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Proceedings of the 2007 National Forum on Contaminants in Fish

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Section II-H
PCBs and Dioxins

Moderator:

Eric Frohmberg, Maine Center for Disease Control

WHO – 2006 Re-evaluation of TEF for Dioxins and Dioxin-Like Compounds

Daniele Staskal, ChemRisk

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Eric Frohmberg, Maine Center for Disease Control

PCB Body Burdens Associated with Adverse Outcome in Epidemiological Studies

Deborah Rice, Maine Center for Disease Control

* This presentation is not included at the request of the author due to pending publication.

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WHO – 2006 Re-evaluation of TEF for Dioxins and Dioxin-Like Compounds

Daniele Staskal, ChemRisk

Biosketch

Dr. Daniele Staskal (Ph.D.) is a Health Scientist with ChemRisk in Austin, TX. Dr. Staskal received her Ph.D. in Toxicology from the Curriculum in Toxicology at the University of North Carolina at Chapel Hill. She began her research by investigating species differences in hepatic toxicity associated with dioxin and dioxin-like compounds with Dr. Linda Birnbaum at EPA. She then transitioned her research focus to investigating the toxicokinetics of brominated flame retardants, also with EPA. Since joining ChemRisk, she has continued her research with both brominated flame retardants and dioxins, focusing primarily on exposure and human health risk issues. She has been involved with the TEF weighting research project for approximately
2 years.

Abstract

Potential health risks associated with exposure to mixtures of dioxin-like compounds (DLCs) are currently assessed using a toxic equivalency factor (TEF) approach. TEFs are single point estimates of the relative potency (REP) of DLCs recommended by the World Health Organization (WHO), based on underlying REP values that represent a heterogeneous dataset ranging across several orders of magnitude. Recently, the WHO re-evaluated the TEF methodology, resulting in a validation of the TEF approach, as well as revised TEFs for some congeners. The WHO also acknowledged the importance of better characterizing variability and uncertainty inherent in the TEFs and indicated that the use of distributions of REPs would provide a means of characterizing such variability and uncertainty. In addition to developing distributions, WHO requested that a weighting scheme, to quantitatively weight studies based on quality and relevance to human health risk assessment, be developed before distributions were used in TEF evaluation.

Therefore, the aim of current investigation was to develop a transparent and reproducible weighting scheme, to apply it to the REP_{2004} database, and to evaluate the impact on the distributions. The proposed consensus-based weighting scheme incorporates several different measures of study quality and relevance, including REP derivation method and quality, as well as endpoint. Multiple iterations and numerical scales were assessed to determine the impact on the REP distributions. This weighting scheme provides an approach for placing greater emphasis on those REP values that are believed to be more well-suited for health risk assessment purposes. Results of weighting will be presented; generally, weighting did not have a major impact on the overall distribution for most congeners. Although the weighting scheme did not have a significant impact on the overall distributions, the use of such a scheme yields a more transparent, reproducible, and consistent method for deriving TEFs from the underlying REP data.

This abstract does not represent U.S. Environmental Protection Agency policy.

WHO – 2006 Re-evaluation of TEFs for Dioxins and Dioxin-Like Compounds

Daniele Staskal, PhD
ChemRisk, Austin, TX
July 25, 2006
Ken Unice, Nigel Walker, Mike DeVito, Linda Birnbaum, Paul Scott, Mark Harris, William Farland, Laurie Haws

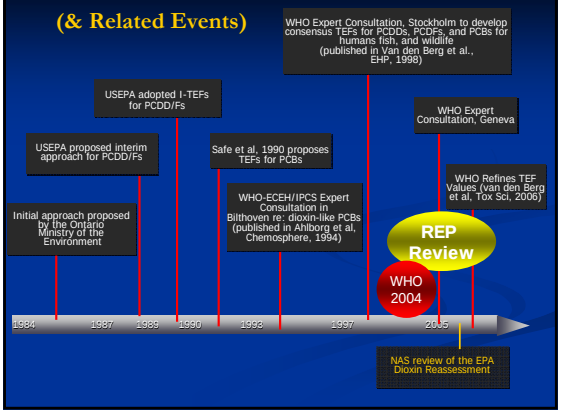
TEF Background

- Currently the standard for evaluating health risks posed by complex mixtures of PCDDs, PCDFs, and dioxin-like PCBs
- Based on evidence indicating that DLCs share a common mechanism of action and elicits a similar spectrum of toxic effects
- Necessary because DLCs occur as mixtures in the environment and there is a lack of complete toxicology data for each congener

TEF Applications

- TEFs play a crucial role in U.S. environmental decision making
- Primary use in the U.S. is in environmental regulation
  - air toxics, site cleanup, issuance of permits, fish advisories, TMDLs, populations exposures, etc.
- In many cases, the use of TEFs is specified in regulations

TEF Timeline
(& Related Events)



WHO Re-evaluation of the TEFs

- October 2004, WHO announced a project designed to re-evaluate the human and mammalian toxic equivalency factors (TEFs) for dioxins and dioxin-like compounds
- Review updated information
- Call for proposals

NAS Review of TEFs

"Overall, even given the inherent uncertainties and limitation, the TEF method, when applied correctly, is a reasonable, scientifically justifiable, and widely accepted method to estimate the relative potency of DLCs on human and animal health" (NAS 2006).

- Considerable uncertainty in selection of TEFs
- Considerable variability in REP data underlying the TEFs
- Better characterize uncertainty in TEF values
  - Consider use of probabilistic distribution of TEFs
  - Establish task force to build consensus probability density functions

REP Database Review

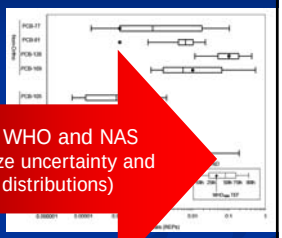
- Review
  - Data entry, repetitive entries, unpublished studies, etc.
- Refine
  - Retained studies which could be used in a quantitative analysis
- Develop unweighted distributions


REVIEW

Development of a Refined Database of Mammalian Relative Potency Estimates for Dioxin-like Compounds

What Did We Learn From the Unweighted Distributions?

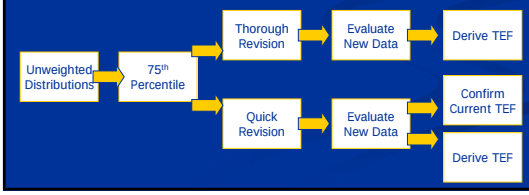
- REPs span orders of magnitude
- PCBs generally have a broader distribution of REPs
- WHO general bound
- WHO generally set at central tendency or lower bound*
  - WHO TEFs for PCBs may be biased low



Results used by WHO and NAS (need to characterize uncertainty and consider using distributions)

WHO Re-evaluation of the TEFs

- Purpose was to consider new scientific information published in the peer-reviewed literature since the time of the last expert consultation held in Stockholm in 1997
  - Methods/approaches for derivation of TEFs (quantitative approaches; uncertainty ranges; weighting factors)
  - Inclusion of mono-ortho PCBs in TEF scheme (role of low level contaminants)
  - Consideration of other dioxin-like compounds



Results of WHO Re-evaluation

- Validation of the TEF approach
- Revised TEFs for several congeners (van den Berg et al 2006)
  - Unweighted REP distributions
  - Expert judgment
  - Point estimates
- Stepwise scale based on half-order of magnitude, log scale (i.e., 0.1, 0.3, etc vs. 0.01, 0.05, etc. previously)
  - Help quantify uncertainty in future

TEF Changes

PCDDs		PCDFs		PCBs	
Congener	TEF	Congener	TEF	Congener	TEF
2378-TCDD	1	2378-TCDF	0.1	PCB77	0.0001
12378-PeCDD	1	12378-PeCDF	0.05 (0.03)	PCB81	0.0001 (0.0003)
123478-HxCDD	0.1	23478-PeCDF	0.5 (0.3)	PCB126	0.1
123678-HxCDD	0.1	123478-HxCDF	0.1	PCB169	0.01 (0.03)
123789-HxCDD	0.1	123678-HxCDF	0.1	PCB105	0.00003
1234678-HpCDD	0.01	123789-HxCDF	0.1	PCB114	
OCDD	0.0001 (0.0003)	234678-HxCDF	0.1	PCB118	
		1234678-HpCDF	0.01	PCB123	
		1234789-HpCDF	0.01	PCB156	
		OCDF	0.0001 (0.0003)	PCB157	
*New TEF for all mono-ortho PCBs=0.00003				PCB167	
				PCB189	

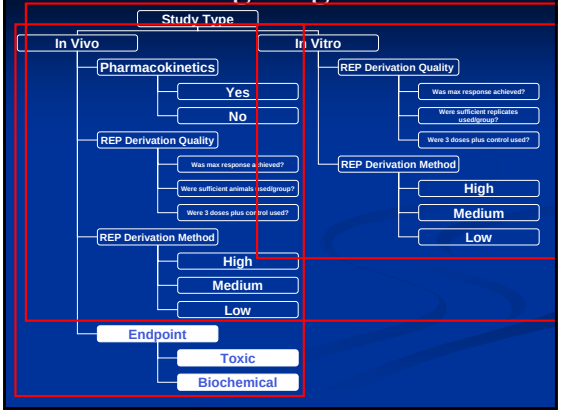
Results of WHO Re-evaluation (Cont.)

