries of surrogate standards #14, #65, and #166.

Laboratories had to demonstrate their ability to meet certain QA criteria regarding resolution, surrogate recoveries, matrix spike recoveries, precision, and detection limits. All labs were also required to participate in a "round robin" quantitation exercise to demonstrate successful application of the congener-specific method. The samples distributed consisted of vials containing different mixtures of Aroclors of concentrations ranging from 500 ng/mL to 50 ng/mL. Several also contained toxaphene, a probable interference for PCBs in the Green Bay samples. Controls also were included. In general, laboratories performed well on the intercomparison, with errors of approximately 20 percent. The presence of toxaphene did not have a significant impact on performance of the method. One laboratory had large errors at low concentrations (error = 50-100 percent). This was largely due to the problem of co-eluting interferences in reagent blanks, and underscored the need for strict control of laboratory contamination when doing congener-specific analyses at trace levels.

This study demonstrated that congener-specific analyses can be used for large scale operations such as monitoring programs. The implementation of these methods requires certain capital investments including chromatographic data processing software, significant time investments, and greater attention to field, reagent, and procedural blanks. In return, laboratories obtained analytical capability that allows for greater flexibility in their projects and contracts and in the use of data. In the case of Green Bay, we generated a "platinum" self-consistent data set that will be used to understand environmental processes for years to come, and introduced several analytical laboratories to state-of-the-art PCB quantitation techniques.

References

De Vault, D.S. and H. Harris, 1989. Green Bay/Fox River Mass Balance River Study, U.S. EPA Great Lakes National Program Office, Report #06-89, Chicago, IL.

Mullin, M, 1985. PCB Workshop, U.S. EPA Large Lakes Research Station, Grosse Ile, MI.

Swackhamer, D.L., 1988. Quality Assurance Document for Green Bay Mass Balance Study: PCBs and Dieldrin, U.S. EPA Great Lakes National Program Office, Chicago, IL.

WHY CONGENER-SPECIFIC ANALYSES?

- **Greatest flexibility for model**
- **Provide valuable data set for future efforts**
- **Allow measures to be correlated to pchem properties which enables extrapolation to other chemicals**
- **To retain involvement of research community**

QUALITY ASSURANCE PROGRAM

To ensure that all data generated in study were of sufficient and comparable quality to be used in the mass balance model.

- **Coordinated 8 laboratories for PCB analyses**
- **Approved all sampling SOPs**
- **Approved all analytical SOPs**
- **Required congener-specific PCB analysis of all air, water, sediment, plankton, and fish samples (thousands!)**
- **Conducted Round Robin for PCB analyses**
- **Visited each lab to aid in troubleshooting problems**

METHOD OF QUANTITATION

(Adapted from Mullin, 1985)

- **Quantitation Standard: 25:18:18 mixture of Aroclors 1232, 1248, 1262 which contains all environmentally-significant congeners**

  Weight-percent of each component characterized for DB-5, DB-1 resolution

- **Internal standard method using IUPAC #30, #204**

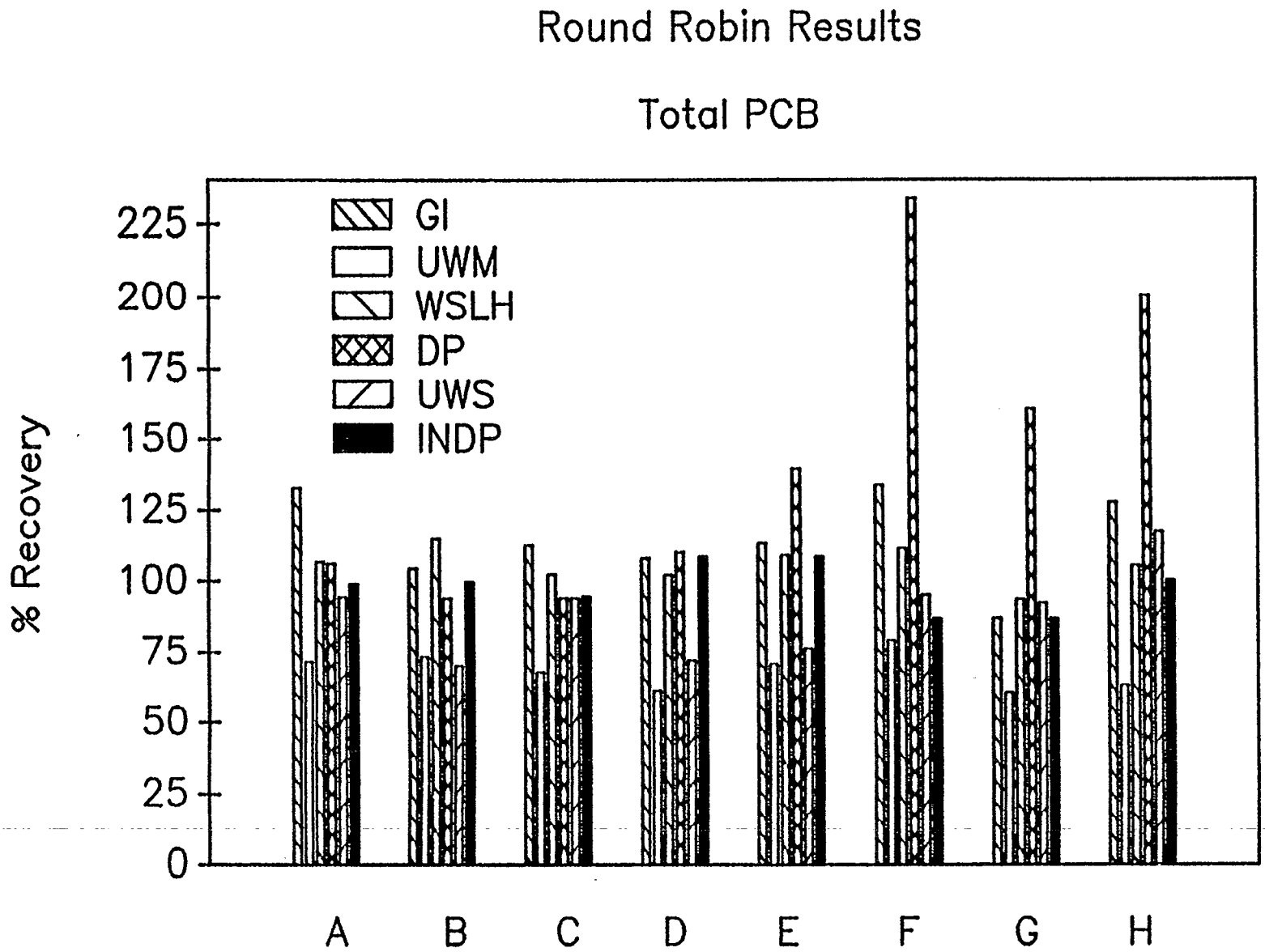
- **Surrogate standards required to monitor recovery efficiencies: IUPAC #14, #65, #166**

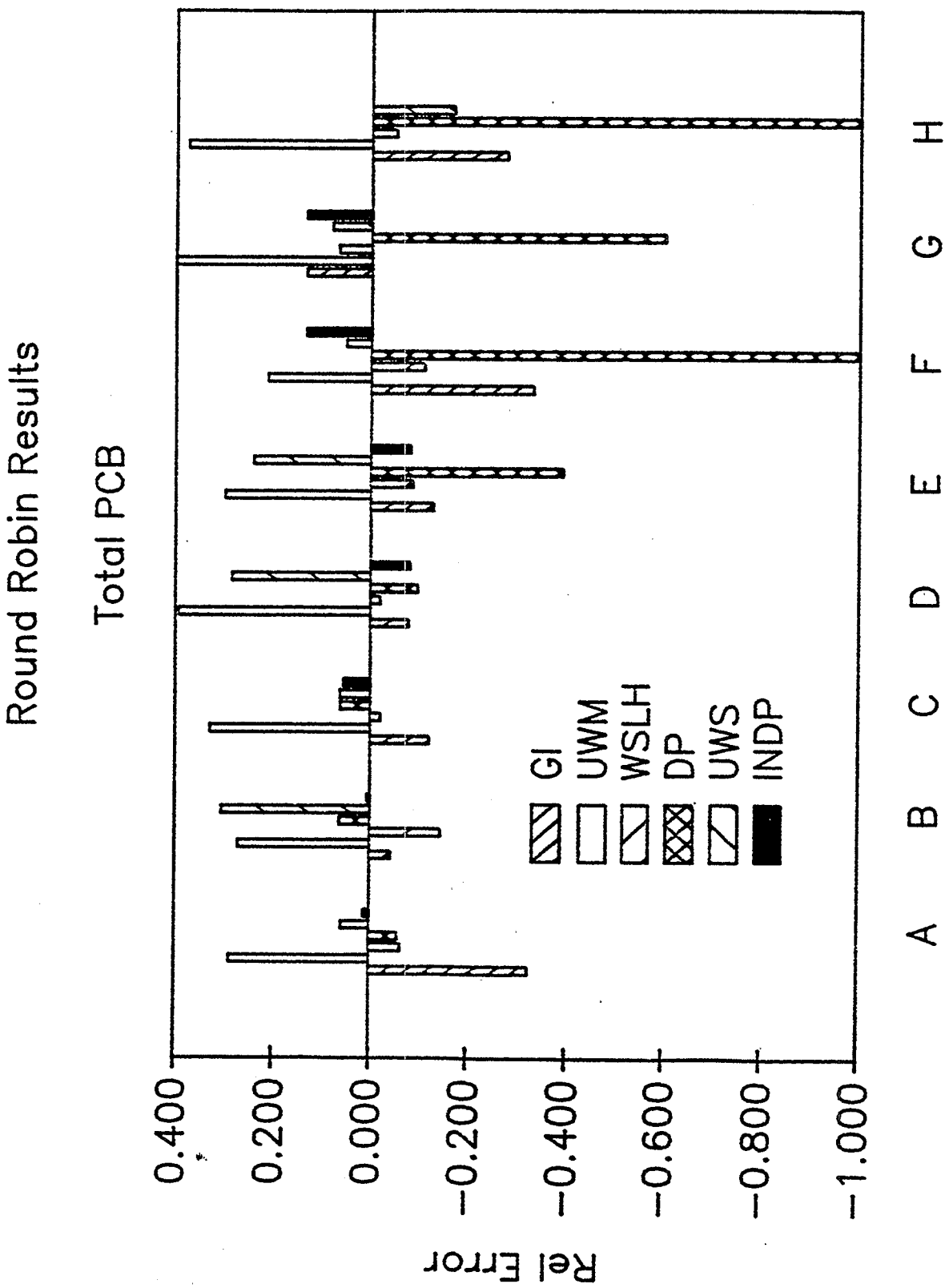
- **All data corrected to surrogate recoveries**

- **Each lab reported 85 congeners (common denominator) using DB-5 column**

QA CRITERIA

- Resolution of congeners #17 and #18
- Surrogate recoveries of 50% $<$R $<$120%
- Spike recoveries of 50% $<$R $<$120%
- Duplicate precision $\pm$50%
- Monitor ratio of #30/#204
- Blanks: $<$10% of samples (peak basis)
- Congener-specific LODs, LOQs


Round Robin Results
Total PCB
% Recovery
225
200
175
150
125
100
75
50
25
0
GI
UWM
WSLH
DP
UWS
INDP
A
B
C
D
E
F
G
H


Round Robin Results
Total PCB
Rel Error
0.400
0.200
0.000
-0.200
-0.400
-0.600
-0.800
-1.000
A
B
C
D
E
F
G
H
GI
UWM
WSLH
DP
UWS
INDP

WHAT DID IT TAKE?

- Required computerized chromatographic acquisition and processing software
- Required greater attention to blanks
- Required extensive implementation time

WHAT DID WE GET?

- "Platinum" data set
- Ability to model congeners, homologs, total PCB
- Upgraded several labs to state-of-the-art

3.6 STATE LABORATORY EXPERIENCE

Brian Bush, Research Scientist V, New York State Department of Health, Wadsworth Laboratories, Albany, NY.

A congener specific analysis for PCBs is described that has been used for the analysis of several matrices, including fish, for the past 10 years in the Wadsworth Laboratories. A 5 g sample of homogenized fish flesh is ground 3 times with anhydrous sodium sulfate and hexane using a Tissuemaster. The hexane extract is evaporated to 2 mL and purified on a calibrated 10 g column of 4 percent deactivated Florisil. A 1:1:1:1 mixture of Aroclors 1221, 1016, 1254, and 1260 (200 ng/mL of each) is used to calibrate the electron capture detector and the gas chromatograph (Aroclor 1221 is incorporated in the mixture because many of our samples are from the Hudson River, which is polluted by mono- and dichlorobiphenyls). The calibration mixture has been carefully characterized using 56 synthetic PCB congeners and with reference to the work of Mullin *et al* and Schultz *et al.* p,p'-DDE, mirex, and hexachlorobenzene also are added to the mixture (10 ng/mL of each). In all on 5 percent phenylmethylsilicone columns, 68 PCB containing peaks are calibrated plus the three other pesticides. A confirmatory column of Apiezon L also is employed. Altogether, 85 PCB congeners, which represent the major compounds distributed in the environment, may be quantified using combined data from each column.

The resultant massive quantity of data requires electronic data processing. We rely on the microprocessor of the Hewlett Packard chromatographs we employ to carry out the primary quantitation, sending the quantitative data to IBM compatible personal computers where they are labelled and formatted in a Lotus 1,2,3 spread sheet (see *Laboratory Lotus, A Complete Guide to Instrument Interfacing*, L.M. Mezei, Prentice Hall, Englewood Cliffs, NJ, 1989). Checking the performance of the system is then simplified and editing is easily carried out by reference to the hard copy chromatogram, all changes being indelibly recorded on the chromatogram, to produce what has been described as "platinum" data. The finished Lotus spread sheet is then easily accessible for data evaluation by investigators in epidemiology, toxicology, and environmental studies.

The minimum detection limit (MDL) at which the probability is <0.01 that the compound is not present and >0.988 that it is present (alpha and beta) is determined by doing seven replicate determinations at a level near disappearance of the signals of the compounds of interest (relative standard deviation >20 percent). The standard deviation of the measurements is multiplied by the Student's t for 6 degrees of freedom and $p=0.01$, the result is defined as the MDL. To obtain a similar value for "total PCB" that is the sum of all PCB, the synthesis of variance theorem is employed. The square of the standard deviation of each PCB congener measured is summed, the square root of this sum is multiplied by Student's t for 6 degrees of freedom, $p=0.01$.

We analyzed 60 striped bass samples from the Hudson River estuary, the NY Bight, and Long Island Sound by the above method ("Polychlorinatedbiphenyl (PCB) Congeners in Striped Bass (*Morone saxatillis*) from Marine and Estuarine Waters of New York State Determined by Capillary Gas Chromatography," Bush, B., Streeter, R.W., and R.J. Sloan, 1989, *Arch Environ Contam Toxicol* 19:49-61) to determine whether the quantity of less toxic PCB derived from Aroclor 1242 would change the estimated risk for human consumption purposes. The samples had been analyzed by a contract laboratory using a packed column method similar to the method of Webb and McCall (1973). The correlation coefficient between our data and the contract laboratory's was 0.91. Congener specific Apiezon L analysis separated 2,2'- and 2,6-dichlorobiphenyl from each other and allowed a typical Hudson River signature to be observed in some fish from as far removed from the river as Mantouk Point (150 miles).

In conclusion, it is possible to undertake accurate multi-component analysis and to make significant discoveries in studies of the environment, toxicology, and environmental health. To do this, electronic data transfer to user friendly PC-based software is mandatory.

3.7 SUMMARY OF QUESTIONS AND RESPONSES[10]

3.7.1. Dr. John Brown of General Electric asked Ted Schwartz about the problem of reporting results in terms of principal components. For example, Dr. Brown stated that there never appears to be a unit describing what the principal component is. Dr. Brown continued, stating that the results are simply a mathematical artifact indicating that a given composition is described in terms of correlation with component 1, component 2, etc.

Ted Schwartz responded that his presentation plotted samples in score terms, which are related to the composition in the parent samples. He indicated that his group has loading terms that do not display any of the particular variables that would influence where the congeners fit in the data space. For example, he stated that if loading terms from the EMAP data set were shown, one could see that the separation was driven by primarily by just two congeners. He stated that when analyzing the congeners in the EMAP program, perhaps one should question whether the most appropriate congeners are being measured.

3.7.2. Jack Moore from IEHR questioned whether the current scientific focus on AHH-active congeners is appropriate; perhaps the wrong congeners are being analyzed and evaluated. Perhaps not enough attention is being given to other congeners (e.g., non-AHH congeners which show tremendous accumulation potential).

Ted Schwartz responded that congeners are measured according to the established benchmark (e.g., the 2,3,7,8-TCDD dioxin). He noted that based upon this benchmark, the congeners are measured for relative importance and influence.

3.7.3. Rich Pruell from EPA's Narragansett Laboratory commented to Mr. Sawyer of FDA that measuring of total PCBs [as Aroclors] may not actually be a "conservative" approach. Mr. Pruell pointed out that in highly altered residues (e.g., lobster tomalley), there can actually be selective enrichment of the AHH-inducing compounds. Thus one may be underestimating the toxicological potential of the mixture.

Mr. Sawyer's response was that a total PCB analysis should include the AHH-active congeners. John Brown of General Electric agreed with the FDA in their total PCB interpretation. He stated that, if the measure of human risk is in terms of the levels of the persistent congeners (as the toxicological data appears to indicate), then the classical approach of examining the major peaks and matching them to an Aroclor standard is actually measuring those peaks that will be persistent and will ignore those peaks that will not

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[10] Ed. note: The question and response portion includes summaries derived from transcribed conversations. The summaries have been carefully edited to present the discussion as accurately as possible. However, these question and response summaries have not been reviewed by the speakers--unlike the proceeding abstracts.

accumulate in humans.