- Consideration of alternative approaches for developing TEF (i.e. development of distributions of REP values)
- Need to develop consensus-based REP weighting factors prior to using distributions of REPs to derive TEFs

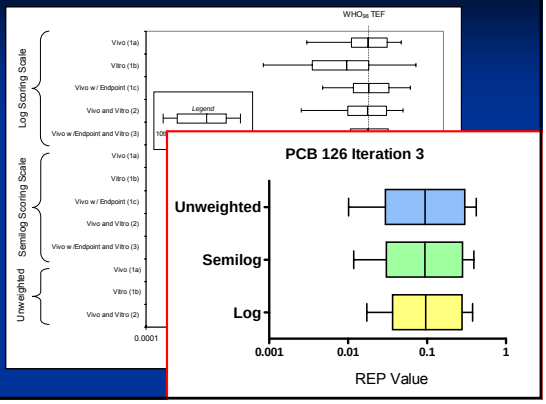
Objective of Weighting

- To develop a transparent, consistent, and reproducible quantitative weighting scheme
- To use these consensus-based weighting factors to develop weighted distributions of REP values
  - Eliminates disagreements over "best" point estimate
  - Reduces variability among congeners (consistent percentile [e.g., 50th, 95th] can be used in deterministic risk assessment)
  - Distributions can be used in probabilistic risk assessment
  - Describe uncertainty in risk estimates
  - Allows regulators to establish target percentile

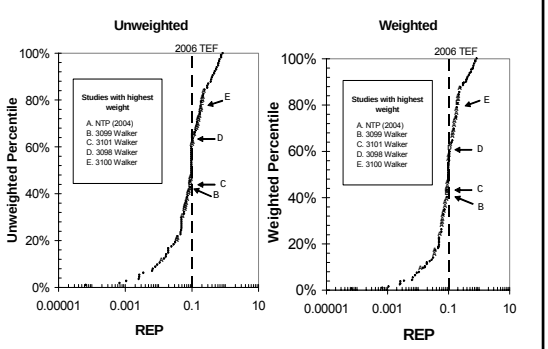
REP Weighting Scheme



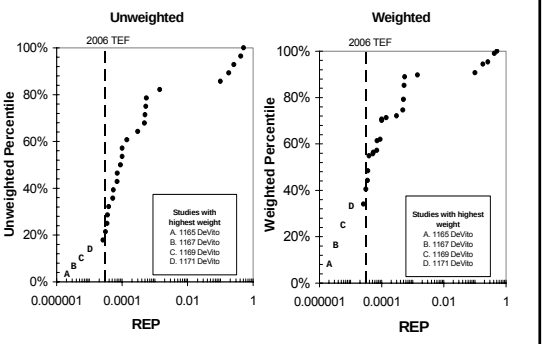
PCB 126



Cumulative REP Distributions for PCB 126

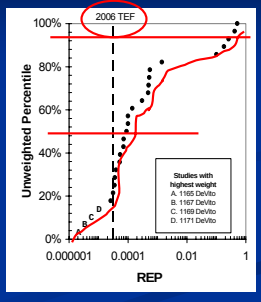


Cumulative REP Distributions for PCB 156

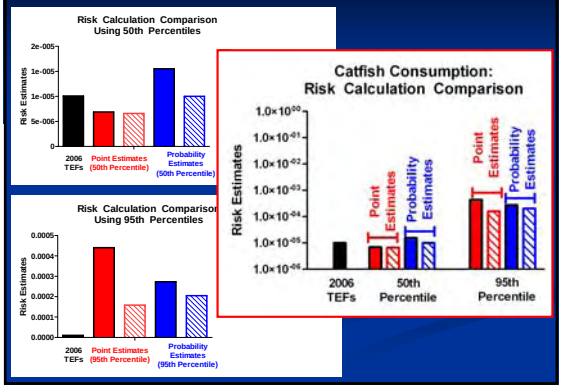


Impact on Risk

- Estimated cancer risk associated with catfish ingestion
- Methods
  - WHO 2006 TEFs
  - Point Estimates
  - Probabilistic Estimates



Preliminary Risk Comparisons



Weighting Conclusions

- Weighting had little impact on the overall distribution of the REPs
  - Results consistent with previous weighting efforts
  - Lack of impact may be do to the inherent variability in the REP values
- Use of weighted REP distributions (rather than point estimates) appears to significantly impact risk calculations*
- Use of a quantitative weighting scheme enhances the transparency in the process for establishing TEFs

Conclusions

- Use of REP distributions could simplify process of developing point estimate TEFs
  - Separates risk assessment from risk management process
  - Provides WHO with a quantitative method for developing TEFs
- By using this approach, regulators, the regulated community, risk managers and the general public can reproduce how TEFs are derived – this provides an additional measure of transparency

Acknowledgements

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Questions and Answers

Q. What is the purity of test material evaluated? If they were less than 99.99% pure, it could account for the mono-ortho compounds found. (Sekerke)

A. The compounds were considered pure by the WHO [World Health Organization], but there is no specific method other than expert judgment. Please consult the toxicology paper by Van Der Berg.

Use of Total-PCB Fish Measurements in Dioxin-Like PCB Related Fish Advisories and Risk Assessment

Satyendra Bhavsar, Ontario Ministry of the Environment

Biosketch

Dr. Satyendra Bhavsar is a Water Modeller in Environmental Monitoring and Reporting Branch of the Ontario Ministry of the Environment (OMOE). He received his B.Eng. in Chemical Engineering from M.S. University of Baroda (India) and his Ph.D. in Chemical and Environmental Engineering from the University of Toronto (U of T, Canada). Dr. Bhavsar worked as a postdoctoral researcher at the U of T and OMOE before assuming his current Water Modeller position. His duties involve undertaking scientific evaluation of the contaminants data collected by the OMOE over last 30 years and providing scientific support to Sport Fish and Biomonitoring Unit (OMOE), which issues fish consumption advisories for more than 1,700 locations in Ontario's inland lakes/rivers and the Great Lakes. Dr. Bhavsar can be reached via e-mail at s.bhavsar@utoronto.ca.

Abstract

Ontario Ministry of the Environment (OMOE) collects fish samples from approximately 1,700 locations in Ontario's inland lakes/rivers and the Great Lakes, analyze the samples for a variety of substances, and provide consumption advice for sport fish-based on health protection guidelines provided by Health Canada (HC). Historically, a wide variety of contaminants, including mercury (Hg), polychlorinated biphenyls (PCBs), dioxins/furans, mirex, photomirex, and toxaphene, have been consumption-limiting chemicals. However, due to recent revisions in HC guidelines and the implementation of our innovative method of overcoming lack of dioxin-like PCB (dl-PCB) measurements, dl-PCB/dioxins/furans, and Hg are the major cause of current advisories.

The current analytical methods for quantifying dl-PCBs are complex and four or five times more expensive compared to total-PCB analysis, which results in limited fish samples analyzed for dl-PCBs. Furthermore, it is a common perception that individual PCB compounds, especially dl-PCBs, rather than total-PCB need to be quantified to predict the environmental hazard because of differences in their toxicity potential and distribution among various environmental matrices, including aquatic food webs. Using the OMOE dataset, we show that the comparatively less expensive and rapid measurements of total-PCB in fish can be used to assess dl-PCB-related toxicological hazard, measured as 2,3,7,8-TCDD Toxic Equivalents (TEQ) (Bhavsar et al. 2007a). The dataset includes total-PCB and dl-PCB measurements in 912 skinless, boneless fillets of 22 different fish species collected from 1996–2004 from 80 locations across Ontario, and they varied over a wide range in length, weight, and PCB concentrations. The possible sources of PCB in the aquatic systems sampled also varied from atmospheric deposition to known recent and/or continuing point sources to combination of atmospheric and point sources.

A regression equation of dl-PCB-related TEQ (i.e., $TEQ_{dl\text{-}PCB}$) to total-PCB in fish has been presented ($TEQ_{dl-PCB} = 2.56\times10^{-5} \times C_{total-PCB}$, $r = 0.89$, $p < 0.001$) (Bhavsar et al. 2007a). The regression was evaluated by applying it to three independent datasets of substantial sizes (n = 55, 141, 176). The $TEQ_{dl\text{-}PCB}$ estimated using the regression and total-PCB measurements were generally within a reasonable factor of 2 of the $TEQ_{dl\text{-}PCB}$ calculated from the dl-PCB measurements. We found that the dl-PCB composition is relatively constant regardless of fish species and total-PCB level (Bhavsar et al. 2007b). The abundance of dl-PCBs expressed as a percentage of total-PCB in fish is generally in the order of PCB- 118 > 105 > 156 > 167 > 123 > 157 ≈ 114 > 189 > 77 > 126 > 81 ≈ 169. The most toxic dl-PCB congeners PCB-126 and PCB-169 contribute on average only 0.027% and 0.004% of total-PCB, respectively. The statistically

significant correlations presented between individual dl-PCB and total-PCB concentrations can be used as a practical tool to estimate dl-PCBs for risk assessment purpose. A comparison of the dl-PCB pattern for the OMOE dataset with other studies suggests that this dl-PCB composition is applicable to fish from North America and perhaps from other geographical regions throughout the world.