3.7.4 John Brown noted that Dr. Bush measured PCB congeners in his fish tissue studies and that the congeners varied tremendously from fish to fish, depending on the depuration that has occurred. He asked how Dr. Bush could infer that the source of these congeners was a capacitor-type PCBs, such as Aroclor 1242--especially since Aroclor 1242 represented 50% of all PCB sales and was widely used throughout the country.

Dr. Bush replied that there were several indications. One was the occurrence pattern of the 2,2,2,6 congener. Another was the presence of all the congeners that belong to 1242 in macroinvertebrate samples. He described a mathematical procedure he used that indicated a strong correlation.

PART FOUR
CASE STUDIES:
HUMAN HEALTH/RISK ASSESSMENT

4.1 CALIFORNIA

Gerald Pollock, Acting Chief, Fish and Sediment Contamination Unit, Pesticide and Environmental Toxicology Section, Office of Environmental Health Hazard Assessment, California EPA, Sacramento, CA

The Department of Health Services (DHS) issued an interim health advisory in 1985 for consumption of contaminated fish in the southern California area based on elevated DDT and PCB levels. The California State Legislature then mandated that DHS conduct a study of chemical contamination of marine fish and conduct a health evaluation.

DHS initiated a series of studies of chemical contamination of marine fish in southern California and the Office of Environmental Health Hazard Assessment (OEHHA; previously in the Department of Health Services) conducted a risk assessment based on the results. Four studies were proposed; an initial pilot study, a comprehensive study and risk assessment, an investigation of commercial fishing in the area, and a study of human breast milk.

The first study, the Pilot Study, was designed to identify the chemicals of concern in fish tissues. A few indicator fish species were sampled at highly contaminated locations and analyzed for the priority pollutants and selected additional pesticides. The results of the Pilot Study identified DDT (and metabolites) and the PCBs as the main chemicals of concern.

The Comprehensive Study followed the Pilot Study and examined the levels of the chemicals of concern in tissues of several fish species from multiple sites. Twenty-four sites were selected for sampling and between 5-10 different species of fish were sampled at a single site. In all, fifteen different species (or groups) of fish were sampled in the study. Sites were selected to represent areas frequented by party boat, private boat, and pier anglers. Fish species were selected to represent those species frequently caught and consumed by anglers.

Tissue samples were obtained from the edible flesh of each fish and composite samples were homogenized and extracted for analysis of DDT and PCB levels. The results indicated significant contamination of some species of fish at several sites. In general, white croaker were the most contaminated species at a given site. This was especially true at highly contaminated sites. The data were used in the OEHHA risk assessment and site/species specific consumption advisories were issued based on the risk assessment.

The risk assessment included evaluation of risks due to consumption of fish contaminated with PCBs. PCB residues were quantitated using an Aroclor 1260 equivalent concentration and the cancer potency factor for Aroclor 1260. However, the evaluation noted problems in addressing risks due to PCB residues. Specifically, the limit of detection for PCBs (50 ppb) was above a human health based level of concern. In addition, it is known that the residues in fish tissues represent a mixture of Aroclor 1242, 1252, and 1260 congeners and are not identical to the original mixtures (e.g., weathered residues).

The Santa Monica Bay Restoration Project conducted a small scale follow-up study in 1991 of chemical contaminants in white croaker (10 sites) and yellow crab (2 sites) in the same area. The SMBRP study quantitated PCB levels using congener specific analyses and summed total Aroclor equivalents. These data will be used in a future risk assessment.

Risk assessment of PCBs in fish tissues presents several problems for the regulator. These problems are scientific and public (communication). The scientific problems involve interpreting the toxicological significance and potential carcinogenic potential of PCB congeners. The use of toxicity equivalent factors has been proposed for use in risk assessment of PCB congeners (congeners with "dioxin-like" activity) to improve this process. However, consensus within the scientific community has not been reached regarding this approach. Still, most agree that improvements in risk assessment of PCB congeners is desirable.

Public problems are more difficult to identify because they involve interpretation of scientific information by a variety of non-scientific sources. Frequently, one "expert" will criticize an evaluation of PCB residues by citing the results as "not state-of-the-art." Such allegations by experts (frequently academics) raise questions of credibility on the part of the public and undermine public confidence in an assessment. Also, it is difficult to explain to a non-scientific population the chemical complexity of PCBs and even more difficult the toxicological uncertainty associated with PCBs. Contradictory statements by experts add to the public's confusion.

The scientific community should determine where we are in the process of interpreting the health significance of PCB residues and chart a course for future changes in the process. We need to agree on a process for conducting risk assessments in the meantime (Do we still use the q* approach using the Aroclor 1260 potency factor?).

We then need to identify how we will move (improve) the risk assessment process and answer key questions in charting this movement. Are we just about ready to use the TEF approach? How do we handle the potential effects caused by "non dioxin-like" congeners?

It is worthwhile for regulatory agencies to invest effort into studying ways to improve the presentation of PCBs to the public. I foresee that we will be going back to previous assessments and doing re-assessments once we have decided on consensus (TEF?) approach and then either issuing new advisories or lifting existing advisories. These actions may

confuse the public who may then feel betrayed.

And the point here, is that it is all in the name of progress. We are moving forward. PCBs are a huge problem and we need to find a way to maintain the public credibility in our process, as much as possible, as we move toward improved methods of risk assessment for the PCBs. Coordination and cooperation by scientists will serve the regulatory community and the public. Workshops like this one serve to facilitate the communication process and coordination among involved scientists during these dynamic times.

INTRODUCTION

STUDY OF MARINE FISH IN SOUTHERN CALIFORNIA

- Focus on risk assessment of PCBS

DESCRIBE A FOLLOW-UP STUDY

- Focus on differences in PCBs analyses

HIGHLIGHT SCIENTIFIC PROBLEMS IN RA OF PCBS

- Focus on reality

HIGHLIGHT PUBLIC PERCEPTION PROBLEMS

- Focus

Study of Chemical Contamination of Marine Fish from Southern California

I. Pilot Study (January 1991)

- Identification of chemicals of concern

II. Comprehensive Study (September 1991)

- Collection of ~4000 fish
- 15 different species; 24 locations
- ~1000 analyses of composite samples
- risk assessment of DDTs and PCBs

III. Data Resources on Commercial Fish (in, preparation)

- Completion of existing data

IV. Contamination of Human Breastmilk (in preparation)

- Epidemiological study
- Collection and analysis of human milk

Site Legend:

1 - Point Dume	13 - Twin Harbor Catalina
2 - Malibu	14 - Point Vicnete
3 - Marina del Rey	15 - Dana Point
4 - Short Bank	16 - Venice Beach
5 - Palos Verdes	17 - LA/LB Breakwater
6 - Redondo Beach	18 - Malibu Pier
7 - White's Point	19 - Santa Monica/Venice Piers
8 - Fourteen Mile Bank	20 - Redondo Piers
9 - Huntington Beach	21 - Cabrillo Pier
10 - Laguna Beach	22 - Pier J (Queen Mary)
11 - Emma/Eva Oil Platforms	23 - Belmont Pier
12 - Horseshoe Kelp	24 - Newport Pier

Matrix of Sites and Fish Species Sampled in the Comprehensive Study of Southern California

Fish (common name)	Site: Party Boat Areas 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Private Boat 16	17	Piers 18	19	20	21	22	23	24	Total # of Sites Sampled Per Species
Sculpin	X		X	X	X	X	X	X	X		X	X		X		X	X			X					14
Rockfishes				3X	X	X	2X	2X				X	X	2X			X								9
Barred sand bass			X						X	X	X	X			X		X					X			8
Kelp bass	X	X	X		X		X		X	X	X	X	X	X	X	X	X								14
Bonito	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	24
Mackerel	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	24
Halibut	X	X	X			X									X			X	X						7
Sand dab							X					X	X												3
Corbina		X				X			X						X	X		X	X	X				X	9
White croaker	X	X	X	X	X		X		X	X	X	X		X	X	X	X	X	X		4XS	X	X	X	20
Queen fish	X	X	X	X	X	X	X		X	X	X			X	X	X	X	X	X	X	X	X	X	X	21
Surfperches	X		X		X	X	X		X	X				X	X		X	X		X	3X	3X	3X	X	16
Barracuda								X							X										2
Opaleye							X						X												2
Halfmoon													X												1
Black croaker		X	X		X						X	X					X					X	X	X	9
Total # of Species Collected Per Site	8	8	10	6	9	8	10	5	9	7	8	9	7	8	10	7	10	7	6	6	5	7	6	7	197

"Setting a health-based trigger level for PCBs, however, is problematic. Using potential risks of 10^{-4}, 10^{-5} or 10^{-6}, the trigger levels for PCBs would be 40 ppb, 4 ppb, and 0.4 ppb, repsectively. Concentrations of 4 ppb and 0.4 ppb are much lower than the MDL in this study...."

"Ultimately, PCBs should be analyzed using congener specific analysis (which can now be achieved analytically) and the results interpreted for each congener. Unfortunately, a generally accepted method for toxicological interpretation of cogener data has not yet been established...."

"Since the health-based trigger levels for PCBs are below the MDL, then the trigger levels for PCBs could be set at the MDL which is the lowest practical analytical value. However, analytical accuracy and reproducibility is generally not good even at the MDL...The trigger level for PCBs must be etablished which take into consideration potential toxicity and analytical accuracy."

"...Therefore, one could propose using the LOQ or PQL as the trigger level (over 200 ppb) for issuing guidance for the PCBs."

"Unfortunately, the theoretical excess cancer risks estimated at these levels are high enough to be of concern as are the theoretical excess risks estimated at the MDL (e.g., 1×10^{-4})."

"Obviously, providing a health-based trigger level for PCBs is problematic...."

"It is proposed that a trigger level of 100 ppb for PCBs be used for providing guidance for fish consumption based on the results of this study...It is important to note that establishing this trigger level does not signify that OEHHA considers this level to be acceptable. OEHHA supports the use of the health-based levels and recommends that methods (analytical and toxicological) be developed which allow for providing consumers with health-based (and, therefore, consistent) guidance."

"It is noteworthy that setting a trigger level for PCBs that takes into consideration the MDL and laboratory performance would limit the use of the level to the particular study being evaluated...That is, the trigger level applies only to the study for which it is being applied...."

"However, immediate and practical needs demand that guidance be provided presently rather than waiting until analytical/toxicological methods for PCBs are developed and/or improved. When newer health-based methods for PCBs evaluation are available, OEHHA will be able to provide improved health-based guidance."

Excerpts from: Pollock, G.A., I.J. Uhaa, A.M. Fan, J.A. Wisniewski, and I. Witherell. 1991. A Study of Chemical Contamination of Marine Fish from Southern California. OEHHA; Cal/EPA. Sacramento, CA.

Establishing "Trigger Levels" for PCBs in Southern California

Criteria	Level ppb	Excess Cancer Risk
Health-Based	4	1×10^{-5}
	40	1×10^{-4}
MDL	50	$\sim 10^{-4}$
Trigger Level	100	2×10^{-4}
LOQ	120	3×10^{-4}
PQL	> 200	5×10^{-4}

MDL: Minimum detection limit
LOQ: Limit of quantitation
PQC: Practical quantitation limit

SITE-SPECIFIC CONSUMPTION RECOMMENDATIONS

SITE	FISH SPECIES	RECOMMENDATION*
Marina del Rey Huntington Beach Fourteen Mile Bank Laguna Beach Redondo Beach Emma/Eva oil platforms Catalina (Twin Harbor) Santa Monica Pier Venice Pier Venice Beach Dana Point	All species	No restrictions
Newport Pier	Corbina	One meal every two weeks
Redondo Pier	"	
Belmont Pier	Surfperches	
Pier J	"	
Malibu Pier	Queenfish	One meal a month
Short Bank	White croaker	One meal every two weeks
Malibu	White croaker	Do not consume
Point Dume	"	
Point Vicente	White croaker	Do not consume
Palos Verdes - Northwest	"	
White's Point	White croaker	Do not consume
	Sculpin Rockfishes Kelp bass	One meal every two weeks +
Los Angeles/Long Beach Harbors (esp. Cabrillo Pier)	White croaker	Do not consume
	Queenfish Black croaker Surfperches	One meal every two weeks +
Los Angeles/Long Beach Breakwater (ocean side)	White croaker Queenfish Surfperches Black croaker	One meal a month +
Horseshoe Kelp	Sculpin White croaker	One meal a month +

* One meal is about six ounces.

\+ Consumption recommendation is for all the listed species combined.

SCIENTIFIC PROBLEMS

Logic - ***Okay***

Analytical Chemistry - ***Okay***

Toxicology - ***Not Okay***

More congener specific data

More endpoints

dioxin-like activity (co-planar)

other toxicities

(basic toxicity mechanisms)

Risk Assessment - ***Not Okay***

TEF for dioxin-like activity?

TEFs for other toxicities? (applied to RfD?)

PUBLIC PROBLEMS

- ***Conflicting experts***

  "not state-of-the-art"
  "obsolete"
  "don't know what they are doing"

- ***Uncertainty***

- ***PCBs are complicated***

- ***Re-issuing or lifting advisories based on changing RA method (TEFs).***

CONFUSION

$$Risk = q^* \times dose$$

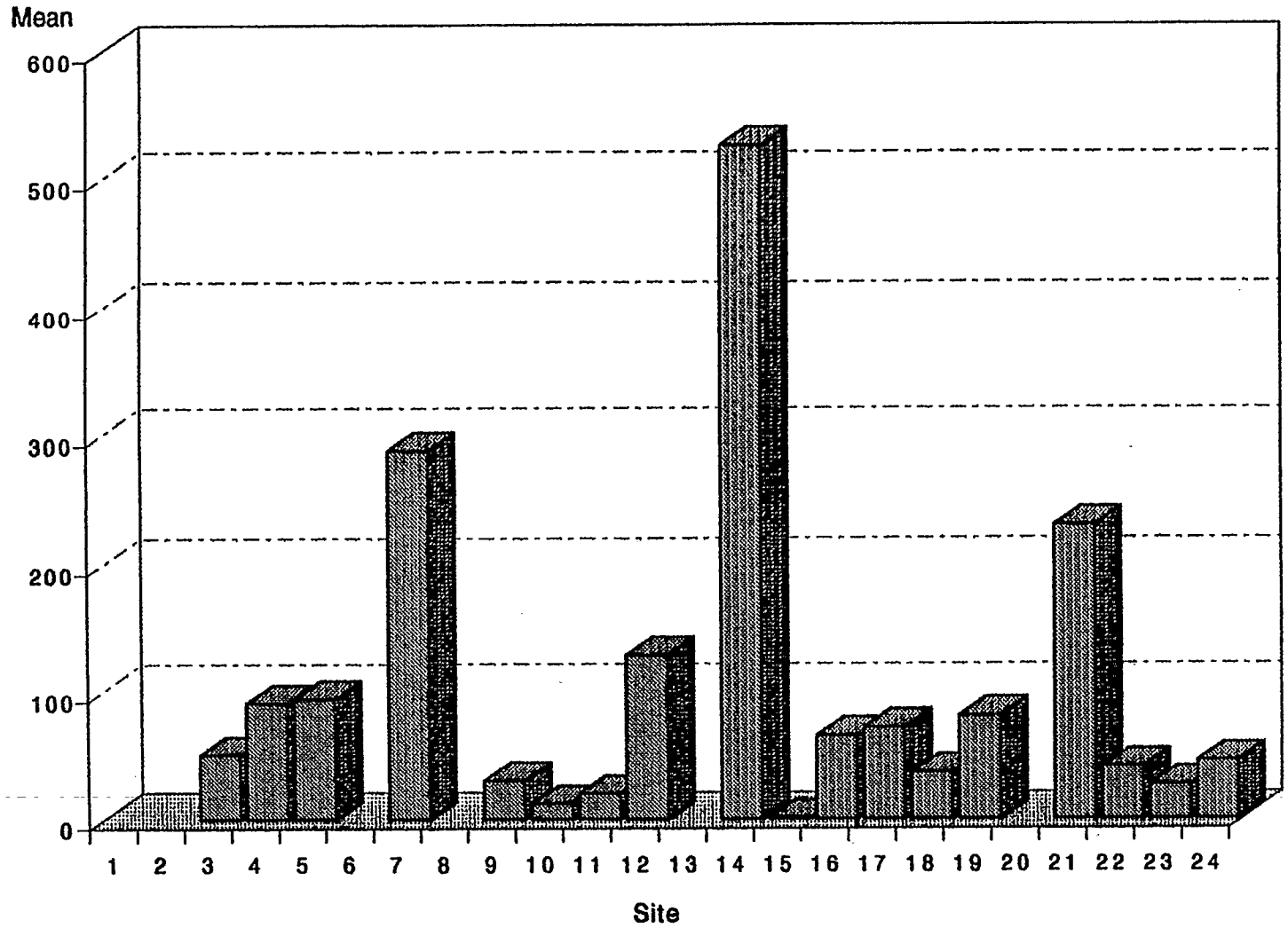
$$Dose\ (exposure) = \frac{[X]\ [consumption\ rate]}{body\ weight}$$

Consumption Rate ➢ *23 g/day (about 1 meal/week)*

[X] ➢ *By analysis*

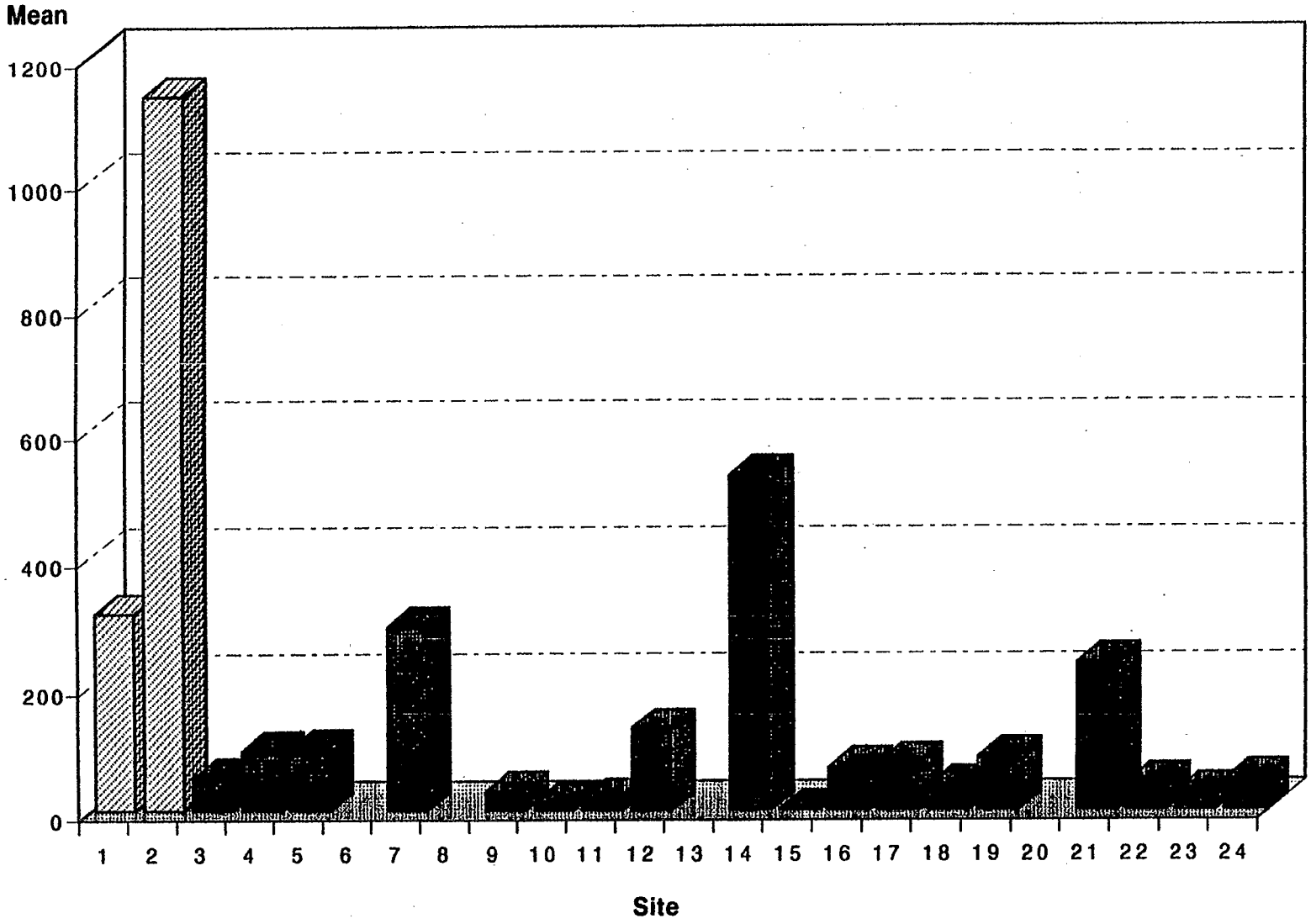
Body weight ➢ *70 kg adult*

Arithmetic mean concentrations* (ppb wet weight) of total PCBs in white croaker muscle tissue collected in southern California



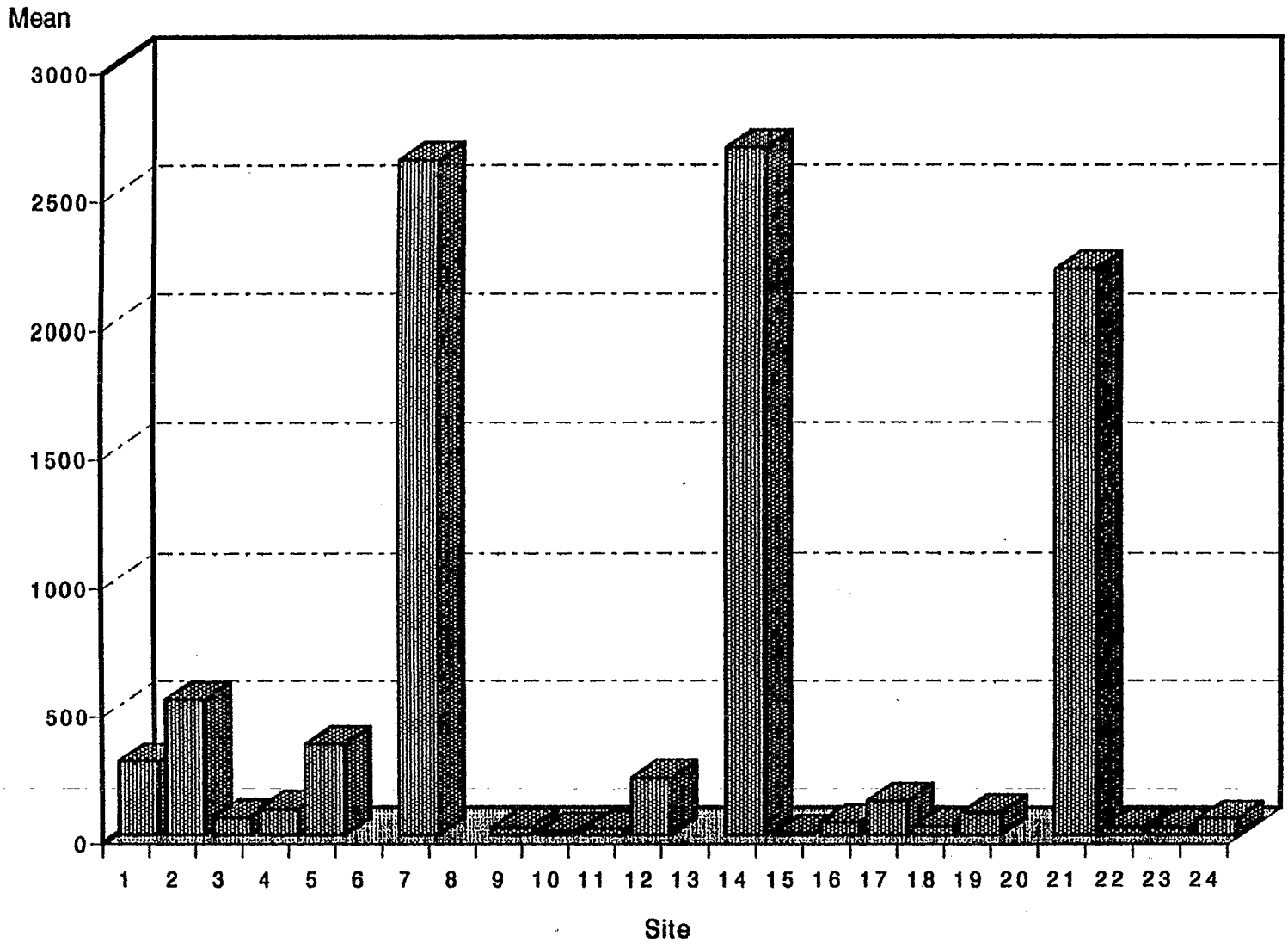
*Means calculated using uncensored data and not adjusted for weight (e.g., all reported values, including values below MDL, 50 ppb).

Arithmetic mean concentrations* (ppb wet weight)
of total PCBs in white croaker muscle tissue collected in southern California



*Means calculated using uncensored data and not adjusted for weight (e.g., all reported values, including values below MDL, 50 ppb).

Arithmetic mean concentrations* (ppb wet weight)
of total DDTs in white croaker muscle tissue collected in southern California



*Means calculated using uncesored data and not adjusted for weight (e.g., all reported values, including values below MDL, 38 ppb).

4.2 TENNESSEE VALLEY AUTHORITY

Janice Cox, Water Management, Tennessee Valley Authority

As a federal resource management agency, the Tennessee Valley Authority (TVA) monitors contaminant concentrations in fish throughout the 7-state Tennessee River basin. Because TVA does not have the authority to issue consumption advisories, it defers to the determinations of the state regulatory agencies when issuing advice on the safety of eating fish from TVA reservoirs. However, differences in the consumption advisory policies of the seven Valley states result in an unlevel playing field with respect to both protection of public health and economic impact on sportfishing interests. These differences in state policies are most apparent when dealing with PCB contamination because PCBs drive the cancer and noncancer risks associated with eating fish from most TVA reservoirs.

To foster consistency in the evaluation of the fish contaminant data it collects, TVA developed a graphic method of reporting risk assessment results to the states. The impetus behind developing a graphic approach was to provide consistency in toxicity assessment while retaining flexibility for the states to choose their assumptions about fish ingestion rate, exposure duration, acceptable risk level, and whether to focus on cancer or noncancer endpoints.

The graphic method presents conclusions from each fish tissue analysis in two nomographs. The first nomograph, based on the aggregate impact of all carcinogens in the sample, shows upper-bound incremental lifetime cancer risk as a function of fish consumption rate. Different curves on the nomograph are used to illustrate the impact of varying exposure duration assumptions. The second nomograph, based on the sum of hazard quotients for each contaminant in the sample, shows the hazard index as a function of fish consumption rate. Various lines on the nomograph can be used to represent the total hazard index and the portion of the total hazard index associated with different classes of endpoints (developmental impacts, hepatic toxicity, etc.). The second nomograph can easily be modified to evaluate potential impact on consumers other than the standard 70-kg adult male.

For communicating with risk managers, this graphic approach is preferable to simply reporting PCB concentrations or point estimates of risk:

- The method evaluates aggregate risks from multiple contaminants. While PCBs are the single largest contributor to the risk from consuming fish from Tennessee Valley waters, DDT, chlordane, lead, heptachlor epoxide, dieldrin, endrin, and mercury are also significant contributors to risk in fish samples from some waters.

- The method moves beyond the black-or-white thinking inherent in defining contaminant concentrations as either "safe" or "unsafe" by illustrating potential risk as a function of exposure; that is, the method makes it easy to determine how much fish consumption is acceptable given a target maximum acceptable risk level.

- The method facilitates identification of the most sensitive adverse health effects, by sample location, so that special "at risk" subpopulations (such as children and pregnant or lactating women) can be targeted for risk management.

- The method helps risk managers put the results of fish tissue studies in perspective by facilitating comparison of the aggregate risks presented by fish consumption with the risks attributable to contaminants in the general food supply. It also provides the technical underpinning for effective risk communication with the public by permitting qualitative and quantitative comparisons with health risks from other sources.

This risk assessment technique was used to evaluate screening-level data collected by TVA in 1990. The results of the risk assessment depended more strongly on PCBs than on any other single contaminant. Using an oral slope factor of 7.7 $(mg/kg/day)^{-1}$, PCBs accounted for most (average 89 percent) of the potential cancer risk from fish consumption. For the recreational fisherman eating one meal of channel catfish per week (30 grams/day), the calculated upper-bound incremental lifetime cancer risks varied by location from 2E-04 to 7E-03. For comparison, the background cancer risk from xenobiotic contaminants in the general food supply, based on FDA market basket studies, is approximately 2E-04.

Using an estimated RfD of 5E-05 mg/kg/day, PCBs also accounted for more than 50 percent of the total hazard index in most of the samples. For the adult fisherman eating one meal of channel catfish per week (30 grams/day), the calculated hazard indexes varied by location from less than 1 to as much as 20. On a basis of "grams of fish per kilogram bodyweight," the average 2-year old child eats about 50 percent more from the meat-fish-poultry food group than does the average adult. Therefore, the hazard index for small children eating channel catfish on a regular basis may be as high as 30 for fish from some locations. For comparison, the background hazard index for adult males from xenobiotic contaminants in the general food supply, again based on FDA market basket studies, ranges from 0.8 to 3 (depending on the assumptions one makes about lead intake and lead toxicity). The background hazard index for the average 2-year old child ranges from 2 to 16 (again depending upon assumptions about lead intake and lead toxicity).

With few exceptions, the sites with elevated (i.e., significantly higher than background food supply) hazard indexes corresponded with the sites that had an elevated cancer risk as well. Incrementally varying assumptions about the estimated RfD for PCBs, the amount of PCBs lost during fillet preparation and cooking, or the exposure duration resulted in a relatively small change in the number of locations where the risk to sportfishermen exceeded the background risk from the general food supply. However, the total array of exposure assumptions taken together can markedly change the risk characterization. Conservative assumptions corresponding to a "reasonable worst case" resulted in 100 percent of sites exceeding the background food supply cancer risk and 73 percent of sites exceeding the background food supply hazard index for an adult consumer.

More moderate assumptions corresponding to a "reasonable best case" resulted in only one percent of sites exceeding the background food supply cancer risk and none of the sites exceeding the background food supply hazard index for an adult consumer.

LIMITATIONS OF FISH CONSUMPTION RATE LITERATURE

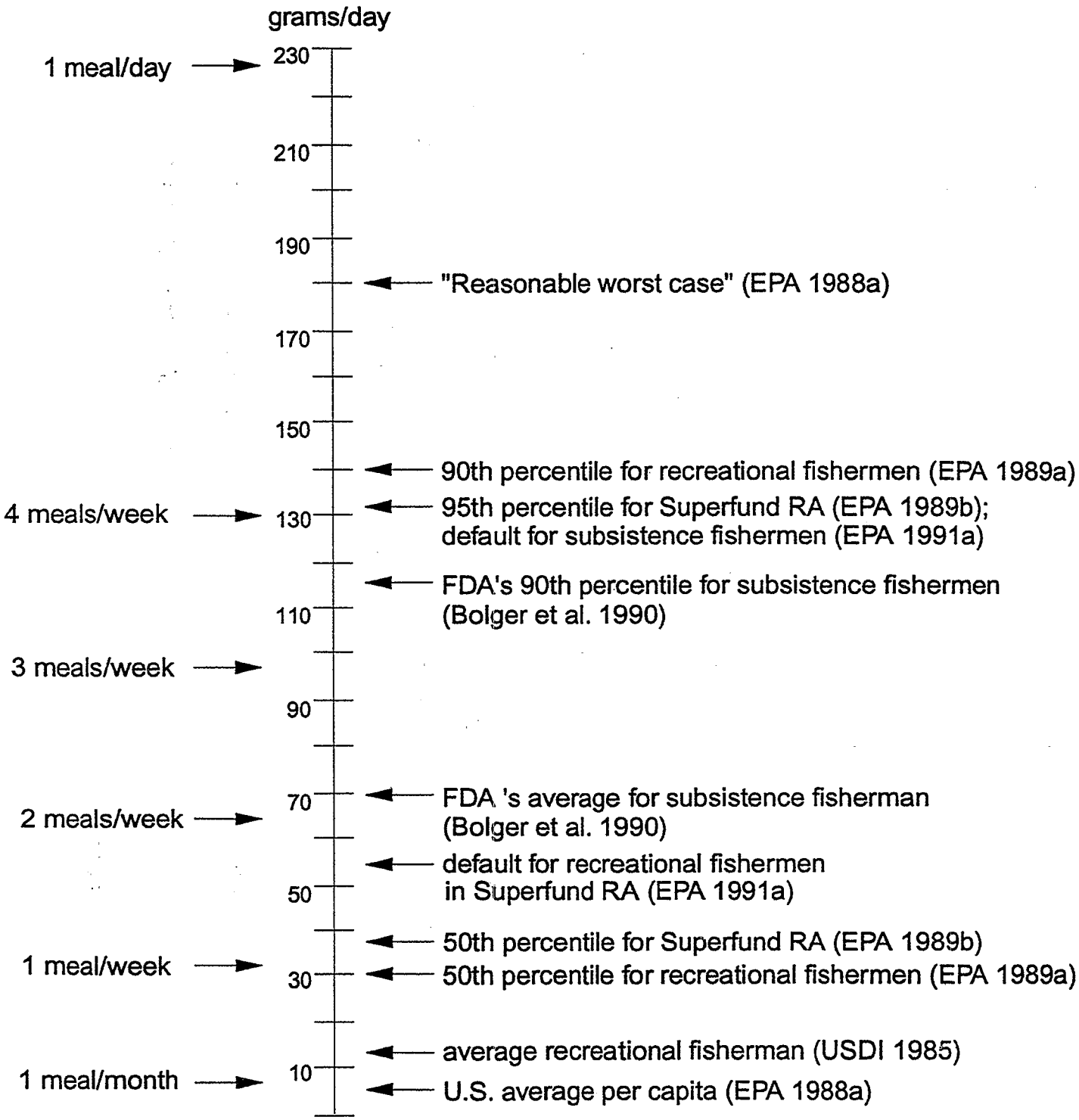
- Most date back to 1970s, while fish consumption has increased rapidly
- Some do not distinguish between freshwater and marine fish
- Many are based on short period recall
- Some take an average of "fish eaters" and "non fish eaters"
- Demographics not representative for all