Use of total-PCB fish measurements in dioxin-like PCB related fish advisories and risk assessment

Satyendra Bhavsar
Al Hayton, Rachael Fletcher, Eric Reiner
Don Jackson, Wolfgang Scheider, Emily Awad

Ontario Ministry of the Environment, Canada
University of Toronto, Canada

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Outline

- Background
  - Sport Fish Contaminant Monitoring Program, Ontario Ministry of the Environment, Canada
- Dioxin-like PCB (dl-PCB) data evaluation
- Fish advisory for dl-PCBs using total-PCB

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OMOE - Sport Fish Contaminant Monitoring Program (SFCMP)

- Monitors contaminants in
  - Sport fish & Juvenile fish
  - Since 1970s
  - Various contaminants (eg, PCBs, dioxins, Hg, pesticides)
  - More than 1700 locations across Ontario and Canadian waters of the Great Lakes
- Assesses health risk
  - Partnership with Health Canada
  - Develop fish advisories
- Provide fish consumption advise to public

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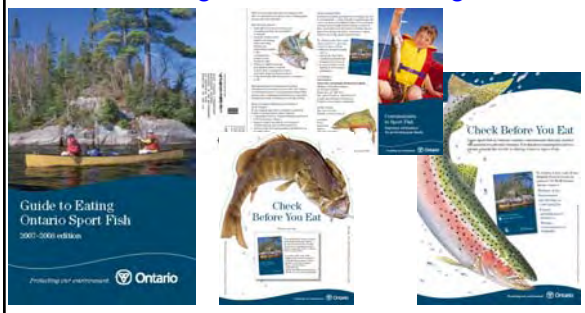
Guide to Eating Ontario Sport Fish
www.ene.gov.on.ca/envision/guide/



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Toxic Equivalents - TEQ

- How toxic chemicals in mixture are compared to most toxic chemical of class
- Uses weighted Toxic Equivalency Factors

$$TEQ = \sum (C_i \times TEF_i)$$

- TEFs: order of magnitude
  - derived from Relative Potency (REPs)
- Requires concentration of individual chemical

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Dioxin-like Compounds

- Dioxins, Furans, dioxin-like PCBs
- High levels in environment including fish
- Major cause of fish advisories in North America
- Dioxin-like PCBs contribute 70-90% of dioxin-like compound related TEQ
- most toxic dl-PCBs are less abundant

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Measuring PCBs in fish

1. Total-PCB → equivalent to Aroclor
2. PCB congeners
   - all major PCBs, not all dl-PCBs
3. Dioxin-like PCBs

- Measuring dl-PCBs is costly
- Limited fish analyzed for dl-PCBs
- All historical and most of current data available as total-PCB or PCB congeners

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Problem

Due to lack of dioxin-like PCB measurements, true risk of these chemicals to human and ecosystem health may not be fully recognized

Research Question

Can we estimate $TEQ_{dl\text{-}PCB}$ using total-PCB measurements for fish?

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Previous attempts

- Correlated TEQ with some dioxin-like congener
  - No real monetary benefit → cost of analyzing some compared to all dioxin-like PCBs would be similar
- Correlated total-TEQ with total-PCB
  - May be affected by variation in dioxins/furans
- Could not generalize due to
  - Small sample size
  - Narrow geographic representation

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Approach

- Analyze dl-PCB & total-PCB OMOE fish data
  - 912 samples
  - Skinless, Boneless Fillet
  - 22 different fish species
  - Collected over last 10 years
  - From 80 locations across Ontario
  - Male:Female → 51:49
  - Length: 20-110 cm (mean: 60 cm)
  - Weight: 100-14000 g (mean: 3000 g)
  - Total-PCB: 20-7500 ng/g ww (mean: 630 ng/g)

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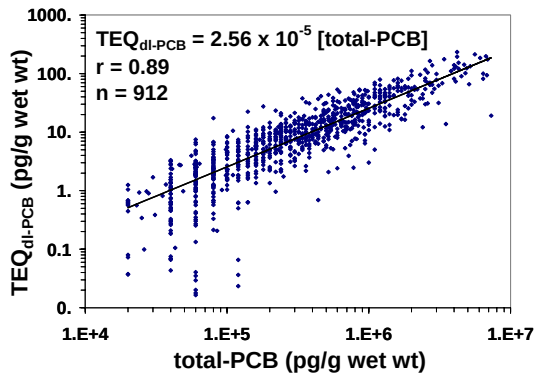

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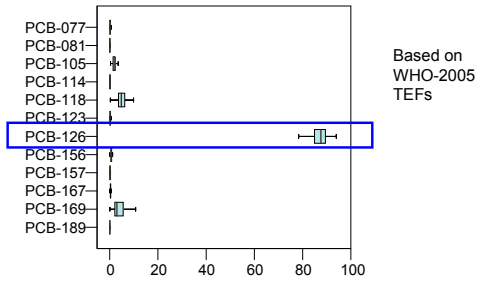
% contribution to $TEQ_{dl\text{-}PCB}$



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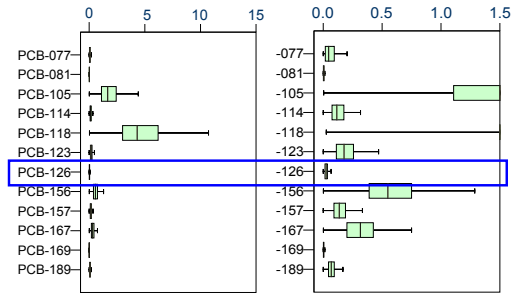
Dioxin-like PCB as % of "total-PCB"



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Evaluation – 1

- USEPA National Lake Fish Tissue Study dataset
- 500 lakes from the lower 48 states
- 56 predator, **skin-on** fish fillet samples with values for all dl-PCB & total-PCB
- 13 fish species
- length: 12-84 cm
- weight: 33-4825 g
- total-PCB: 10-700 ng/g ww

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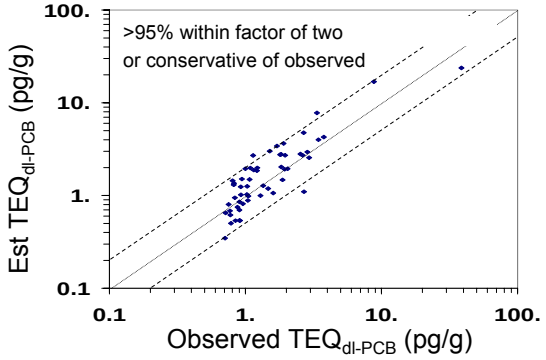

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Evaluation – 2

- Lake Ontario lake trout **whole-fish** data
  - Huestis et al. (JGLR, 22:310-330, 1996)
- 22 sets of annual mean values
- total 141 samples
- total-PCB: 2000-9500 ng/g

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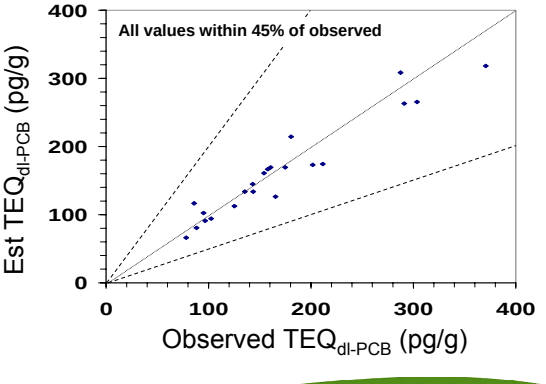

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Evaluation – 3

- USEPA National Lake Fish Tissue Study
- 175 **bottom-dweller, whole-fish** samples
- 10 fish species
- length : 14-85 cm
- weight : 20-10000 g
- total-PCB: 9-1266 ng/g ww

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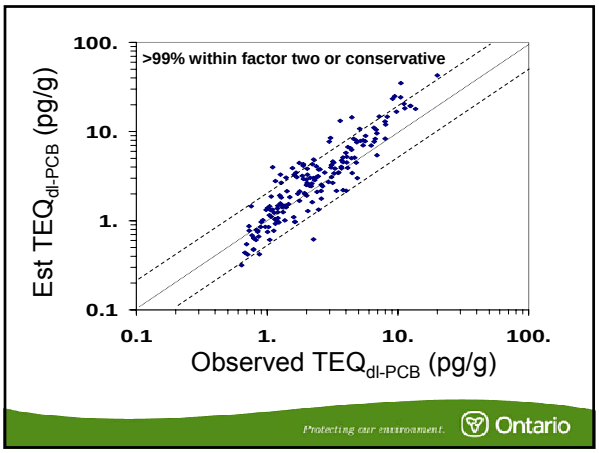

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Composition of Dioxin-like PCBs in Fish: An Application for Risk Assessment

SATYENDRA P. BHAVSAR,*,†,‡,§ RACHAEL FLETCHER,§ ALAN HAYTON,§ ERIC J. REINER,§ AND DONALD A. JACKSON†

Department of Ecology and Evolutionary Biology, University of Toronto, Toronto, Ontario M5S 3G5, Canada, and Environmental Monitoring and Reporting Branch and Laboratory Services Branch, Ontario Ministry of the Environment, 125 Resources Road, Toronto, Ontario M9P 3V6, Canada

It is widely accepted that a congener-specific analysis of polychlorinated biphenyls (PCBs), rather than traditional Aroclor equivalent total PCB analysis, is required for risk assessment. This is based on the fact that environmental processes alter the original distribution of PCB congeners in Aroclors and that toxicity varies considerably among the congeners with dioxin-like PCBs (dl-PCBs) generally being among the most toxic. Using the largest known dl-PCB fish dataset, here we present a likely composition of dl-PCBs in fish. In contrast to common perception, we found that the dl-PCB composition is relatively constant (within approximately a factor of 2) regardless of fish species and total PCB level. The abundance of dl-PCBs expressed as a percentage of total PCB (25–75 quartile range) in

the trade name Aroclor in North America. PCB mixtures have been used for a variety of applications largely based on their chemical stability and physical properties. Their stability is also responsible for their continued presence in the environment even decades after extensive regulatory actions and an effective ban on their production in the 1970s (*1*). Although the levels of PCBs in various environmental matrices have decreased dramatically since peaking in the 1970s (*1*–*3*), their current levels in fish are a major cause of fish consumption advisories in North America (*4*, *5*).

Environmental levels of PCBs are traditionally measured as total PCB based on Aroclor equivalent analysis, as opposed to congener-specific concentrations, due to analytical limitations and/or cost differentials (*6*). Many studies have shown that physical, chemical, and biological processes alter the distribution of PCB congeners in Aroclor after release into the environment (*7*–*9*). In addition, it is well-recognized that the potential for adverse effects varies considerably among PCB congeners (*10*). For these reasons, congener-specific PCB analysis is recommended for risk assessment purposes (*6*, *11*–*13*). Although the U.S. Environmental Protection Agency (U.S. EPA) has encouraged states to develop the capability to conduct congener-specific tissue analysis, the higher cost of the analysis has restrained most contaminant monitoring agencies to total PCB measurements with a limited number of fish samples being analyzed for congener-specific PCBs (*6*). In addition, even a congener-specific analysis does not normally determine environmentally relevant and toxicologically important low ppt levels of dioxin-like PCBs (dl-PCBs). Dioxin-like PCBs are a group of 12 PCBs that share a common toxic mechanism with the most toxic dioxin compound (i.e., 2,3,7,8-tetrachlorodibenzo-*p*-dioxin or 2,3,7,8-TCDD) and generally are among the most toxic PCB congeners as they incur toxic effects at relatively lower concentrations than those of non-dl-PCBs (*9*, *14*).

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ESTIMATING DIOXIN-LIKE POLYCHLORINATED BIPHENYL TOXIC EQUIVALENTS FROM TOTAL POLYCHLORINATED BIPHENYL MEASUREMENTS IN FISH

SATYENDRA P. BHAVSAR,*†‡ ALAN HAYTON,‡ ERIC J. REINER,§ and DONALD A. JACKSON†
†Department of Ecology and Evolutionary Biology, University of Toronto, Toronto, Ontario M5S 3G5, Canada
‡Environmental Monitoring and Reporting Branch, Ontario Ministry of the Environment, 125 Resources Road, Toronto, Ontario M9P 3V6, Canada
§Laboratory Services Branch, Ontario Ministry of the Environment, 125 Resources Road, Toronto, Ontario M9P 3V6, Canada

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Abstract—Polychlorinated biphenyls (PCBs) are 209 related compounds, a dozen of which are known as dioxin-like PCBs (dl-PCBs) and are among the most toxic PCBs. Polychlorinated biphenyls contribute to many adverse effects to human health, including cancer, and are a major cause of fish advisories in North America. It is a common perception that individual PCB compounds, especially dl-PCBs, rather than total PCBs need to be quantified to predict the environmental hazard because of differences in their toxicity potential and distribution among various environmental matrices, including aquatic food webs. Because the current analytical methods for quantifying dl-PCBs are complex and four- to fivefold more expensive, limited fish samples are analyzed for dl-PCBs. Using what likely is the largest dl-PCB fish data set (n = 912) with a wide distribution of fish species (n = 22), size (19–112 cm), weight (100–14,300 g), sex, and PCB contamination level (20–7,300 ng/g wet wt), we show in the present study that the comparatively less expensive and rapid measurements of total PCBs in fish can be utilized to assess dl-PCB–related toxicological hazard, measured as 2,3,7,8-tetrachlorodibenzo-*p*-dioxin toxic equivalents (TEQs). A regression equation of dl-PCB–related TEQs (i.e., $TEQ_{dl\text{-}PCB}$) to total PCBs in fish is presented ($TEQ_{dl\text{-}PCB} = 12.56 \times 10^{-5}[C_{tot\text{-}PCB}]$, $r = 0.89$, $p < 0.001$). The regression was evaluated by applying it to three independent data sets of substantial sizes (n = 55, 141, and 176). The $TEQ_{dl\text{-}PCB}$ estimated using the regression and total PCB measurements were within a reasonable factor of two to three of the $TEQ_{dl\text{-}PCB}$ calculated from the dl-PCB measurements. The successful evaluation indicates versatility of the regression.

Keywords—Toxic equivalents Polychlorinated biphenyls Dioxin-like polychlorinated biphenyls Fish advisory Analytical method

Calculation of fish advisory levels

- Tolerable monthly intake from Health Canada
- Use 100% of TMI for sport fish consumption
- 227 g fish meal size
- 70 kg body weight
- Assume fish meal size proportional to body wt
- Fish advisory levels (8 meals/month)
  - Total-PCB → 153 ng/g
  - Dioxins/furans/dl-PCBs (total-TEQ) → 2.7 pg/g

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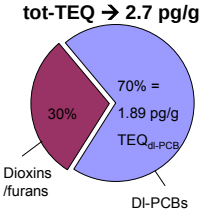
Fish advisory for dl-PCBs from total-PCB

Allowable tot-TEQ → 2.7 pg/g



$TEQ_{dl\text{-}PCB} = 2.56 \times 10^{-5}$ [total-PCB]

1.89 / 2.56×10^{-5} pg/g

Equivalent allowable total-PCB

74 ng/g

Compare with allowable total-PCB (from HC TMI) → 153 ng/g

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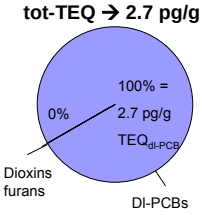
Fish advisory for dl-PCBs from total-PCB

Allowable tot-TEQ → 2.7 pg/g



$TEQ_{dl\text{-}PCB} = 2.56 \times 10^{-5}$ [total-PCB]

2.7 / 2.56×10^{-5} pg/g

Equivalent allowable total-PCB

105 ng/g

Compare with allowable total-PCB (from HC TMI) → 153 ng/g

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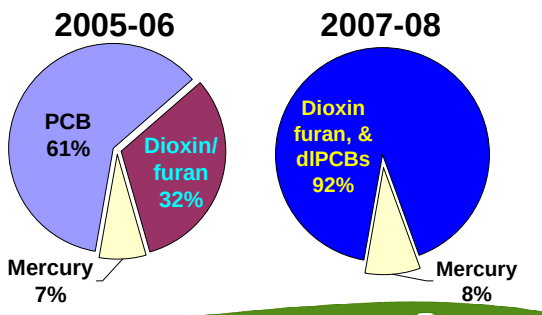
Contributions to advisories
(Lake Ontario)



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Summary

- Cost effective method is presented to estimate TEQ for dioxin-like PCBs
- Comprehensive dataset of OMOE was used
- $TEQ_{dl\text{-}PCB} = 2.56 \times 10^{-5}$ [total-PCB]
- Successful evaluation across three independent datasets indicates versatility of the correlation
- Implementation of correlation in fish advisories
  - Resulted in more stringent total-PCB consumption limit
  - Alleviates deficiencies in risk assessment because of lack of expensive dl-PCB measurements

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Contact Information

Satyendra Bhavsar
Ontario Ministry of the Environment
Water Monitoring and Reporting Section
Environmental Monitoring and Reporting Branch
125 Resources Road, Toronto, ON M9P 3V6
Tel: (416) 327-5863 Fax: (416) 327-6519

E-mail: satyendra.bhavsar@ontario.ca
sportfish.moe@ontario.ca

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Questions and Answers

Q. We analyzed 101 PCB and dioxin samples in Delaware and forced the data through 0 as well. The slope is 2.56 x 10^{-5} and our R was a little better. There are situations, however, where no substitutes are possible, such as reductions of oddball congeners in some people. It is extremely useful for source fingerprinting. (Greene)

A. I agree. This measurement is an alternative when funding for full analyses is not available.

Q. The National Lake Fish Tissue Study is not necessarily representative of the PCBs and Arochlors used in the United States. A lot of U.S. PCBs are in estuaries and not lakes. Your regression line is spread at the bottom. Have you ever analyzed the lower levels of contamination versus the higher level concentrations? (Brodberg)

A. It may be that, at low concentrations, the error analytically increases dynamically. Also the non-detects are represented in the low concentrations, and it is not clear how to handle non-detects in this manner. At lower levels, however, the TEQ [toxic equivalency] is below 1 and is less of a concern.