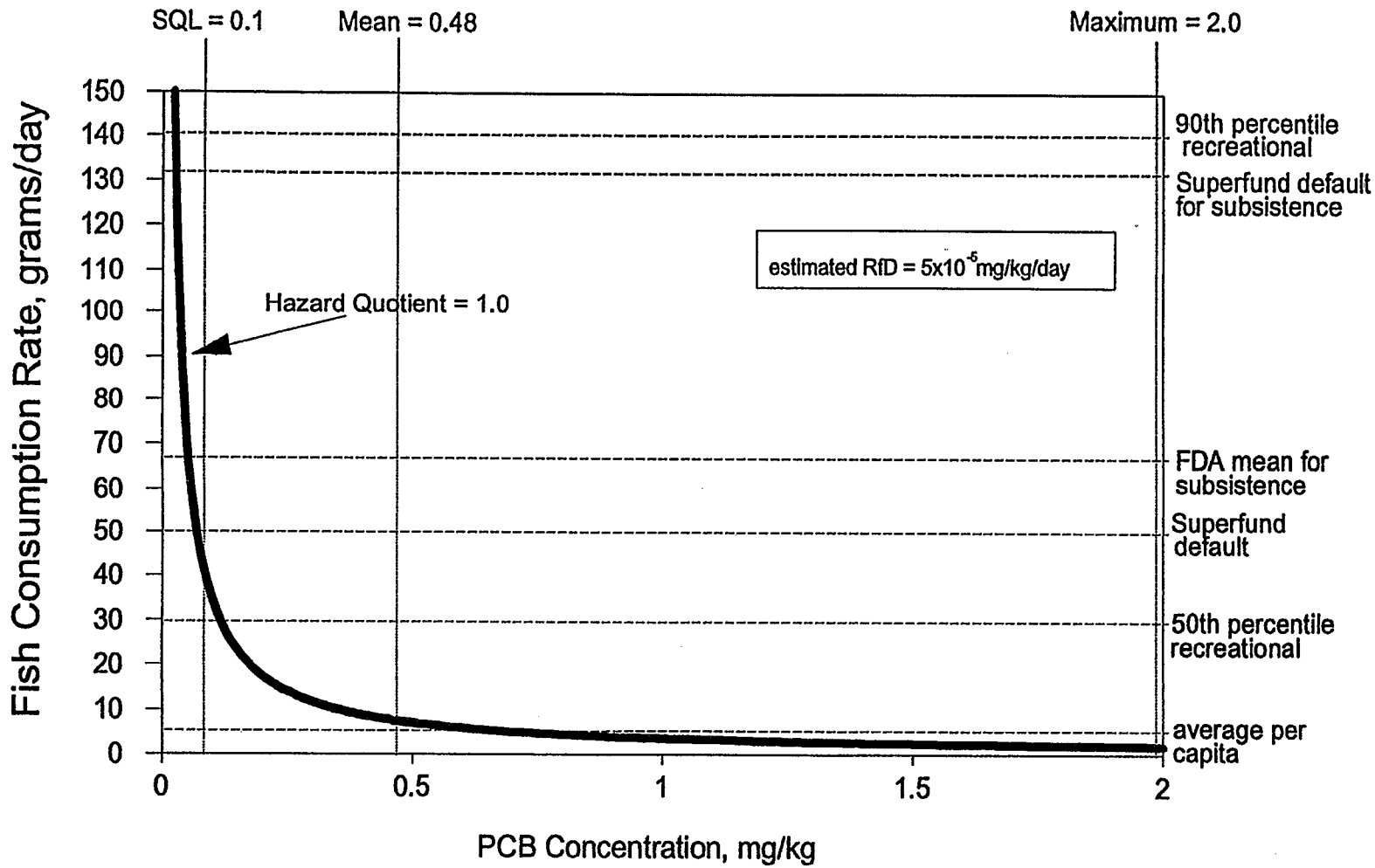
COMPARED TO FDA MARKET BASKET SURVEYS, RECREATIONAL FISHERMEN IN THE TENNESSEE VALLEY MAY BE GETTING SIGNIFICANT "ADD-ON" DOSES OF:

- Mercury
- Dieldrin
- Lead
- Endrin
- Chlordane
- Heptachlor epoxide
- DDT, DDD & DDE
- PCBs

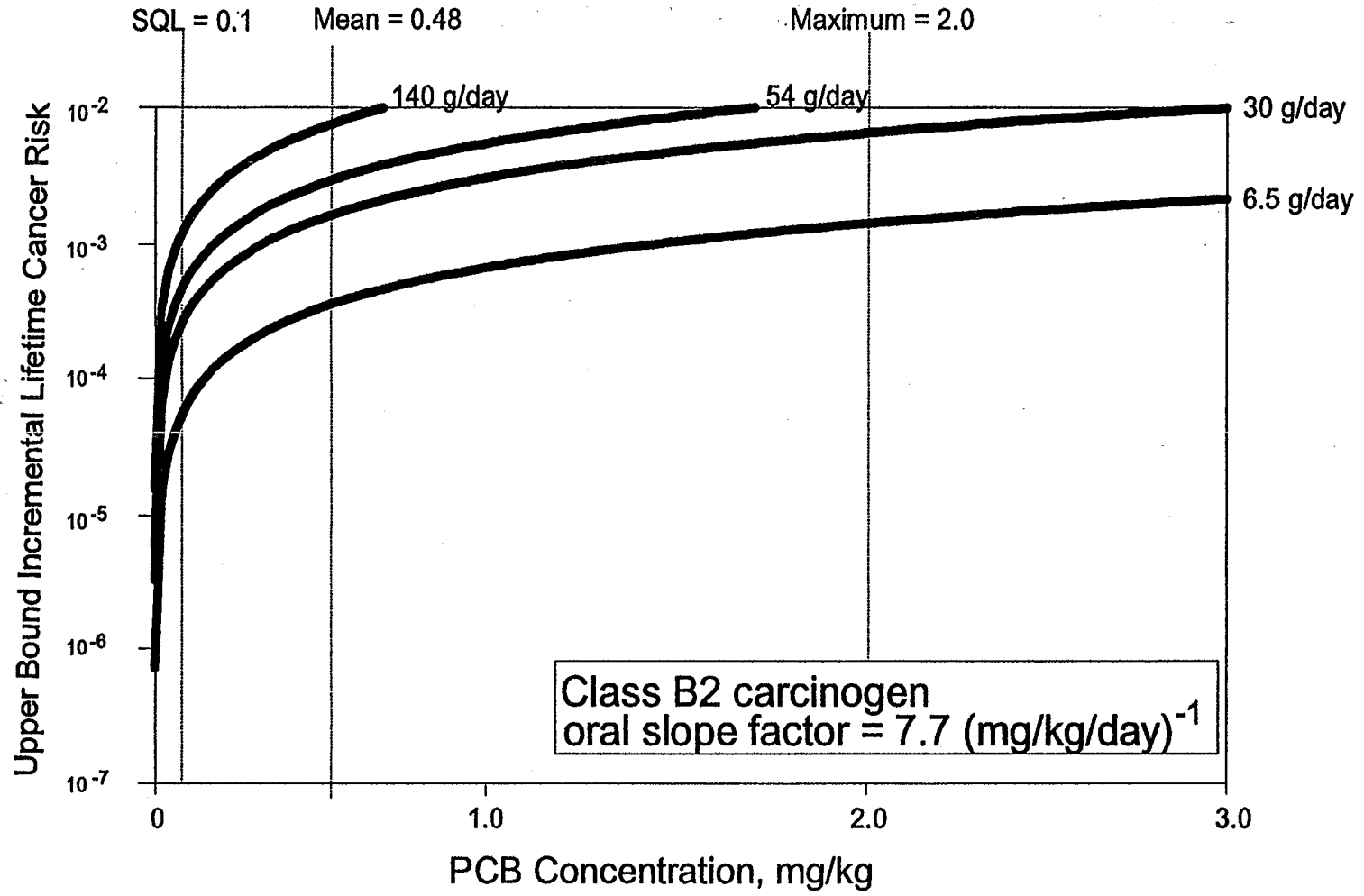
Comparison of Assumed Fish Consumption Rates

(Note: Typical "meal" size assumed to be 0.5 pounds)

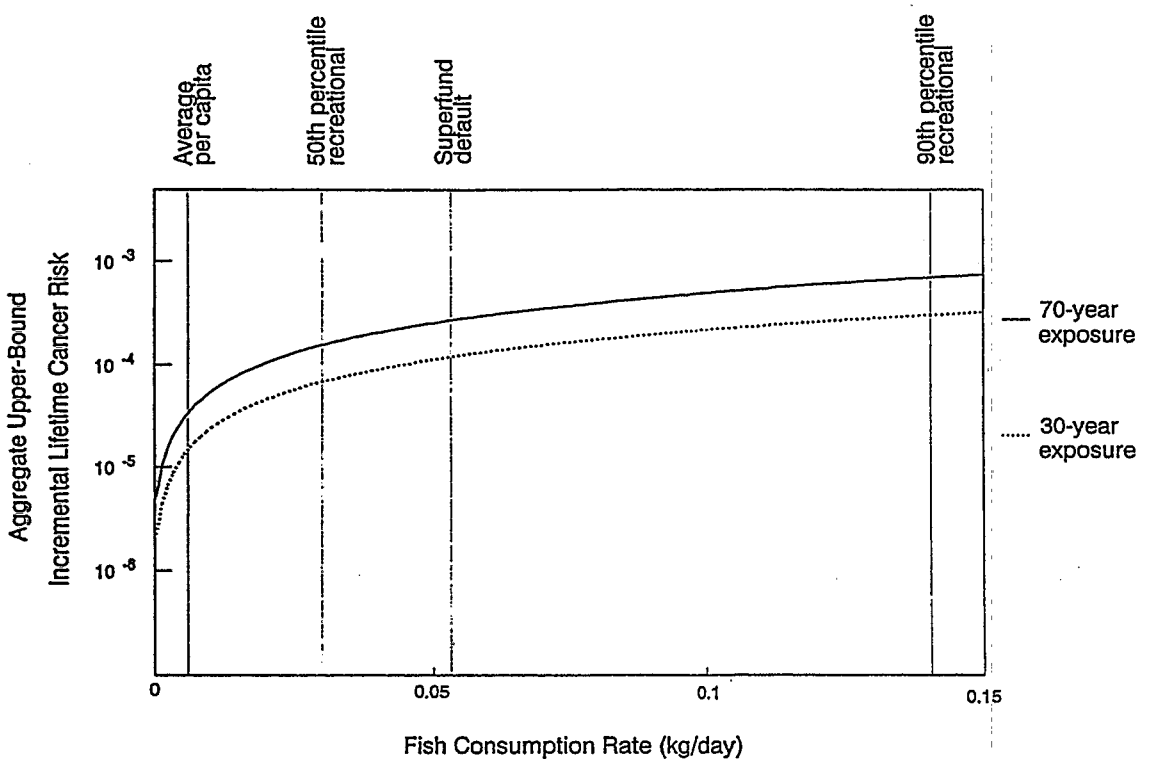


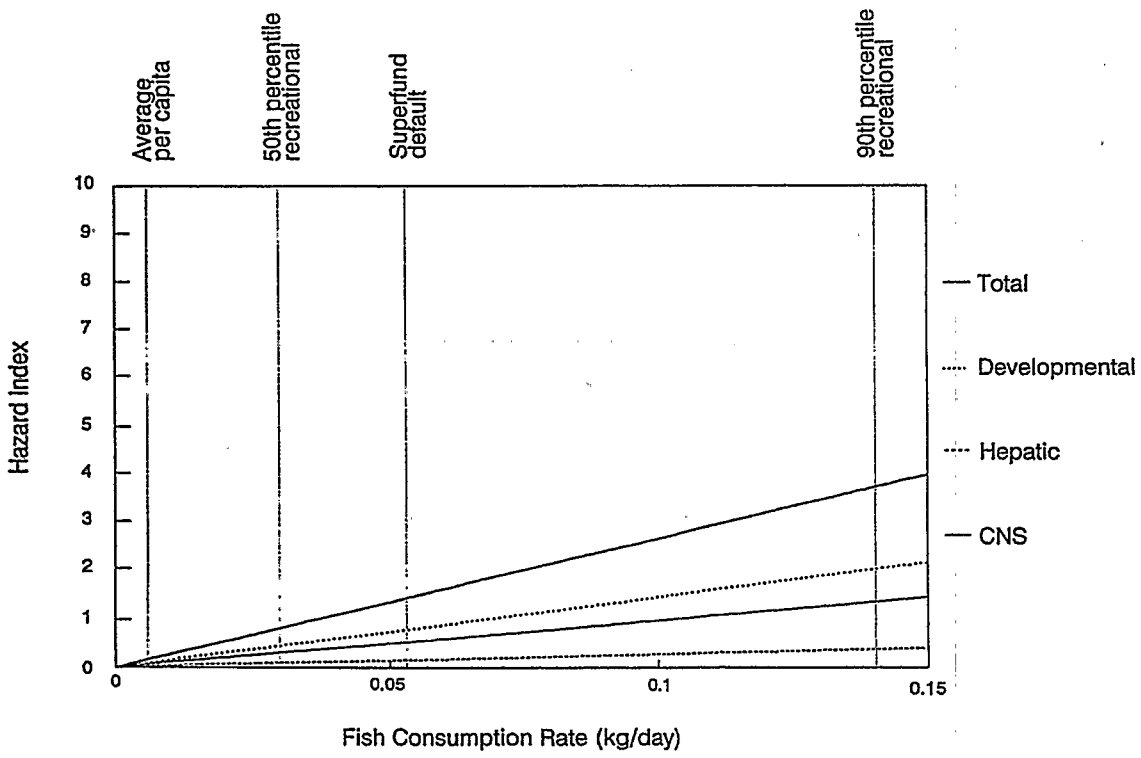


Effects of PCB Concentration and Fish Consumption Rate on Hazard Quotient.



Effects of PCB Concentration and Fish Consumption Rate on Incremental Lifetime Cancer Risk





Risk Characterization for Elk River Mile 41

4.3 DELAWARE

Richard W. Greene, Environmental Engineer, Watershed Assessment Branch, Delaware Department of Natural Resources and Environmental Control[11]

Recreational and commercial fishing are important water-dependent activities in the Delaware Estuary. There are growing concerns, however, regarding chemical contamination of resident and migratory fish in the system and potential health effects to anglers who may consume their catch. New Jersey and Pennsylvania have both issued health advisories on the consumption of catfish and white perch from the Estuary based on exceedence of the FDA Action Level for PCBs. Furthermore, the United States Fish and Wildlife Service detected elevated levels of PCBs in whole body striped bass taken from the system. In response to these and similar findings, the State of Delaware conducted a pilot study of PCB contamination in striped bass taken from the spawning ground adjacent to Wilmington, Delaware in May of 1991. The results of that work lead state officials to further investigate the problem. A more detailed study was undertaken in two areas of the Estuary in 1992 that targeted the size ranges of striped bass most likely to be eaten by Delaware fishermen. The two size categories selected for study were fish that were of a size legal in Delaware's commercial fishery (those between 18 and 28 inches TL) and fish legal for recreational harvest (minimum size 28 inches TL).

A total of 79 fish were obtained for the study. Forty-nine fish (25 commercial size and 24 recreational size) were obtained from mid-Delaware Bay in February and March of 1992 as a part of commercial American shad by-catch. The remaining thirty fish (25 commercial size and 5 recreational size) were obtained from the spawning ground area in May of 1992 by the Division of Fish and Wildlife. The 25 commercial size fish from the Bay were grouped into 5 composite samples of 5 fish each. Equal mass aliquotes of muscle tissue were taken from each fish. This same compositing scheme was used for the 25 commercial size fish from the spawning ground. The 24 recreational size fish from the Bay were also grouped into 5 composite samples, this time, however, one of the samples only contained 4 fish while the others contained 5. The remaining 5 recreational size fish from the spawning ground were treated as individual samples. The decision was made not to sacrifice 20 additional recreational size fish from the spawning ground because of concerns over preservation of existing spawning stock. In all, 20 samples were prepared for analysis, 14 five-fish composites, 1 four-fish composite, and 5 individual fish.

The specific objective of this study was to fully characterize the PCB content of striped bass to help support a credible human health risk assessment. The chemical characterization is expected to be coupled with a consumption survey to further refine the risk projections. The available literature suggested that a congener-specific and homolog-specific analysis would provide the information of greatest utility for this study. Decision

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[11] Roy W. Miller of the Division of Fish and Wildlife, Delaware Department of Natural Resources and Environmental Control was a coauthor of the paper.

criteria used in specifying which congeners to analyze were: 1) coplanar structure, 2) whether the congener is a principal component of commercial Aroclor mixtures, 3) whether the congener had been reported in related studies involving fish of the same or similar species and, 4) whether the congener had been detected in human blood serum, adipose tissue, or mother's milk. In addition, at least two congeners were selected from each chlorination level to allow for homolog determination. Use of these criteria resulted in the selection of 47 congeners out of a possible 209.

All twenty samples were analyzed for mono-ortho and di-ortho PCB congeners, additional congeners that met the selection criteria, PCB homologs, DDT and its metabolites, dieldrin, chlordane, and percent lipid. Because of budget constraints, only four of the samples, one from each sample area and size category, were analyzed for the non-ortho substituted PCB congeners.

Total PCB varied among the 20 samples from a low of 0.463 ppm to a high of 2.253 ppm. Although mean values on the spawning grounds were nominally higher (1.07 ppm) than from Delaware Bay (0.732 ppm), ANOVA and nonparametric tests revealed that these differences were not statistically significant (alpha=0.05), nor was there a statistically significant difference in mean PCB concentrations of commercial size fish versus recreational size fish. Although total PCB content did not differ between size or location, the level of chlorination in the recreational size fish from the spawning grounds (58 percent) was statistically higher than any of the other categories (between 55 and 56 percent). This finding is believed to have important implications to risk projections. Namely, some evidence exists (IEHR, 1991) to suggest that only PCB mixtures with an overall level of chlorination of approximately 60% represent a threat of cancer in animals. Other evidence suggests that the cancer effects of PCBs are determined not so much by level of chlorination, but more fundamentally by the extent to which individual congeners attain coplanar conformation and hence, structural similarity to 2,3,7,8-TCDD. These issues are explored as a part of the risk assessment portion of the Delaware Estuary Striped Bass Study.