Measures of PCBs in Edible Fish Tissues: A Comparative Risk Analysis

Kevin Connor, Geomatrix

Biosketch

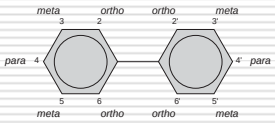
Dr. Kevin Connor (Ph.D.) is a Senior Scientist with Geomatrix Consultants, working in Folsom, CA. Dr. Connor received his B.S. degree in Environmental Toxicology at the University of California at Davis, and earned a Ph.D. in Toxicology at Texas A&M University. He has worked professionally in human health risk assessment and regulatory toxicology for more than 10 years. Dr. Connor's core expertise stems from his graduate work on the molecular toxicology of polychlorinated biphenyls (PCBs) and related persistent organic compounds, and he has conducted numerous analyses on the human health risks associated with the presence of these compounds in soils, sediment, fish, and shellfish. At Geomatrix, his duties have expanded to include the risk assessment for chemicals used in manufacturing consumer products.

Abstract

Several analytical methods are available for quantifying polychlorinated biphenyls (PCBs) in fish and shellfish. These methods have been used to provide measures of PCBs that are expressed in terms of the original Aroclor mixture, individual PCB congeners or homologs, or an estimate of total PCB based on regression analysis. The choice for analysis is driven by many considerations, including cost; however, it is important to consider the requirements of the current approach to human health risk assessment for PCBs, as developed by U.S. Environmental Protection Agency (EPA). This includes a toxic equivalency (TEQ) approach for the coplanar PCB congeners, where the mixture has been heavily degraded or weathered. In this analysis, we contrast the PCB health risk estimates obtained using fish tissue data from a New Jersey waterway and a PCB concentration term derived from each of following analytical approaches: 1) a National Oceanic and Atmospheric Administration (NOAA) estimate of the total PCB based on 18 congeners, 2) an estimate of the total PCB based on the sum of 38 analyzed congeners, and 3) the sum of 9 homolog groups. In each case, the coplanar (or dioxin-like) congeners were subtracted from the total PCB mass to arrive at a non-coplanar total, in accordance with EPA guidance. These three approaches yielded similar estimates of the total non-dioxin-like PCBs for a variety of fish species, while the totals quantified as Aroclor 1248, 1254, or 1260 were typically >5-fold lower. Based on these results, the choice of analytical approach applied to the measurement of PCBs in fish and shellfish should be guided by the composition of the PCB mixture and the requirements of the risk assessment methodology.

MEASURES OF PCBS IN EDIBLE FISH TISSUES: A COMPARATIVE RISK ANALYSIS

Kevin Connor, Ph.D.
Geomatrix Consultants, Inc. Folsom, CA
kconnor@geomatrix.com



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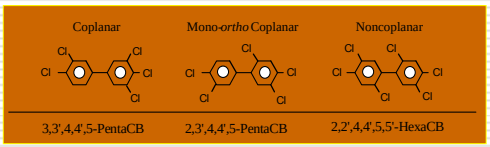
Polychlorinated Biphenyls (PCBs)

- Complex family of compounds
- Structurally related to polychlorinated dibenzo-*p*-dioxins, furans, and diphenyl ethers
- Regulated as carcinogens



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Aroclors

- Commercial PCB mixtures used in the U.S.
- Aroclors 1232, 1242, 1254, and 1260 contained 32, 42, 54, and 60% chlorine
- Well-characterized with respect to mammalian toxicology (cancer and non-cancer endpoints)
- Are often used as a primary method of quantifying PCBs in the environment

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Aroclor Approach to Cancer Risk Assessment

(Aroclor Dose) x (Aroclor Cancer Slope Factor [CSF]) =

PCB risk

- Aroclor is quantified as Aroclor 1242, 1248, 1254, or 1260
- Choice of CSF (Aroclor-based) is made from following categories:
  - High risk & persistence: 2.0 $(mg/kg\text{-}d)^{-1}$
  - Low risk & persistence: 0.4 $(mg/kg\text{-}d)^{-1}$
  - Lowest risk & persistence: 0.07 $(mg/kg\text{-}d)^{-1}$

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Aroclor Analysis: Potential Problems

- Individual PCB congeners may undergo selective degradation and partitioning
- Different Aroclor sources may co-mingle
- Non-Aroclor sources of PCBs may exist

Composition of Aroclors released into environment may become obscured

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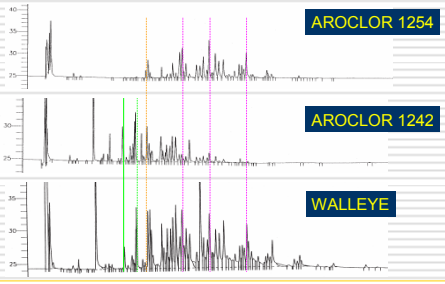
Aroclor Signatures Can Persist in Fish



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Implications for Analysis

- Can create difficulty and uncertainty in choosing Aroclor standard
- Aroclor-based methods may underestimate total PCB mass
- Will increase uncertainties in the contribution of "dioxin-like" congeners to total PCB risk

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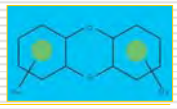
PCB Cancer Risk Assessment (U.S.EPA 1996)

May Require Two Analytical Endpoints:

1) TEQ = Σ [Coplanar PCB_i x TEF_i]

2) Σ [Non-coplanar PCBs]

- TEQ approach particularly recommended when:
  - PCB profile no longer resembles Aroclor
  - Site/system contains complex mixture of PCDD/Fs and PCBs



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Cancer Risk Assessment for "Dioxin-like" PCBs Can Use TEFs

Congener	1997 TEF	2005 TEF
3,4,4',5-TCB (81)	0.0001	0.0003
3,3',4,4'-TCB (77)	0.0001	0.0001
3,3',4,4',5-PeCB (126)	0.1	0.1
3,3',4,4',5,5'-HxCB (169)	0.01	0.03
2,3,3',4,4'-PeCB (105)	0.0001	0.00003
2,3,4,4',5-PeCB (114)	0.0005	0.00003
2,3',4,4',5-PeCB (118)	0.0001	0.00003
2',3,4,4',5-PeCB (123)	0.0001	0.00003
2,3,3',4,4',5-HxCB (156)	0.0005	0.00003
2,3,3',4,4',5'-HxCB (157)	0.0005	0.00003
2,3',4,4',5,5'-HxCB (167)	0.00001	0.00003
2,3,3',4,4',5,5'-HpCB (189)	0.0001	0.00003

- TEF is expression of relative potency as compared with 2,3,7,8-TCDD
- TEQ = Σ [PCB_i x TEF_i]
- TEQ Dose x TCDD CSF = PCB risk

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If TEQ Approach is Applied…

- Coplanar (or "dioxin-like", DL) congeners should be removed from the estimate of total PCB mass that is used in Aroclor–based approach
- Noncoplanar PCB mass:

  Estimate of PCB Total – Σ [DL congeners]

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Measurement of Total PCB Mass

- Aroclor analysis (Method 8082)
- Individual Congeners (Method 1668)
  - Full analysis (209 possible congeners)
  - Subset of key congeners
- Homologs (Method 1668)
  - Nine homolog classes, *mono*- through *nona*-chlorinated

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Measurement of Total PCB Mass : Regression Methods

- "NOAA" method (Method 1668; 18 key congeners* and linear regression)
  - Regression analysis based on extensive fish data based representing multiple sites
  - (Σ [18 select PCB congeners] x 2.2) + 81
  - Cost-effective and likely accurate, but not a standard method of estimation

* Includes PCBs 8, 18, 28, 44, 52, 66, 101, 105, 118, 128, 138, 153, 170, 180, 187, 195, 206, and 209

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Case Study: Lower Passaic River

Photo courtesy of Project Navigator, LTD; Passaic River Restoration

- Highly industrialized river, with multiple inputs
- PCDD/Fs, possibly other "dioxin-like" compounds in sediment and biota
- PCB analysis as Aroclors often returning results below limits of detection

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Methods

Samples:

- 5 blue crab samples
- 17 fish fillet samples: striped bass, perch, and bluefish

PCB analyses:

- Aroclors 1248, 1254, and 1260
- 38 individual PCBs
  - 12 coplanar PCB congeners
  - 26 non-coplanar PCB congeners*
- All 9 homolog classes (*mono-* to *nona*-chlorobiphenyls)

* Included PCBs 1, 3, 8, 15, 18, 28, 44, 52, 66, 87, 90, 101, 128, 138, 153, 170, 180, 183, 184, 187, 194, 195, 202, 206, 207, and 209.