Total coplanar PCB was found to increase with increasing total PCB. Toxicity equivalents for the 4 samples selected for full PCB characterization ranged from 61 pptr to 95 pptr. The mono-ortho congeners were found to represent roughly two-thirds to three-quarters of the computed toxicity equivalents. Of this percentage, congeners 126, 105, 118, and 167 predominated.

Excess lifetime cancer risk was estimated by combining mean contaminant concentrations, standard exposure factors, and potency slopes. The linearized, multistaged model of carcinogenesis was used. Four separate fish consumption scenarios were considered within each of four separate hazard/potency scenarios. Fish consumption scenarios considered included one 8 oz meal/yr, two 8 oz meals/yr, one 8 oz meal/mo, and one 8 oz meal/wk. The four hazard/potency scenarios considered included:

A: $q^* = 7.7$ applied to total PCB for all samples, regardless of level of chlorination. (traditional EPA policy on PCBs)

B: $q^* = 7.7$ applied to total PCB, but only for samples with level of chlorination approximately equal to 60 percent

C: $q^* = 1.9$ applied to total PCB, but only for samples with level of chlorination approximately equal to 60 percent (IEHR recommendation)

D: Toxicity Equivalence approach. TEFs from Safe combined with q^* of 2,3,7,8 TCDD of 1.56E+05

Method A and Method D yielded similar risk estimates. Because neither is dependent on level of chlorination, they would both apply to the entire study area. Both methods A and D project cancer risk in excess of 1-in-100,000 assuming as little as one 8 ounce meal of striped bass per year. At a top end consumption of one 8 ounce meal per week, risk projections increase to in excess of 1-in-1000 using both of these methods.

Method B and C are based on the premise that only PCB mixtures with approximately 60% chlorination represent a cancer hazard. The recreational sized striped bass from the spawning ground was the only category which met this criterion. Using Method B for those fish, it only takes one 8 ounce meal per year to exceed a 1-in-100,000 risk, whereas it takes two 8 ounce meals per year to exceed this same risk level using Method C. If Method B or C are used, the assessor must still consider the cancer risk associated with chlorinated pesticides in the stripers taken in the Delaware Bay. Due to chlorinated pesticides alone, a person would have to eat one 8 ounce meal of striped bass per week taken from the Bay in order for their cancer risk to exceed in 1-in-100,000 level.

Although Delaware has not taken an official position on this matter, management options being considered include the following:

- Limited consumption advisory for entire geographic region (based on Method A or D).
- Limited consumption advisory for spawning ground only (based on Method B or C).
- No advisory - "wait it out" until fish consumption survey is complete and consensus reached on PCB risk assessment.

Upon completion of the fish consumption survey, Delaware intends to further refine its current risk estimates through a probabilistic risk analysis. Such an approach allows the assessor to construct a more complete picture of the risk continuum based upon assumed probability distributions of the various exposure factors. An illustrative example was prepared as a part of this study to suggest potential future refinements.

KEY FEATURES

* REPLICATE COMPOSITE SAMPLING DESIGN

* 2 SIZE CLASSES AND 2 LOCATIONS

* CONGENER SPECIFIC AND HOMOLOG SPECIFIC PCB ANALYSIS

* RESULTS CONSIDERED IN CONCERT WITH CONSUMPTION DATA

* PROBABILISTIC RISK ANALYSIS

PCB CONGENER SELECTION CRITERIA

* COPLANARS (NON–ORTHO SUBSTITUTED, MONO–ORTHO SUBSTITUTED, DIORTHO SUBSTITUTED)

* PRINCIPLE AROCLOR CONSTITUENT

* PREVIOUSLY REPORTED IN FISH

* PREVIOUSLY REPORTED IN HUMAN SERUM, MOTHERS MILK OR TISSUE OF HEAVY FISH CONSUMERS

* AT LEAST 2 CONGENERS FROM EACH HOMOLOG LEVEL

RESULT: 47 CONGENERS OF A POSSIBLE 209

ANALYTICAL METHODS

ANALYTE	METHOD	DETECTION LEVEL
Mono–ortho PCBs, Di–ortho PCBs, and Pesticides	HRGC/LRMS	1–10 ppb
Non–ortho PCBs	HRGC/HRMS (isotope dilution)	2 pptr
PCB Homologs	EPA 680	1–10 ppb

RESULTS
PCB CHARACTERIZATION

*NO SIGNIFICANT DIFFERENCE IN TOTAL PCB BETWEEN SIZE CLASSES OR LOCATION.

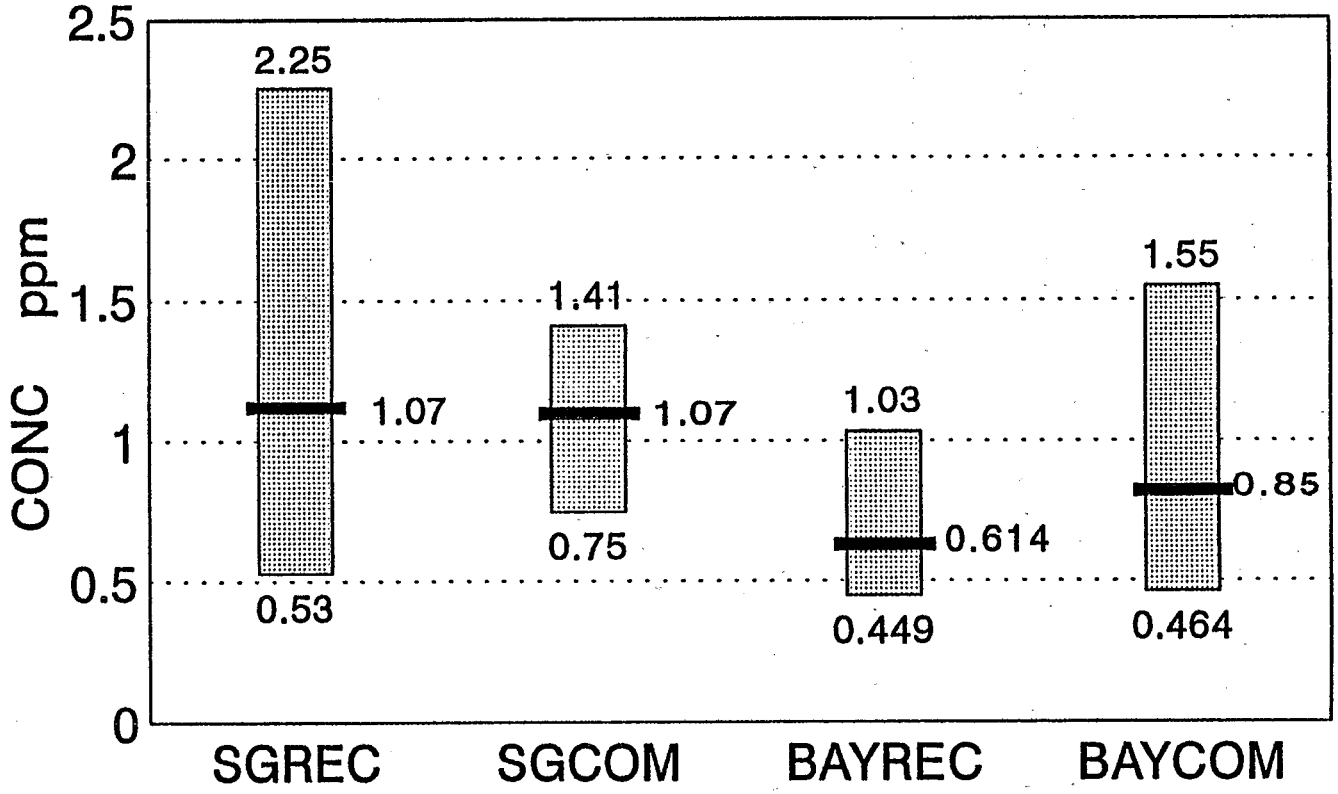
*RECREATIONAL SIZE STRIPERS FROM SPAWNING GROUND EXHIBIT STATISTICALLY HIGHER LEVEL OF CHLORINATION THAN OTHER CATEGORIES.

*INCREASES IN COPLANAR PCB CONTENT ARE CORRELATED WITH INCREASES IN TOTAL PCB.

*MONO-ORTHOs REPRESENT ROUGHLY 66% TO 75% OF THE TOXICITY EQUIVALENTS; NON-ORTHOs REPRESENT ROUGHLY 20 TO 30%; DI-ORTHOs GENERALLY COMPRISE <5%.

*CONGENERS 126, 105, 118, AND 167 MAKE UP THE MAJORITY OF THE TOXICITY EQUIVALENTS.

VARIATION IN PCB CONTENT
BY SIZE CLASS AND LOCATION



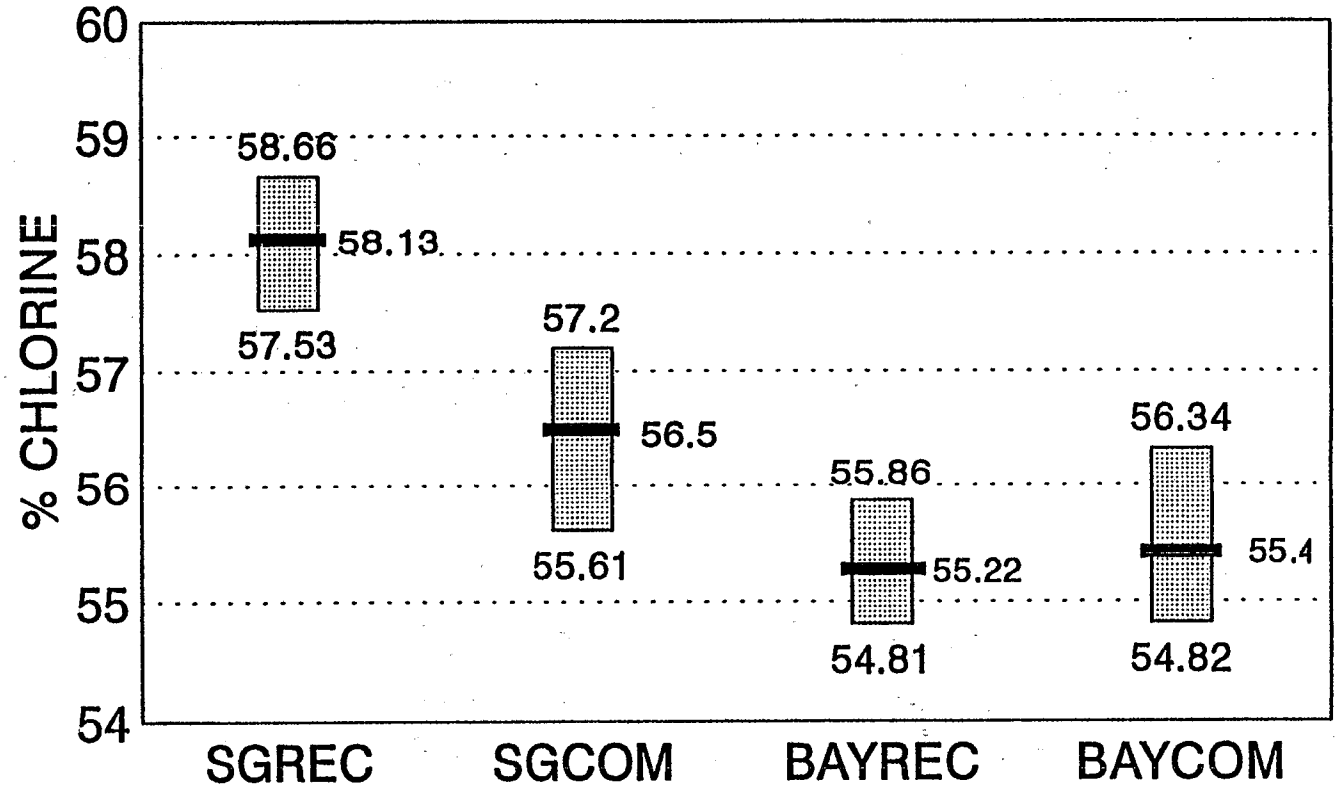
PCB HOMOLOGS
DATA REDUCTION

$$\text{LEVEL OF CHLORINATION IN SAMPLE } j = \sum_{i=1}^{10} A \times B$$

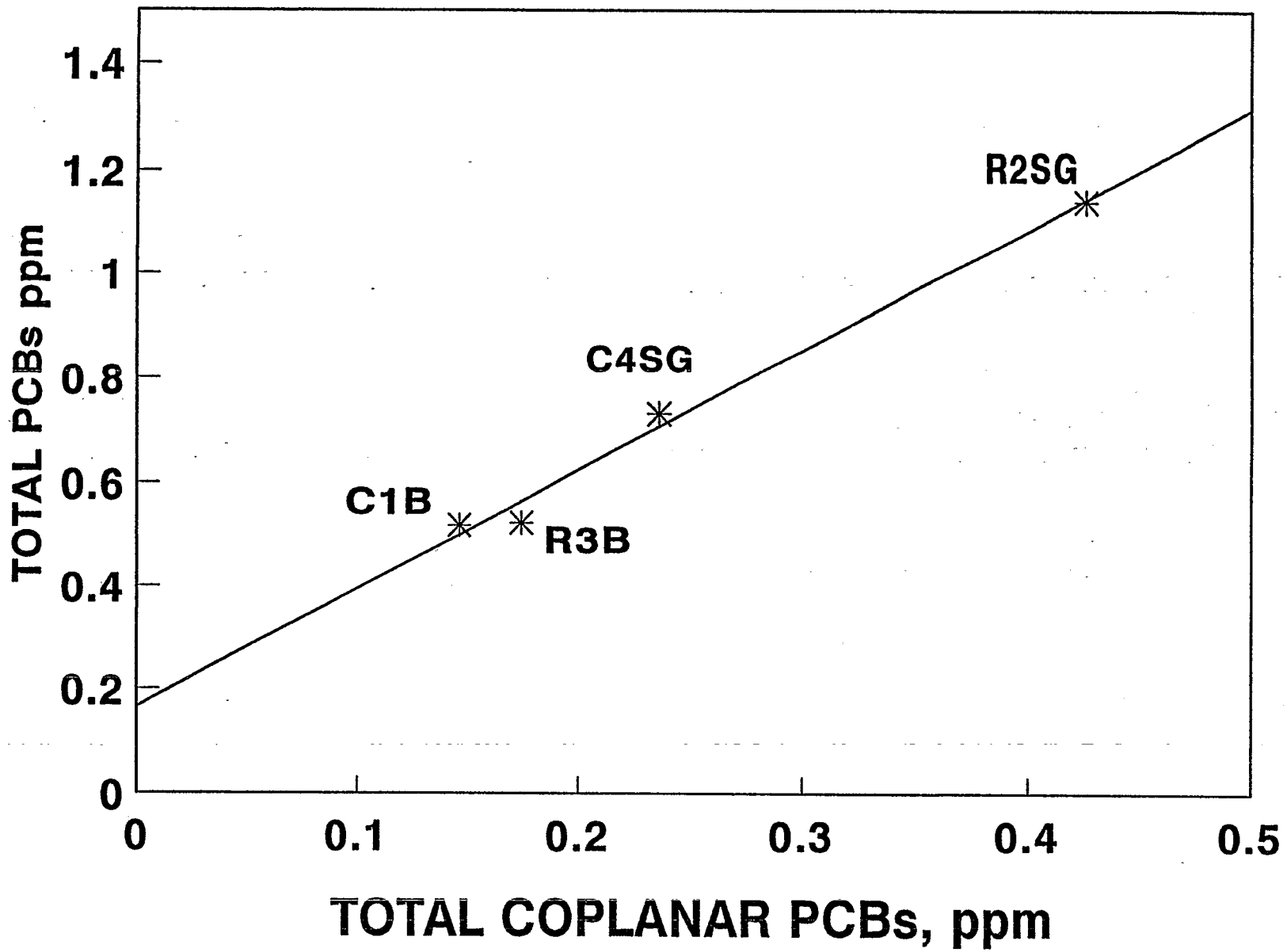
$$A = \%\ \text{CHLOROBIPHENYL } i \text{ IN SAMPLE } j = \frac{\text{CONC. OF CB } i \text{ IN SAMPLE } j}{\text{TOTAL PCB IN SAMPLE } j} \times 100$$

$$B = \text{MASS FRACTION OF CHLORINE IN CB } i = \frac{i \times \text{M.W. OF CHLORINE}}{\text{M.W. OF CB } i}$$