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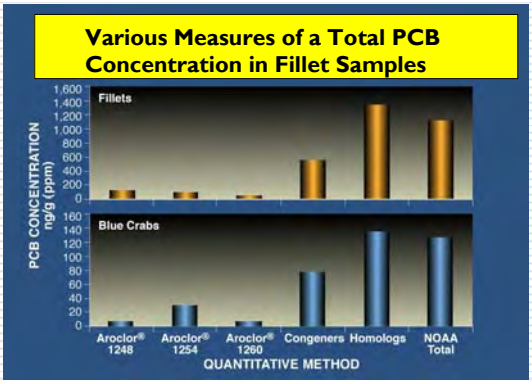
Various Measures of a Total PCB Concentration in Fillet Samples



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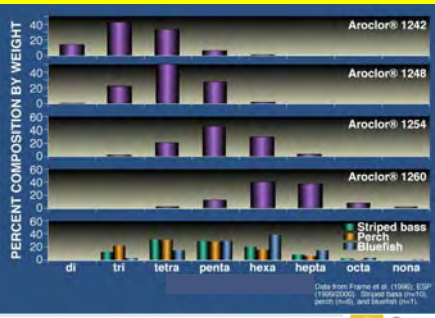
Homolog Profiles for Common Aroclors and Edible Fish from the Lower Passaic River



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Methods (cont.): Estimates of Total Noncoplanar PCB Mass

- Σ [26 Non-coplanar PCBs]
- Σ [9 homologs] – Σ [DL congeners]
- "NOAA total" – Σ [DL congeners]

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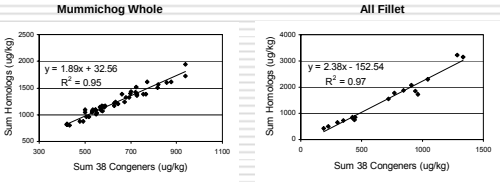
Regression Analysis



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Various Estimates of Total Nondioxin-like Noncoplanar PCB Mass (µg/kg) in Passaic River Fish: Various Estimates

Fish fillet type	"NOAA" PCB total – Σ DL	Regression of 38 Congeners – Σ DL	Sum of Homologs – Σ DL
Adult striped bass (n=10)	980	947	946
White perch (n=6)	1,996	2,246	2,228
Bluefish (n=1)	873	NA	873
All fillets (n=17)	1,332	1,479	1,384

DL: "Dioxin-like" PCBs
NA: Not applicable, sample size did not permit regression analysis
NOAA: National Oceanic and Atmospheric Administration

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Summary

- PCB analysis on Aroclor basis may not accurately quantify PCB mass in fish and shellfish samples
- Choice of analytical method can have significant effect on magnitude of the risk estimates
- In this case study, methods based on homolog totals or key congener/regression analysis (e.g., "NOAA method") yielded better and comparable estimates of the total PCB mass

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Recommendations

- Consider the history and context of PCBs in system (e.g., presence of other 'dioxin-like' compounds)
- Preliminary data evaluation (i.e., comparison against Aroclor standard using homolog profiles or chromatograms)
- If difficulties arise in Aroclor analysis, determine if it is due to weathering/degradation or commingling
- Combination of methods may therefore seem appropriate, but multiple factors, including needs of risk assessment should be considered, e.g., Beliveau (2001) decision tree, to arrive at reliable, but cost-effective approach

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Future Work

- Regression analyses appear to offer potential cost-effective and accurate means of measuring non-coplanar PCB total
- Possible advancement: Tailor the list of 18 – 20 "key" congeners to the media under study (soil, sediment, fish, shellfish) and the nature of the PCBs released
- As database grows, consider use of regression equations derived from site data as basis for future investigations

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Acknowledgments

Coauthors: Michelle Everson, Steave Su, Brent Finley
Also: Paul Scott, Alta Laboratories, and Tierra Solutions

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Questions and Answers

Q. How are you quantifying cancer risks for non-coplanars?

A. Presumably you would add the non-coplanars together.

Q. What is the ballpark cost of congener analyses and homolog analyses?

A. For congener analyses, the cost is approximately $1,200 to $1,300. Arochlors cost approximately $1,300 per sample.

Consistent Advice for Striped Bass and Bluefish along the Atlantic Coast

Eric Frohmberg, Maine Center for Disease Control

Biosketch

Dr. Eric Frohmberg (Ph.D.) is a Toxicologist with the Maine Environmental and Occupational Health Program. He has been involved in the development of fish consumption advisories and the Bureau's Center for Disease Control's Fish Advisory Communication Program. This work has included the development of new brochures, testing efforts with low-literacy focus groups, and surveys to evaluate the effectiveness of the risk communication program.

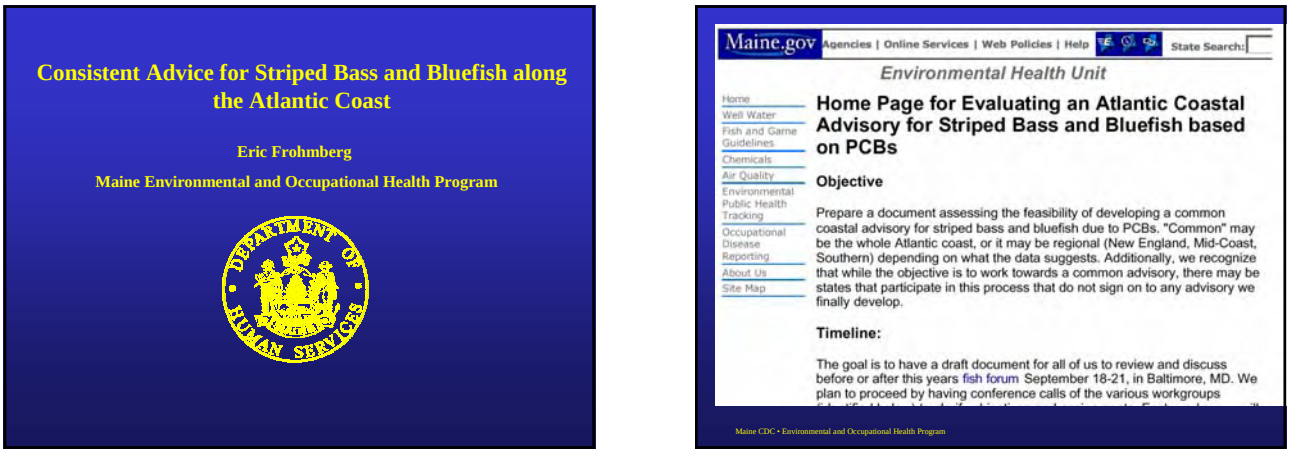
Abstract

Eric Frohmberg will present the methodology and results to date on the Workgroup for Evaluating an Atlantic Coastal Advisory for Striped Bass and Bluefish based on polychlorinated biphenyls (PCBs). The process is in the third year, and the methodology, results, timeline, and next steps will be presented and discussed. In particular, size dependence of PCB concentrations in bluefish and the risks and benefits of striped bass and bluefish consumption have been included in the evaluation. A body burden approach to evaluating the risks of PCBs will be included and will be discussed by Deborah Rice in the following talk.

Consistent Advice for Striped Bass and Bluefish along the Atlantic Coast

Eric Frohmberg

Maine Environmental and Occupational Health Program



Outline/Status

How Organized

What has happened/where we are

Status: 9 out of 11 states agreed to advisory in Dec.
NY and Mass comments.
New data from NY.