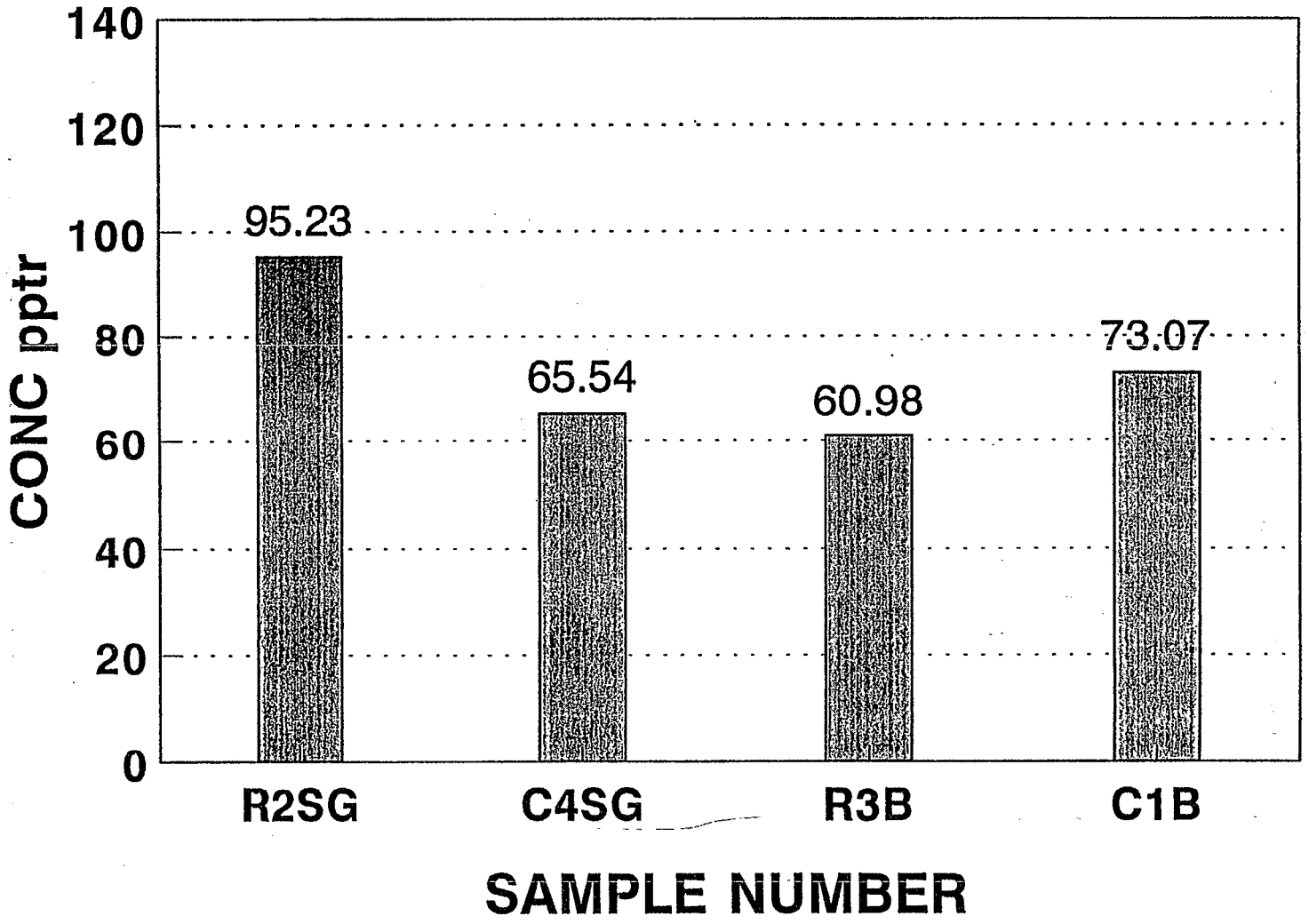
VARIATION IN PERCENT CHLORINATION
BY SIZE CLASS AND LOCATION



TOTAL PCBs VERSUS TOTAL COPLANAR PCBs

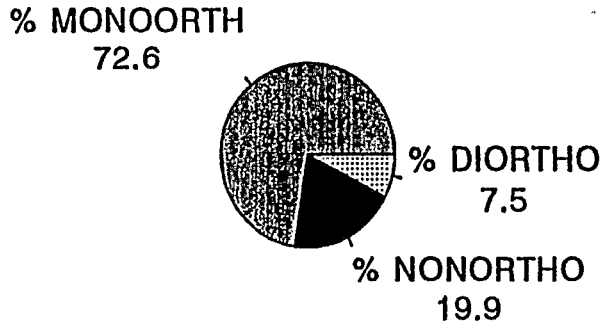


TOXIC EQUIVALENTS OF AHH-ACTIVE PCBs

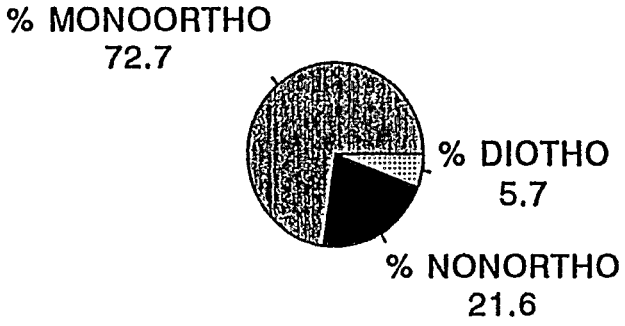


TE = (TEF) x (CONC)

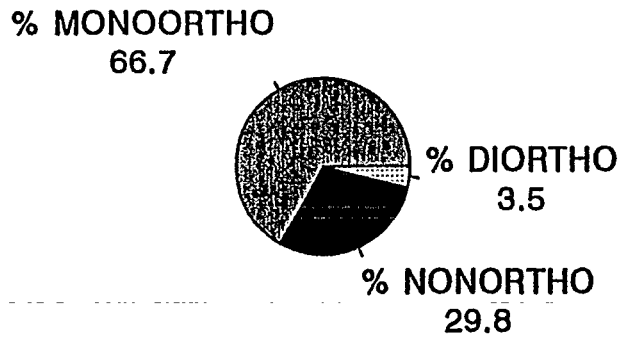
CONTRIBUTION OF COPLANAR PCBs TO TOXICITY EQUIVALENTS



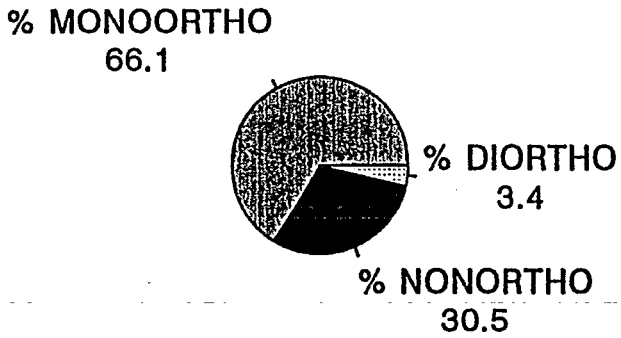
SAMPLE R2SG



SAMPLE C4SG



SAMPLE R3B



SAMPLE C1B

QUANTITATIVE RISK ASSESSMENT
FOR CHEMICALLY CONTAMINATED FISH

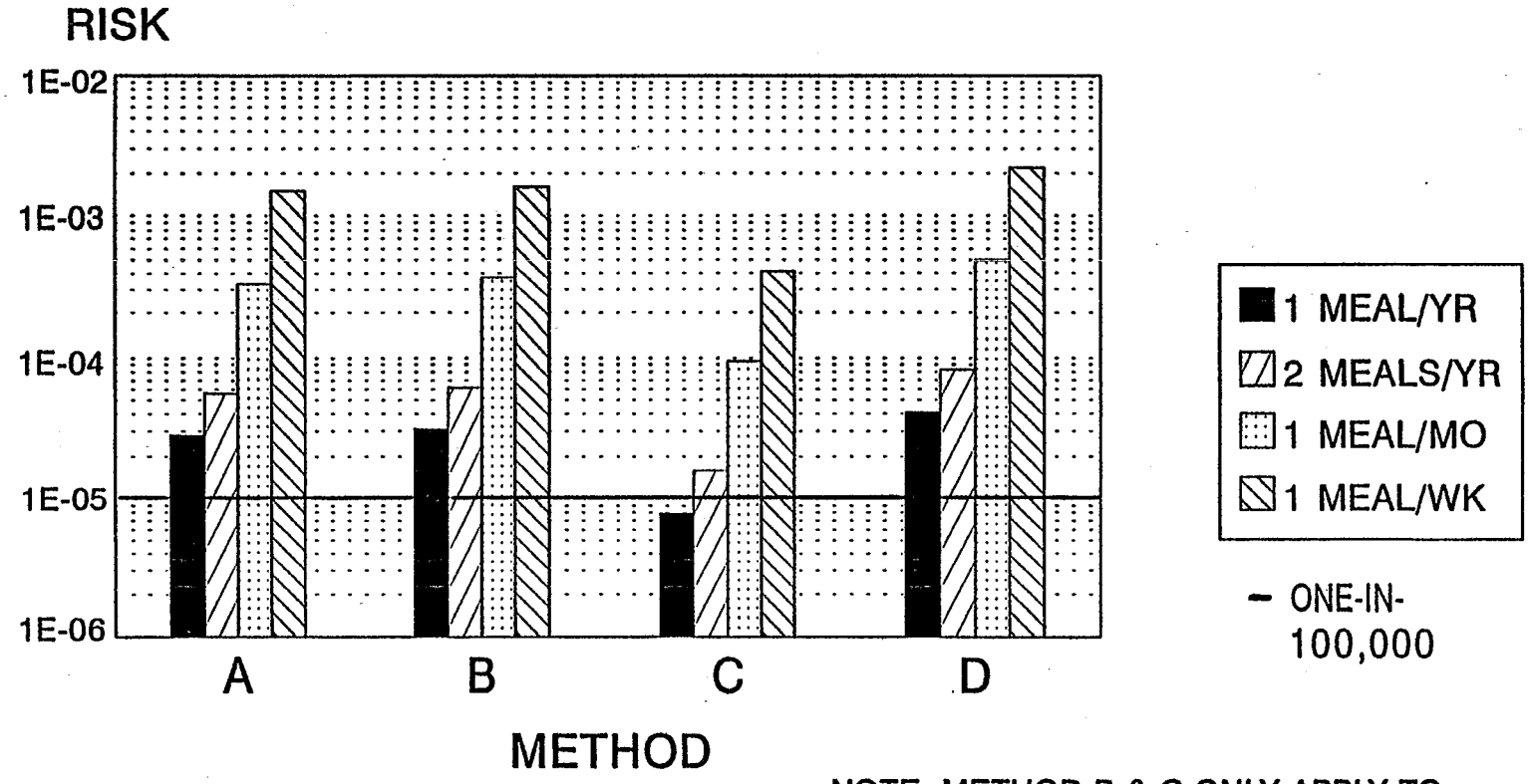
$$\text{EXCESS LIFETIME CANCER RISK} = \frac{C \times CR \times ED \times DF}{BW \times LT} \; q^*$$

C = CONC. OF CONTAMINANT IN FISH, ppm or mg/kg
CR = HUMAN CONSUMPTION RATE OF FISH, kg/d
ED = DURATION OVER WHICH EXPOSURE OCCURS, yrs
DF = DIET FRACTION OF FISH DERIVED FROM THE PARTICULAR WATERBODY, unitless
BW = BODY WEIGHT OF FISH CONSUMER, kg
LT = LIFETIME DURATION, yrs
q* = CANCER POTENCY SLOPE, 1/(mg/kg/d)

EXPOSURE FACTORS

FACTOR	ASSUMED VALUE
CR	one 8 oz meal/yr two 8 oz meals/yr one 8 oz meal/mo one 8 oz meal/wk
ED	30 yrs
DF	1
BW	70 kg
LT	75 yrs

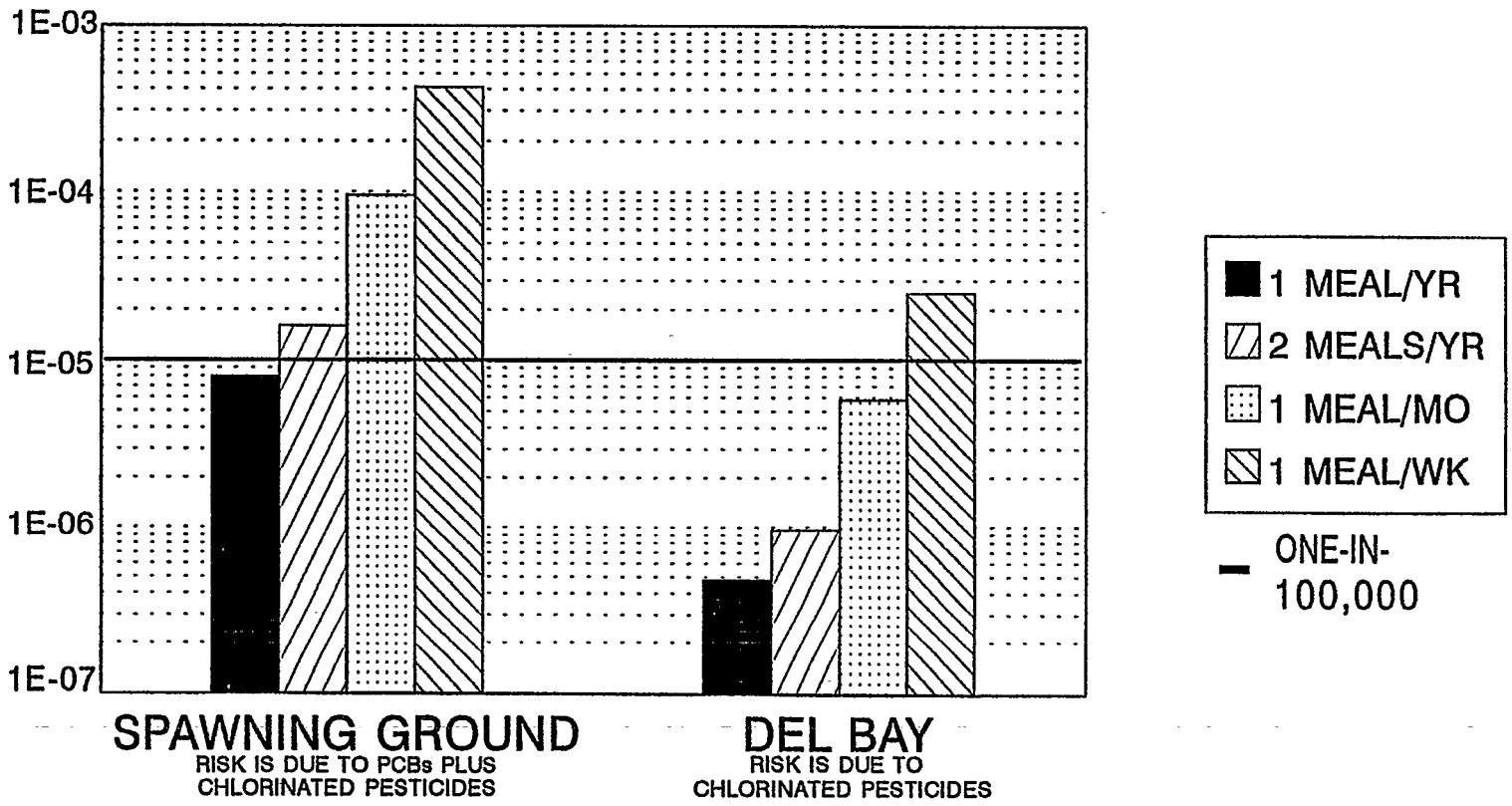
COMPARISON OF CANCER RISK PROJECTIONS
DELAWARE ESTUARY STRIPED BASS



MEAL = 8 OUNCES

NOTE: METHOD B & C ONLY APPLY TO
RECR SIZE FISH FROM SP GROUND

COMPARISON OF CANCER RISK PROJECTIONS SPAWNING GROUND VS DELAWARE BAY METHOD C



SUMMARY

- CONSIDERABLE UNCERTAINTY CURRENTLY SURROUNDS PCB RISK ASSESSMENT. THIS UNCERTAINTY HAMPERS RISK MANAGEMENT AND COMMUNICATION.

- MAXIMUM OPPORTUNITY (FOR STATES) TO REDUCE UNCERTAINTY IS THROUGH USE OF IMPROVED ANALYTICAL METHODS AND FISH CONSUMPTION SURVEYS, ALTHOUGH THIS WILL TAKE TIME AND MONEY.

- GEOGRAPHICALLY-TARGETED, INTENSIVE STUDIES PROVIDE A MUCH STRONGER INFORMATION BASE UPON WHICH TO ASSESS POTENTIAL FISH CONTAMINATION PROBLEMS.

- IMPERATIVE TO TAKE A TEAM APPROACH.

4.4 MICHIGAN

John L. Hesse, Chief, Site Assessment Section, Michigan Department of Health

The Great Lakes have received considerable attention and publicity in terms of fish contaminant problems, perhaps more than any other region of the nation. Part of this attention is because the Great Lakes represent the largest freshwater resource in the world. They have also been more thoroughly studied than other areas.

Some of the nine Great Lakes jurisdictions initiated fish consumption advisory programs more than 20 years ago, dating back to the discovery of mercury and PCBs in fish in 1970. This presentation will focus on how Michigan and other Great Lakes states have issued advisories in the past and will provide a preview of a proposed advisory protocol currently being considered for uniform application by all states in the region.
While a few isolated advisories have been issued because of DDT, chlordane, toxaphene, mercury, and dioxins in the Great Lakes over the years, PCBs continue to be the primary chemical group responsible for most consumption advisories.

Trend monitoring conducted by EPA and other agencies provides clear evidence of rather dramatic declines of PCB levels since the mid-1970's, approximating a 90 percent drop in concentrations found in many popular Great Lakes sport fish species. During this same time interval, however, epidemiologic and toxicologic research into the potential health effects of PCBs on animals and humans has increased our level of understanding about fish consumption patterns, specific congener toxicities, possible modes of action, and most sensitive endpoints of concern. It is appropriate that we continue to use this new information in refining our "risk management" criteria and strategies (i.e., fish consumption advisories).

In the 1970's, when pesticide and PCB levels were the highest in Great Lake's fish, most of the states which had advisory programs in place depended largely upon FDA Action Levels as the basis for advice to anglers. It seemed to make sense that advice to people who were eating sport-caught fish should be comparable to protection being provided through regulation of fish being sold commercially.

By 1978, with the expanded use of risk assessment in our regulatory programs, Michigan started to more critically evaluate the trigger levels for our advisories. When FDA was ordered by the courts in 1979 to raise their action level for mercury from 0.5 ppm to 1.0 ppm due to economic impacts upon marine fisheries, Michigan decided not to adopt the new standard for fish advisories because we felt that the toxicology of mercury supported continued use of 0.5 ppm as a trigger level.

In 1979, when FDA issued notice of an intent to lower the PCB action level from 5 ppm to 2 ppm, Michigan began our own evaluation of the PCB trigger level and decided to adopt the 2 ppm value in 1981 for fish advisory purposes. FDA's decision to lower the standard to 2 ppm didn't occur until 1983.

As part of an initiative to establish new guidelines for surface water quality discharge limits, Michigan had adopted a standardized cancer risk estimation procedure and a level of acceptable risk of 1 X 10^{-5}. Using assumptions and cancer risk models which were fairly well accepted in 1981, we concluded that 2 ppm for PCB and 0.3 ppm for chlordane each approximated a 10^{-5} cancer risk and that they were appropriate trigger values for fish consumption advisories. Similarly, we adopted a 10 part per trillion advisory level for dioxin based upon a 10^{-5} estimated cancer risk. We recognize, however, that the application of more conservative models and assumptions since the early 1980's have increased the estimated risk at these levels. As I will discuss later in my presentation, this may be irrelevant because of a tentative decision by the Great Lakes states to use adverse reproductive outcomes rather than cancer risk estimates as the principal basis for fish consumption advisories.

Because differing approaches to fish advisories by neighboring jurisdictions causes unnecessary confusion for the public, all of the Lake Michigan states (Michigan, Indiana, Illinois, and Wisconsin), began an effort in the early 1980's to reach consensus on issues associated with sampling, analysis, and advisory criteria. The U.S. EPA Region V office provided assistance, and, by 1985, we had actually reached agreement on all major Lake Michigan fish monitoring and consumption advisory issues.

The Lake Michigan states knew that the FDA Action Levels were being criticized as being out-dated and perhaps not adequately protective of the developing fetus and of anglers who tend to eat more fish than the general public. On the other hand, we wanted to retain some association with how fish from the Great Lakes or other area waters were being regulated for commercial sale.

To partially take into account the extra sensitivity of the fetus and higher average consumption rates of anglers compared to the general public, we decided to initiate a "no consumption" advisory for women and kids when only 11-49 percent of the samples for a species exceeded any of the FDA action levels. At this frequency, the general population was advised to eat no more than 1 meal per week. When 50 percent of the samples exceeded an FDA action level, a "no consumption" advisory was issued that applied to everyone.

While this lacked a true scientific basis, we felt that it would be less confusing to the public than completely divorcing ourselves from the FDA regulatory numbers. A survey in Wisconsin conducted in 1985 showed that about 90 percent of anglers surveyed were aware of the consumption advisories and 60 percent were modifying their consumption patterns accordingly. We feared that we would lose voluntary compliance with the advisories if we changed to a system that treated anglers grossly different from consumers of commercially harvested fish from the same waters.

The Lake Michigan states also began to annually pool monitoring data and coordinate sampling plans. This all worked out so well in Lake Michigan that the Governors of all the

Great Lakes states signed an agreement (Governors' Great Lakes Toxic Substances Control Agreement, 1986) mandating common fish consumption advisories on each of the Great Lakes. While the jurisdictions were able to comply with the spirit of the agreement by the 1987 fishing season with advisories that were essentially uniform, we have not been able to reach agreement on common criteria, even after several years of effort.

For several years, we have essentially maintained a moratorium on significant changes to the Great Lakes advisories pending final development of uniform criteria. We have added species to the advisory as necessary but have hesitated to delist species as contaminant levels have declined (because of the likelihood of new criteria being more conservative).

In 1993, the Great Lakes Sport Fish Advisory Task Force, currently co-chaired by the Wisconsin Department of Health and Social Services and the Wisconsin Department of Natural Resources, has tentatively reached agreement on a Protocol for a Uniform Sport Fish Consumption Advisory for the Great Lakes' region (GLSFATF, 1993). The proposed protocol will likely be undergoing peer review in next few months and hopefully will be ready for implementation for the 1994 advisories.

The proposed protocol involves use of a Health Protection Value (HPV) of 0.05 ug/kg/day maximum ingestion of PCBs. The goal of the advisories will be to keep the PCB ingestion via sport fish consumption below 3.5 ug PCB per day for a 70 kg person. The Health Protection Value approach primarily focuses on protection against neuro-developmental effects in infants born to exposed mothers. The selected value is from an aggregate of several human and animal studies showing similar thresholds of effects. The protocol assumes an average meal size of 227 gms (1/2 lb) and an average adult weight of 70 kgs.

Perhaps unique to our proposal, we would be using a 50 percent estimated reduction factor for residues in the untrimmed raw fillet due to losses through trimming and cooking. Recent research at Michigan State University (Zabik, M.E., *et al.*, 1993), coupled with other research on contaminant reductions, support at least a 50 percent reduction as a conservative estimate. The draft EPA Sampling and Guidance Manual (US EPA, 1993) cites 60-90 percent reductions possible through trimming and cooking but does not propose an adjustment to the screening values.

The protocol establishes 5 advisory categories for different rates of consumption (unrestricted; 1 meal/week; 1 meal/month; 6 meals/year, and; no consumption). Fish are placed into these groupings according to concentration ranges that would not result in ingestion of more than 3.5 ug PCBs/day. Provisions are made for adjustments in the advisory if PCBs are not the predominant contaminant in fish from a specific location.

Due to the high level of uncertainty associated with cancer risk projections, the Great Lakes Task Force has rejected use of such extrapolations as the primary basis for PCB or other organochlorine compound fish consumption advisories . However, the advisory

information provided to the public will include general statements about potential cancer risks from fish consumption. As presented earlier, emphasis will be given to protection against adverse reproductive impacts and other non-cancer endpoints, and by doing so, other potential adverse effects will be minimized also.

Persons interested in obtaining a copy of the Proposed "Protocol for a Uniform Great Lakes Sport Fish Consumption Advisory" should write to James F. Amrhrein, Wisconsin Department of Natural Resources, Bureau of Water Resources Management, 101 S. Webster Street, Box 7921, Madison, WI 53707-7921.

References Cited

Great Lakes Council of Governors. "The Great Lakes Toxic Substances Control Agreement," May 21, 1986.

Great Lakes Sport Fish Advisory Task Force. "Proposed protocol for a uniform sport fish consumption advisory," Draft, March 1993.

US EPA. "Fish sampling and analysis: A guidance document for issuing fish advisories," Draft, Office of Science and Technology, February, 1993.

Zabik, M.E., M.J. Zabik, and H. Humphrey. 1993. "Assessment of contaminants in five species of Great Lakes fish at the dinner table," Part I, Final Report to the Great Lakes Protection Fund, March, 1993.

4.5 SUMMARY OF QUESTIONS AND RESPONSES[12]

4.5.1. A representative from the Massachusetts Division of Marine Fisheries asked Dr. Pollock how he deals with the issue of risk comparisons. How are the viewpoints of colleagues who favor the use of risk comparisons factored into risk assessments and risk communication work?

Dr. Pollock stated that there have been suggestions about comparing exposures due to fish consumption to other sources of exposure; however, at this point, such comparisons have not been used in California. In part, this is because a total diet approach might be needed and that is not being done.

4.5.2. Dr. Bolger then commented to the panel about several difficulties facing people involved with risk assessment. Some methodologies, developed years earlier, are not well suited for evaluating environmental contaminants where we are evaluating degrees of risk, rather than a simple question of "safe or unsafe." Other approaches (e.g., probability distributions) may require further education of those who must use the assessment.

The second comment focused on the use of a nomogram, which describes all the data in one pictorial representation. Nonetheless it is difficult to interpret the resulting nomograph because it is based on aggregate risk.

Ms. Cox acknowledged that there may be difficulties associated with adding all of the hazard quotients to obtain a hazard index. However, she believed that this is a standard protocol used in the Superfund program.

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[12] Ed. note: The question and response portion includes summaries derived from transcribed conversations. The summaries have been carefully edited to present the discussion as accurately as possible. However, these question and response summaries have not been reviewed by the speakers--unlike the proceeding abstracts.

PART FIVE
APPENDICES

A.1 Speakers Biographies

Elizabeth Southerland, Ph.D.

Elizabeth Southerland currently directs EPA's Risk Assessment and Management Branch within the Office of Water's Office of Science and Technology. The Branch is responsible for directing sediment contamination programs and evaluating risks associated with chemical contaminants in fish.

Dr. Southerland graduated with a Ph.D. in Environmental Engineering from Virginia Polytechnic Institute and State University in 1980. She worked in State government and in consulting engineering prior to joining EPA.

Rick Hoffmann

Rick Hoffmann organized the PCB workshop. Mr. Hoffmann is an environmental scientist in EPA's Risk Assessment and Management Branch. The Branch is located in the Office of Science and Technology within the Office of Water. The Branch is responsible for directing sediment contamination programs and evaluating risks associated with chemical contaminants in fish. Mr. Hoffmann works on fish contamination issues.

Prior to that, Mr. Hoffmann worked in EPA's San Francisco region where he held various positions relating to water quality planning and pollution control as well as overall environmental impact assessments. He has also worked for the Hawaii State Department of Health. Mr. Hoffmann received a B.A. in Zoology from California State University at San Diego and an MPH from the University of Hawaii's School of Public Health, with an emphasis in environmental/occupational health.

Mitchell D. Erickson, Ph.D.

Mitchell D. Erickson is a Group Leader for Environmental Chemistry in the Environmental Research Division at Argonne National Laboratory, Argonne, IL. His current research interests focus on the improvement of radio analytical methods (with an emphasis on faster and less expensive routine methods) and the evaluation, design, and testing of sensors and samplers for use in subsurface monitoring (specifically for interfacing to cone penetrometers). He also provides technical contributions on PCBs,

PCDDs, PCDFs, and other environmental pollutants through presentations, publications, and consulting.

He is the author of *Analytical Chemistry of PCBs,* first published in 1986, and is currently working on the second edition for Lewis Publishers. He also authored the book *Remediation of PCB Spills* (Lewis, 1993).

John H. Craddock, Ph.D.

John H. Craddock is founder and principal of Craddock Associates, Incorporated Regulatory and Environmental Consultants based in St. Louis, MO. Dr. Craddock also is a Senior Consultant with RegNet Environmental Services in Washington, DC. Dr. Craddock has more than 30 years experience in the chemical industry, including wide-ranging involvement with state and federal regulatory and compliance issues. For the past 13 years, he has worked closely with federal and state agencies responsible for regulating toxic chemicals, particularly PCBs. For more than 12 years, he has managed PCB regulatory and compliance issues for Monsanto Company in St. Louis.

Dr. Craddock was an active member of the Chemical Manufacturers Association PCB Panel since its inception in 1980 and its chairman from 1984 to 1992. Working closely with the EPA in the development of all major federal PCB regulations since 1981, he has led industry advocacy efforts to develop cost-effective, technically achievable rules. He received his B.S. in Chemistry from Memphis State University and his Ph.D. in Chemistry from Vanderbilt University.

P. Michael Bolger, Ph.D., D.A.B.T.

P. Michael Bolger is the Chief of the Contaminants Standards Monitoring and Program Branch in the Center for Food Safety and Applied Nutrition of the U.S. Food and Drug Administration (FDA) in Washington, DC.

Dr. Bolger received his B.S. in Biology from Villanova University and his Ph.D. in Physiology and Biophysics from Georgetown University. After a two year postdoctoral position with the Department of Physiology in the Georgetown University Medical Center, Dr. Bolger became a staff fellow in toxicology with the Bureau of Foods in the FDA. Upon completion of the staff fellowship, he accepted a position as a toxicologist with the contaminants branch at FDA. Over the last decade, Dr. Bolger has been involved in a number of hazard/risk assessments of food contaminants, including PCBs. Dr. Bolger is a board certified toxicologist by the American Board of Toxicology. Dr. Bolger is currently Chief of the Contaminants Standards Monitoring and Programs Branch, which is responsible for the monitoring and hazard/risk assessment of environmental contaminants in the food supply.

Vincent James Cogliano, Ph.D.

Vincent James Cogliano is the Chief of EPA's Carcinogen Assessment Statistics & Epidemiology Branch. In this capacity, he is responsible for evaluating human studies and using human and animal studies to estimate the risks to human health from exposure to environmental pollutants.

Dr. Cogliano received his Ph.D. in Operations Research from Cornell University in 1982. From 1981 to 1983, he worked as a manufacturing engineer for the IBM Corporation in New York. In 1983, he moved to the Washington area and began working for the U.S. Environmental Protection Agency, where he has held positions in the Office of Pesticide Programs; the Office of Policy, Planning, and Evaluation; and the Office of Health and Environmental Assessment.

John L. Cicmanec, D.V.M.

John L. Cicmanec is a Veterinary Medical Officer of the Systemic Toxicants Assessment Branch in the Environmental Criteria Assessment Office of EPA's Office of Research and Development in Cincinnati, Ohio.

Dr. Cicmanec is a Research Veterinarian who presently works as a risk assessor in the Cincinnati office of EPA. Prior to joining the staff of the Environmental Criteria Assessment Office he directed the operation of the research animal facility of EPA in Cincinnati. Prior to the 8 years that he has spent with EPA, he spent 16 years at a clinical veterinarian and study director for private animal research contract firms in the Washington, DC area. During this time, as a study veterinarian, he conducted a subchronic reproductive research study involving the effects of Aroclor 1254 on a large group of rhesus monkeys. Dr. Cicmanec is a Diplomate of the American College of Laboratory Animal Medicine. In addition to his veterinary training, he received a M.S. from the University of Michigan Medical School.

Donald G. Barnes, Ph.D.

Donald G. Barnes has held numerous senior science advisory positions with the U.S. Environmental Protection Agency in Washington, DC, including EPA's Science Advisory Board (SAB). The SAB, which are organized into nine committees, is composed of 16 staff members and a Board of more than 300 distinguished scientists and engineers. The SAB committees meet 50 to 60 times a year and produce nearly 40 reports annually. Dr. Barnes currently serves as a member of the EPA Risk Assessment Forum and the Risk Assessment Council. He also participated in the development and adoption of EPA risk assessment guidelines for cancer, exposure assessment, and complex mixtures.

Dr. Barnes is an international expert in the toxicology, exposure, and risk assessment of 2,3,7,8-tetrachlorodibenzo-p-dioxin, and has published more than a dozen papers on the subject. He served as a consultant to the World Health Organization on "dioxin" in municipal solid waste combustion and as a contaminant in human milk. He also led a successful effort to develop an international consensus on "Toxicity Equivalency Factors" (TEFs) for conducting risk assessments for 210 "dioxins and furans." Dr. Barnes represented EPA for more than a decade on an interagency science panel established by the White House to address Agent Orange.

He received his B.A. in chemistry from the College of Wooster and his Ph.D. from Florida State University with a major in chemistry and a minor in physics.

Theodora (Theo) Colborn, Ph.D.

Theo Colborn, a Senior Fellow with the W. Alton Jones Foundation and the World Wildlife Fund, manages their Toxics and Wildlife Program. In 1985, she was awarded a Fellowship at the Congressional Office of Technology Assessment. In 1987, she moved to the Conservation Foundation where she provided scientific guidance for the book, *Great Lakes, Great Legacy?*, released in 1990 in collaboration with the Institute for Research and Public Policy, Ottawa, Canada. Recently, Dr. Colborn edited a book, *Chemically Induced Alterations in Sexual and Functional Development: The Wildlife/Human Connection*. Dr. Colborn has testified before the U.S. House and Senate, lectured extensively, and served in an advisory capacity to state, Federal, and international groups concerning the non-cancer hazards of exposure to toxic chemicals. Currently, Dr. Colborn serves on the Science Advisory Committee of UNEP's Marine Mammal Plan Task Force; she also serves on the Science Advisory Consultant Group authorized under the Great Lakes Critical Program Act of 1990 for the Agency for Toxic Substances and Disease Registry. She holds an adjunct faculty position with George Mason University and is a member of the Rocky Mountain Biological Laboratory, the Colorado Field Ornithologists, and the Society of Environmental Toxicology and Chemistry.

Dr. Colborn earned a Ph.D. in Zoology (distributed minors in epidemiology, toxicology, and water chemistry) at the University of Wisconsin-Madison; an M.A. in Science at Western State College of Colorado (fresh water ecology); and a B.S. in Pharmacy from Rutgers University College of Pharmacy.

John F. Brown, Jr., Ph.D.

John F. Brown Jr. is the Manager of Health Research for General Electric Corporate R&D in Schenectady, NY. Dr. Brown received his B.S. from Brown University and Ph.D. from MIT, both in chemistry, and later took postdoctoral training in clinical pathology at the SUNY Upstate Medical School in Syracuse. Except for his post-doctoral training, Dr. Brown's entire professional career has been spent in various research or research management positions at General Electric, where he was initially concerned with chemical synthesis and molecular structure, and more recently with medical diagnostics, and health risk assessment and environmental biodegradation, especially as it relates to PCBs.

Dr. Brown has served as a member of an NHLBI study of blood-compatible materials, the MIT SCEP Study of Critical Global Environmental Problems, and the recent IEHR Workshop on Hydrophobic Organic Chemicals Bioaccumulation. He also has served as Natural History Chairman for the Adirondack Mountain Club, Chairman of the Schenectady Museum Nature Preserve Committee, and long-time member of both the Niskayuna (Town) and Schenectady (County) Environmental Management Councils.