Status/Timeline/Next Steps

Organization

Data Workgroup

Biology Workgroup

Toxicology Workgroup

Advisory Workgroup

Organization Workgroup

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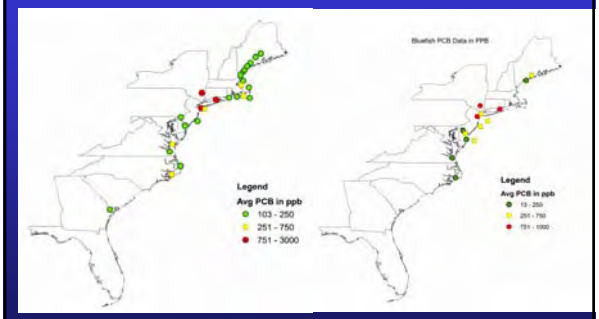
Data



Striped Bass

Bluefish

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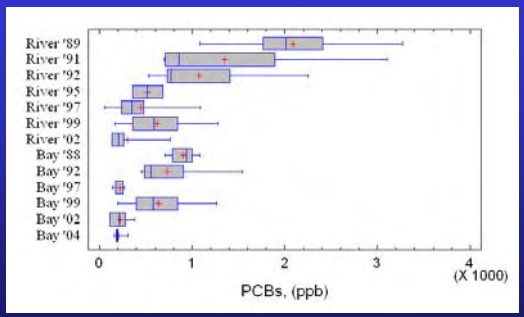
Data



Striped Bass: Delaware Estuary

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Size Dependence in Bluefish

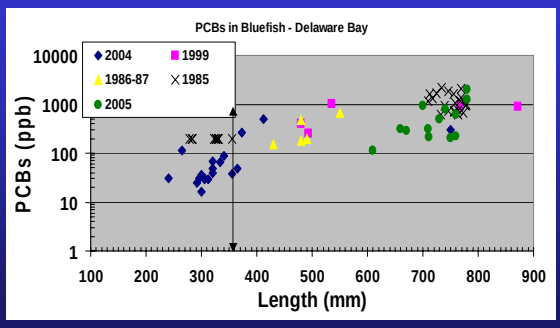

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Figure 1. Major Spawning Stocks of Atlantic Striped Bass

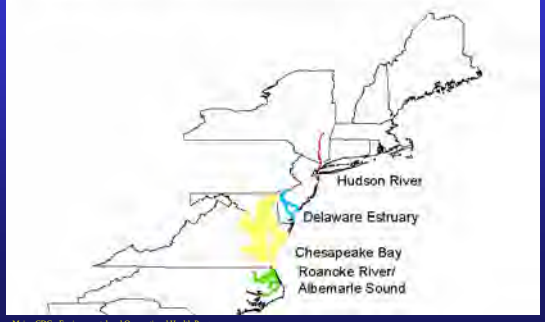

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Figure 2: Summer Distribution of Adult Female Striped Bass

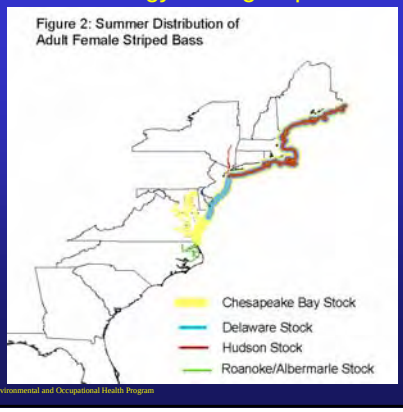

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Figure 3: Winter Distribution of All Stocks Adult Female Striped Bass

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Toxicology: Risk Based Approach

	EPA Non-Cancer Action Level		EPA Cancer Action Level		Great Lakes Protocol
	W/out cooking loss	50% cooking loss	W/out cooking loss	50% cooking loss	
One meal/ week	43 ppb	86 ppb	11 ppb	22 ppb	60-200 ppb
One meal/ Month	173 ppb	346 ppb	43 ppb	86 ppb	210-1000 ppb
No Consumption					> 1,900 ppb

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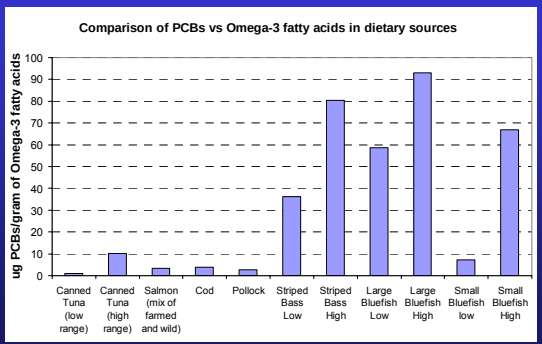
Toxicology: Benefits



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Advisories

Procedures variable from state to state, advisories aren't that different

Summarize data on cooking loss

Think about age breakdowns to specify who you want to protect and to simplify communication

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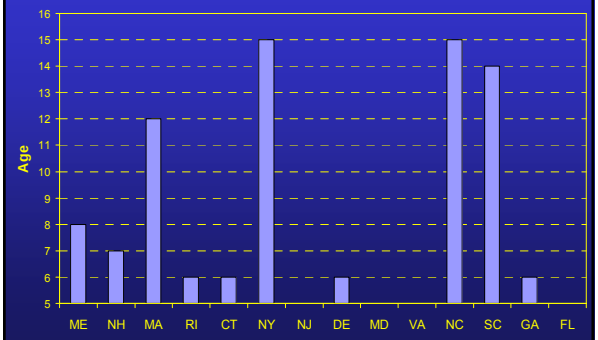
State by State variations in Age Definitions of a "Child"



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Status/Next Steps

- **Data from NY**
- **Review body burden text and incorporate into a tox chapter**
- **Discuss size breakdown for bluefish**
- **Review and re-write organizational chapter**
- **Timeline? – End of Summer/Fall**

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Thanks

Gary Buchanan (NJ), Brian Toal (CT), Rick Greene (DE), Ron Sloan (NY), Ashok Deshpande (NOAA), Gary Ginsburg (CT), Deb Rice (ME), George Henderson (FL), Rich McBride (FL), Byron Young (NY), Victor Crecco (CT), Paul Caruso (MA), Sharee Rusnak (CT),Tony Forti (NY)

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Questions and Answers

Q. How certain are you on the migrations in and out of state waters? Are there telemetry data? (David)

A. There were several tag and recapture data, but I am unclear of the sensitivity for striped bass. No data are available for the Maine and New England populations, because the population collapsed. In the past, the population came from Chesapeake Bay. This may still be the migration route. We also believe some are fish coming up from the Roanoke.

A. For Long Island Sound striped bass, PCB levels average 0.21 to 0.25 ppm. (Forti)

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PCB Body Burdens Associated with Adverse Outcome in Epidemiological Studies

Deborah Rice, Maine Center for Disease Control

Biosketch

Dr. Deborah Rice (Ph.D.) is currently a Toxicologist with the Maine Center for Disease Control and Prevention. Previously, she served as a risk assessor in the area of neurotoxicology with the National Center for Environmental Assessment at EPA, where she was involved in health assessments of PCBs and methylmercury. Dr. Rice was a research scientist in the Toxicology Research Division of Health Canada for more than 20 years, where she headed a research program focused on characterizing nervous system impairment produced by developmental exposure to the major environmental pollutants PCBs, methylmercury, and lead. Dr. Rice is currently an Associate Editor for the journals *Neurotoxicology* and *Environmental Research*. Dr. Rice received her Ph.D. in Toxicology from the University of Rochester.

Abstract

There is a large experimental literature documenting behavioral effects associated with developmental exposure to polychlorinated biphenyls (PCBs). Several longitudinal prospective studies have also documented developmental neurotoxicity associated with PCB exposure, mostly as a result of *in utero* exposure. Studies in the United States (Michigan and Oswego, NY), Germany, and the Netherlands found adverse effects as a result of PCB exposure, from early infancy to 11 years of age (Michigan) or 9.5 years of age (Oswego, NY). Deficits included neuromotor effects during infancy; lowered IQ; deficits in memory, attention, and language processing; failure of impulse control and other executive functions; and effects on sexually dimorphic behavior. In most cases, data were not presented in such a way that the dose-response relationship, including evidence of a threshold, could not be determined. However, decrement in IQ at 3.5 years of age in the Dutch study, as well as several measures on the Oswego study, were presented as histograms, allowing estimates of an effect level. Additionally, an increase in otitis media in an Inuit population was amenable to dose-response estimation. The body burden data (lipid-adjusted blood concentrations) could then be compared with data from the National Health and Nutrition Examination Survey (NHANES) based on the appropriate congeners analyzed in each study. In the Dutch and Inuit studies, blood levels were generally higher than in the United States, and a no-effect level was not identified. The effect level, which is contingent upon the way in which the subjects were grouped, was between the 90th and 99th percentiles of U.S. women of child-bearing age based on the NHANES data. In the Oswego study, body burdens were comparable to the general U.S. population, and an effect level was identified for several endpoints and at various ages that corresponded to blood levels below the 5th percentile of U.S. women based on the NHANES. In fact, there was evidence on some measures that effects were observed at the 1st percentile. Although these histogram-based estimates are certainly not the optimal way to determine effect levels, it seems reasonable to conclude that a substantial fraction of women of childbearing age in the United States has a body burden of PCBs that may produce adverse effects.