Ted R. Schwartz

Ted Schwartz is the Chief Chemist of the U.S. Department of the Interior Fish and Wildlife Service's National Fisheries Contaminant Research Center (NFCRC) in Columbia, Missouri. Mr. Schwartz is responsible for the administration and management of the Chemistry Division of NFCRC. He evaluates and determines the nature, extent, and limits of equipment, facilities, and data needed to accomplish the Division's goals. He is responsible for staff development and direction of chemistry research. His

personal research interest is in the interpretation of complex environmental patterns of organic residues in aquatic ecosystems using chemometric data analysis techniques.

Mr. Schwartz received a B.S. degree in Chemistry from the California State University at Humboldt in 1978, and a M.S. degree in Organic Chemistry at the University of Missouri in 1982.

Margaret M. Krahn, Ph.D.

Margaret Krahn serves as the Assistant Program Manager of the Environmental Conservation Division's Environmental Chemistry Program. This program is located at the Northwest Fisheries Science Center of the National Marine Fisheries Service, which is a part of the National Oceanic and Atmospheric Administration in Seattle, Washington.

Dr. Krahn has developed state-of-the-art methods for determining trace organic contaminants, such as polynuclear aromatic hydrocarbon metabolites and coplanar PCBs in marine samples. Among the techniques she uses are high-performance liquid chromatography, fluorescence spectrometry, photodiode array (ultraviolet) spectrometry, gas chromatography, and mass spectrometry. Dr. Krahn has played a key role in developing new screening methods to rapidly determine contaminant levels in bile and tissues from marine animals and in marine sediments. In addition, she has developed and automated procedures for the cleanup of sediment and tissue extracts before analysis by gas chromatography/mass spectrometry. She has published extensively and many of her published methods have been adopted for use by government, academic, and private laboratories.

Prior to joining the Environmental Conservation Division in 1978, Dr. Krahn taught chemistry at the University of Delaware. She earned her B.S. in Chemistry from the University of Minnesota and her Ph.D. in Organic Chemistry from the University of Washington.

Leon D. Sawyer

Leon D. Sawyer is the Branch Chief of the Methods Research Branch, Division of Pesticides and Industrial Chemicals at the Food and Drug Administration's Center for Food Safety and Applied Nutrition in Washington, DC.

Mr. Sawyer has worked for the U.S. Food and Drug Administration for 29 years; specifically, he has worked 25 years as a chemist, research chemist or scientific coordinator, and the last four years as a supervisory chemist in FDA's Division of Pesticides and Industrial Chemicals. He has been involved with analytical and regulatory issues relating to PCBs since their identification as environmental contaminants in 1969 and has actively participated in numerous workshops and symposia relating to them. He served as an Associate Referee in the Association of Official Analytical Chemists (currently *AOAC International*) on four different residue topic areas, and he has served for 18 years (1971-1989) as the Associate Referee on PCBs. During this time, two AOAC Collaborative Studies on the analysis and quantitation of PCBs were conducted which are recognized as "Official Methods of Analysis" by *AOAC International*. Also during this time period, investigations were initiated on an individual congener approach to PCB identification and quantitation, which will be the subject of this presentation.

Brian Bush, Ph.D.

Brian Bush is a Senior Research Scientist for organic analytical toxicology for the New York State Department of Health, Wadsworth Laboratories in Albany. Dr. Bush also is an associate professor at the School of Public Health Sciences, State University of New York at Albany. Dr. Bush has published nearly 70 professional articles on organic analysis topics including a number of articles on PCB analysis. He received his B.S. (with honors) in Chemistry from the University of Leeds, the United Kingdom and received his Ph.D. in the Analysis of Steroids also from the University of Leeds in the United Kingdom. Dr. Bush is a Fellow of the Royal Society of Chemistry and a Member of the Society for Analytical Chemistry.

Gerald Pollock, Ph.D.

Gerald Pollock is a Staff Toxicologist and Acting Unit Chief of the Fish and Sediment Contamination Unit for the California EPA, Office of Environmental Health Hazard Assessment, Pesticide and Environmental Toxicology Section in Sacramento. Presently, he is responsible for the evaluations of human health hazards associated with consumption of chemically contaminated seafood. He also managed the Department of Health Service's studies of the contamination of fish in southern California and Monterey Bay. He has conducted risk assessments of consuming fish contaminated with DDT, PCBs, and dioxins, and has served as a consultant to the Committee on Wastewater Management for Coastal Urban Areas of the National Research Council. Previously, Dr. Pollock has held positions as both an Assistant Professor of Toxicology in the Regional Program in Veterinary Medicine at the University of Idaho, and as a Research Supervisor for Animal Metabolism at Diamond Shamrock Corporation.

Dr. Pollock received both his B.S. in Biochemistry and his Ph.D. in Pharmacology and Toxicology from the University of California at Davis. He is a Diplomate of the American Board of Toxicology.

Janice P. Cox

Janice P. Cox is currently a Project Leader for the Tennessee Valley Authority's Water Resource Issues Analysis projects. She developed the issues analysis format to identify and evaluate -- on a watershed-wide basis -- sources of impacts to water quality and their potential for impact on public health. Issues analyses have been used for defining needs for monitoring, resource protection, and impact mitigation projects.

Ms. Cox currently is a member of TVA's Hiwassee River Action Team, charged with identifying water resource problems and building inter-agency coalitions to implement solutions on a watershed basis. Previously, she was an Associate Editor for the International Journal of Childbirth Education, 1986-1988, which focused on the potential impacts of environmental stresses on fetal development and birth outcomes.

Ms. Cox received a B.A. in Chemistry from the University of Arkansas, an M.S. in Phycology from the University of Arkansas, and a C.E. in Risk Assessment, Toxicology, and Risk Communication from The Johns Hopkins University.

Richard W. Greene

Richard W. Greene is an Environmental Engineer for the State of Delaware Department of Natural Resources and Environmental Control's Watershed Assessment Branch. His principal focus is the assessment of ecological and human health risks associated with toxics in surface water, sediment, and biota. Mr. Greene has been instrumental in developing Delaware's Toxics in Biota Program and was involved in all three fish consumption advisories issued for Delaware waters. Most recently, he was the driving force behind the transition to a risk-based approach to evaluating fish contaminant data in Delaware. As part of Delaware's transition to a risk-based approach, Mr. Greene identified the important link between PCB analytical methods and subsequent risk characterization.

John L. Hesse, M.S.

John L. Hesse is an Environmental Health Administrator within the Michigan Department of Public Health, currently serving as Chief of the Site Assessment Section. Mr. Hesse has been with the Department of Public Health for 14 years. Prior to this, he worked for 11 years with the Michigan Department of Natural Resources in toxic chemical monitoring and control. He was involved with the identification of the PCB problem in the Great Lakes in 1970 and assisted in the passage of legislation at the state and Federal level to ban the use of PCBs. As one of two primary program areas under his supervision, Mr. Hesse is currently principal investigator of a cooperative agreement from the Federal Agency for Toxic Substances and Disease Registry for Michigan to conduct health assessments at Superfund contamination sites. He also coordinates the fish consumption advisory program for the State of Michigan. Mr. Hesse works closely with other members of the Division of Health Risk Assessment who are involved with ongoing investigations to determine human health effects of eating Great Lake fish.

Mr. Hesse received his B.S. from Utah State University and his M.S. in Aquatic Biology from Michigan State University.

Deborah L. Swackhamer, Ph.D.

Deborah L. Swackhamer is an Associate Professor at the University of Minnesota. She directs the Environmental Chemistry Program in the Division of Environmental and Occupational Health, School of Public Health. Dr. Swackhamer's research interests include studying the chemical and biological processes that control the fate of hydrophobic contaminants in aquatic systems. For the past 15 years, one of her greatest emphases has been the processes controlling PCB behavior in the Great Lakes. Her current research is on PCB accumulation by phytoplankton.

She received her B.A. in Chemistry from Grinnell College and her M.A. and Ph.D. degrees from the Water Chemistry Program at the University of Wisconsin-Madison. After doing postdoctoral work at Indiana University in Bloomington, she joined the faculty at the University of Minnesota in 1986.

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AGENDA: PCB WORKSHOP

PCBs in FISH TISSUES--
Exchanging Information Between Data Generators and Data Users

A forum to discuss current PCB issues regarding analytical methods for fish tissues and considerations for human health assessments.

DAY 1 MONDAY MAY 10, 1993

PART I: INTRODUCTION To PCBs & FISH

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1. Welcome & Introduction
   9:00--9:20
   {Dr. Elizabeth Southerland, EPA}
   {Mr. Rick Hoffmann, EPA}
   Topic: Welcome; Workshop purpose; EPA programmatic overview.

2. Introduction to PCBs and Analytical Methods
   9:20--9:50
   {Dr. Mitchell D. Erickson, Argonne National Lab}
   Topic: Structure, chemistry, & analysis of PCBs.

3. Overview: Occurrence of PCBs in Fish Tissues
   9:50--10:35

   A. Temporal Trends of PCBs in the Environment
      9:50--10:15
      {Mr. John H. Craddock, Regulatory Network, Inc.}

   B. PCB Trends in Great Lakes Fish
      10:15--10:35
      {Mr. David Devault,
      EPA's Great Lakes National Program Office}

4. Overview of PCB toxicology

10:50--11:15

*{**Dr. Mike Bolger**, Food and Drug Administration}*

Topic: Introduction to PCB toxicology; FDA uses of PCB data

5. PCB Criteria for Water

11:15--11:40

*{**Ms. Jennifer Orme Zavaleta**, EPA}*

Topic: Overview of PCB regulatory criteria

11:40--12:00 Responses to Introductory Remarks

PART II: PCB TOXICITY & HEALTH EFFECTS

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6. PCB Toxicity: Recent Evaluations of Human Health Effects

1:00--4:30

A. Regulatory Update: Human Carcinogenicity Effects

1:00-1:25

*{**Dr. Jim Cogliano**, EPA}*

Topic: Current/Anticipated cancer value; recent information

B. Regulatory Update: Non-Carcinogenic Effects

1:25--1:50

*{**Dr. John Cicmanec**, EPA}*

Topics: proposed RfD for Aroclor 1016, other

C. Update: Toxicity Equivalents for PCBs

1:50--2:15

*{**Dr. Donald Barnes**, EPA}*

D. Animal/Human Health Connection

3:00--3:25

*{**Dr. Theo Colborn**, W. Alton Jones Foundation}*

E. Industry Research

2:35--3:00

*{**Dr. John Brown**, GE R&D Center}*

Topics: Longitudinal medical studies; PCB accumulation patterns; other

F. 3:30--4:30 Questions/ Discussions

DAY 2 TUESDAY MAY 11, 1993

PART III: ANALYTICAL METHODS

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7. PCB Analyses--An Overview

8:00--8:15

*{**Dr. Mitch Erickson**, Argonne National Lab}*

Topic: Introduction of analytical methods panel

8. Methods Panel--Aroclor vs. Congener Methods vs. Other Methods

8:15--11:30

A. Recent PCB Research

8:15--8:40

*{**Mr. Ted Schwartz**, U.S. Fish & Wildlife Service}*

Topic: Further comparisons of aroclor versus congener-specific analyses in fish; pattern recognition

B. FDA Method for Analyzing PCBs

8:40--9:05

*{**Mr. Leon Sawyer**, U.S. Food & Drug Admin.}*

Topic: FDA method for "total PCBs"--Aroclor-based; comparisons to congener-specific analysis

C. "Performance-based" Methods

9:05--9:30

*{**Dr. Peggy Krahn**, NMFS/NOAA}*

Topic: Performance-based methods used by NMFS--total aroclor & congeners; method advances

D. EPA's Green Bay PCB Study--Congener Analyses

9:30--9:55

*{**Dr. Deborah Swackhamer**, University of Minnesota}*

Topic: Measuring specific congeners--lessons from 7 lab. QA for EPA's Green Bay PCB mass loading study

E. State Lab Experience
10:15--10:35
*{**Dr. Brian Bush**, NY State Wadsworth Lab}*
Topic: Congener-specific analyses in New York

10:35--11:30 Methods Panel Discussion

PART IV: CASE STUDIES--Human Health/Risk Assessment

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9. Risk Assessment Panel--
Case Studies of PCB Risk/ Health Assessments
1:00-3:30

A. California
1:00--1:25
*{**Dr. Gerald Pollock**, Cal EPA}*
Topic: PCB risk assessment in Southern California

B. Tennessee Valley Authority
1:25--1:50
*{**Ms. Janice Cox**, TVA}*
Topic: Recent TVA fish risk assessment, PCB emphasis

C. Delaware
1:50--2:15
*{**Mr. Richard Greene**, Delaware Water Resources}*
Topic: Recent PCB assessments in Delaware

D. Michigan
2:15--2:35
*{**Mr. John Hesse**, Michigan Dept. of Public Health}*
Topic: Fish advisories for the Great Lakes: Past and Proposed Methodologies

2:35--3:45 Panel Discussion

PART V: CONCLUDING REMARKS

3:45--4:15
{Dr. Elizabeth Southerland, EPA}
Topic: Summarize meeting; Follow-up activities

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Appendix A.5 - PCB Workshop Report Summaries from EPA's Risk Assessment Forum

Neurotoxic Effects Summary

On September 14 and 15, 1992, EPA's Risk Assessment Forum sponsored a workshop on the developmental neurotoxic effects of PCBs (57 FR 39200, August 28, 1992). The meeting was held in Research Triangle Park, NC, and was chaired by Linda Birnbaum and Carole Kimmel of EPA. Participants from academia, industry, and state and federal government brought expertise from a wide range of disciplines to the discussion. Members of the public and EPA scientific staff attended the workshop as observers.

The report collects workshop papers and discussion on principles and methods for evaluating data from animal and human studies. The report also summarizes data from other information discussed at the workshop for characterizing risk to human development, growth, survival, and function following exposure to PCBs prenatally or to infants and children. EPA complied several issues papers on various aspects of PCB toxicity and especially on developmental neurotoxicity, as a framework for workshop discussion. These issue papers were distributed to all invited participants, who then submitted pre-meeting comments.

As outlined in the issue papers, the purpose of this workshop was to arrive at a general "sense of the meeting" regarding the current state of the science on neurotoxic effects associated with prenatal and perinatal exposure to PCBs. EPA did not expect participants to reach a common position on all of the issues before the group. Because PCBs are present in air, water, and food, information developed at the workshop will assist EPA in evaluating the effects of PCBs in these media and will serve as a basis for protecting public health from PCBs occurring in these media.

Recent studies defined the issues selected for workshop analysis. Data from rodents and monkeys have demonstrated that prenatal and perinatal PCB exposure results in neurotoxicity in the offspring. Related effects have been reported in human studies. For example, human poisonings (Yusho and Yucheng) have led to developmental delays and impairment in neurobehavioral indices in offspring of exposed women. Also, relatively low levels of exposure to PCBs in cohorts in Michigan and North Carolina have suggested neurobehavioral deficits in infants and younger children. Thus, the public health consequences of exposure to developmental neurotoxicants such as PCBs are potentially significant.

These observations pose several questions regarding the use of PCB data for assessing risk of neurotoxic effects because of prenatal or perinatal exposure:

- Are all PCBS alike in these effects or, if not, are any useful structure/activity relationships discernable?

- What are the dose/response relationships?

- Are there populations at special risk due to elevated exposure or to inherent sensitivity?

- What are the endpoints of greatest concern and greatest sensitivity?

These questions are important because of the persistence of PCBs in environmental media such as water and air, and the nature of the data available on PCBs and developmental neurotoxicity; *i.e.*, many studies are available on various mixtures but little or no information is available regarding specific congener effects on the developing organism, or the mechanism of action of PCBs.

Availability: The full report, *Workshop Report on Developmental Neurotoxic Effects Associated with Exposure to PCBs* (EPA/630/R-92/004, May 1993), is available from EPA's Center for Environmental Information in Cincinnati, Ohio at (513 569-7562.

Toxicity Equivalency Summary

On December 11 and 12, 1990, EPA's Risk Assessment Forum held a workshop on toxicity equivalency factors for PCB congeners. The purpose of the workshop was to examine the existing toxicity and exposure data base on PCBs to ascertain the feasibility of developing toxicity equivalency factors (TEFs) for PCB congeners. Given the widespread acceptance and acknowledged utility of the TEF method for assessing risks associated with exposures to complex mixtures of chlorinated dibenzo-p-dioxins and dibenzofurans, some experts have urged development of comparable TEF schemes for other structurally related chemicals, such as PCBs. Information from the workshop will contribute to Risk Assessment Forum recommendations on whether to pursue development of a TEF scheme for PCBs.

EPA's Risk Assessment Forum assembled approximately 30 experts in the field of PCB toxicity and mechanisms of action, environmental exposure, and analytical methods for measuring PCBs in human and environmental samples. Dr. Donald Barnes chaired the workshop. After presentations by Dr. Barnes and Dr. Stephen Safe, the participants divided into two work groups: the Work Group on Exposure/Analytical Issues, chaired by Ms. Ann Alford-Stevens; and the Work Group on Toxicity/Mechanisms of Action Issues, chaired by Dr. Linda Birnbaum. The groups discussed the following questions:

- Is the existing data base on toxicity and mechanisms of action sufficient to support a TEF scheme for PCBs?

- What is known about environmental exposures to specific PCB congeners?

- What analytical methods are available to identify and quantify individual congeners in environmental matrices?

- What are the important data gaps and what research is needed to fill them?

On the second day of the workshop, all participants reconvened and the Work Group chairs led the discussion of each group's finding and recommendations. Dr. Barnes closed the meeting with a summary of the workshop's conclusions and recommendations, which are contained in the full report.

Availability: The full report, *Workshop Report on Toxicity Equivalency Factors for Polychlorinated Biphenyl Congeners* (EPA/625/3-91/020, NTIS Order No. PB 982-114529, June 1991), is available from the National Technical Information Service at 1-800-553-6847.