PCBs are developmental neurotoxicants

- Large experimental literature, including characterization of multiple mechanisms of action
- Four longitudinal prospective studies documenting effects from infancy into school age
  - Michigan
  - Oswego, New York
  - The Netherlands
  - Germany
- PCBs are also carcinogenic and immunotoxic, and decrease thyroid hormones

Summary of selected effects across studies

	Michigan	Oswego	Netherlands	Germany
Study population	eaters and non-eaters of Lake Michigan fish	eaters and non-eaters of Lake Ontario fish	general population, half breast-fed, half not	general population
Number of subjects	325	309	418	171
PCB analysis	packed-column GC, Aroclors 1016 and 1260 as references	cord blood: 68 congeners or congener pairs	cord and maternal blood: 118, 158, 153, 180	cord and maternal blood, breast milk: 138, 153, 180
Infant neurological status	abnormal responses	abnormal responses	abnormal responses	
Fagan test of recognition memory	impaired	impaired		no effect (poor control)
Bayley Scales of Infant Development	no effect		lower score	lower score

Summary of selected effects across studies

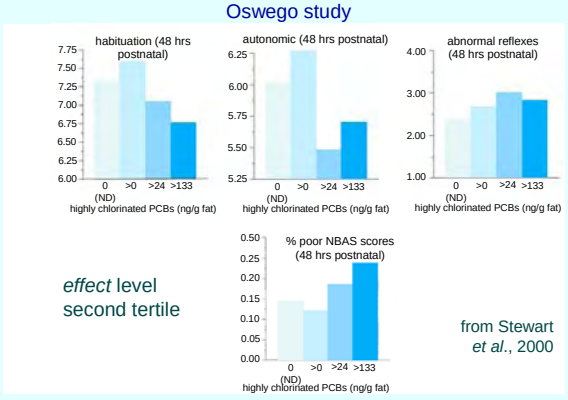
	Michigan	Oswego	Netherlands	Germany
Cognitive effects 3–4 years	lower IQ	lower IQ	lower IQ	lower IQ
Cognitive effects 4–7 years		McCarthy: no effect on IQ	lower IQ in less-advantaged children	non-significant negative effect on IQ
Cognitive effects in later childhood	decreased full-scale and verbal IQ		impaired executive function	
Attention/response inhibition/processing speed	vigilance task: increased errors of commission	vigilance task: increased errors of commission	vigilance task: increased errors	
	effects on other tasks	DRL:impaired impulse control	simple reaction time: impaired	

Strategy for estimating effect levels from epidemiological studies

- Most studies and endpoints provided no information on the dose-effect relationship
- For some endpoints, data were presented as histograms
- Most emphasis placed on the Oswego study
  - US study
  - Low body burdens
  - Histograms presented for a number of endpoints at various ages
- Other available data were from the Dutch and Inuit studies
  - Higher body burdens
  - No-effect level not identified

Abnormal neurological status during infancy

Oswego study

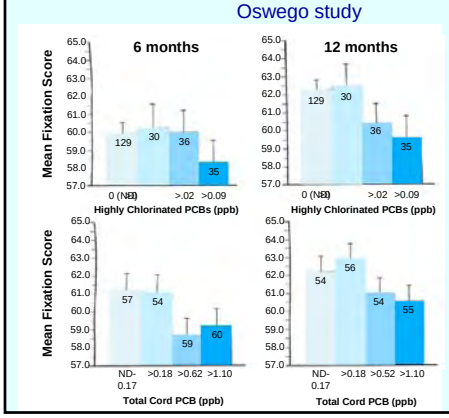


effect level second tertile

from Stewart *et al.*, 2000

Poorer recognition memory during infancy

Oswego study

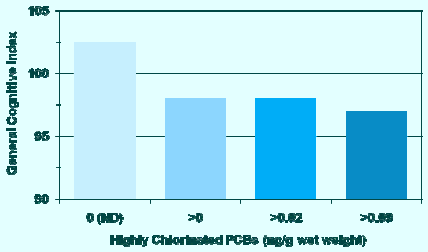


effect level second tertile

from Darvill *et al*., 2003

Decreased IQ at 3 years associated with prenatal PCB exposure

Oswego study



effect level first tertile

from Stewart *et al*., 2003

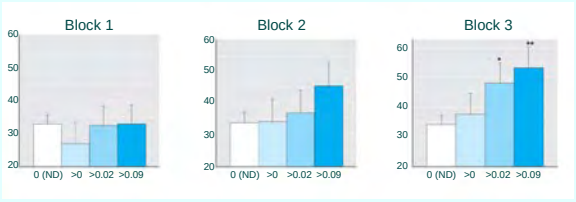
Vigilance Task

- Computer game
- Respond to specific symbol (cat), not to others (pig, rabbit, ram, wolf)
- Measure reaction time
  - errors of omission
  - errors of commission
- More errors at 4, 8, 9.5 years old

Increased errors of commission on a vigilance task at 4.5 years

Oswego study

effect level first tertile

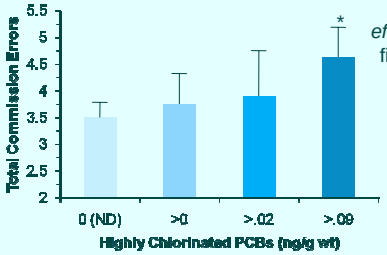


Highly Chlorinated PCBs (ng/g wt)

from Stewart *et al*., 2003

Increased errors of commission on a vigilance task at 8 years

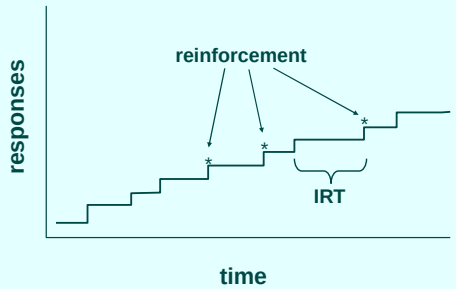
Oswego Study



effect level first tertile

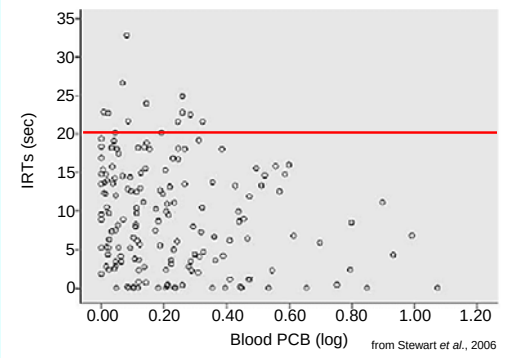
from Stewart *et al*., 2005

DRL Performance



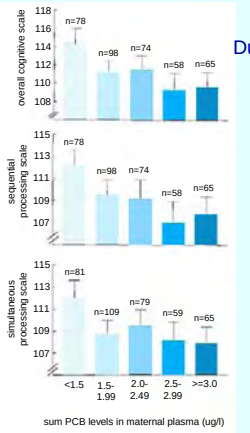
Poorer performance on DRL at 9 years

Oswego study



Decreased IQ at 3.5 years

Dutch study in the general population

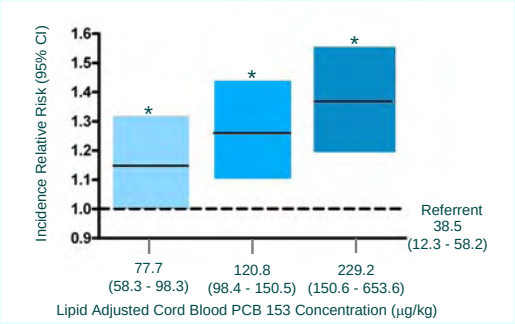


effect level
second quintile

no information on lowest group with respect to possible threshold

from Patandin *et al.*, 1999

Incidence Relative Risk of Acute Otitis Media In Inuit Children with Prenatal Exposure to PCBs



from Dallaire *et al.*, EHP 114:1301-1305, 2006

Comparison of effect levels in epidemiological studies and NHANES

- Based on comparison of appropriate congeners in blood
  - Oswego: 7-9 chlorine atoms in cord blood, lipid adjusted and compared to U.S. women
  - Dutch: congeners 118, 138, 153, 180, wet weight, compared directly
  - Inuit: congener 153, lipid adjusted, compared directly
- Effect level
  - Dutch and Inuit: lowest comparison group (no no-effect level)
  - Oswego: second non-zero tertile
    - Not most sensitive
    - Effects observed consistently based on histograms
    - Not always statistically significant

Highly chlorinated PCB congeners in the Oswego study and NHANES

Congener	Oswego	NHANES	NHANES 50th % (ng/g lipid)
170/190	√	√	
172	√	√	
174	√		
177	√	√	
178		√	3.7
179	√		
180	√	√	
181/187	√	√	
183	√	√	
185	√		
189		√	3.7
194	√	√	
195	√	√	
196/203	√	√	
199	√		
200	√		
201	√	√	
206	√	√	

Highly chlorinated PCB tertiles in cord blood from Oswego study

PCB Measurement	1st Non-Zero Tertile	2nd Tertile	3rd Tertile
ng/g lipid (group mean)	0-23.2 (10.5)	23.3-132.7 (50)	>132.7 (899)
ng/g serum (group mean)	0.001-0.02 (0.009)	0.02-0.09 (0.043)	>0.09 (0.61)

Group mean data for wet weight measurements provided verbally by Dr. Stewart

Group mean data for lipid-adjusted measurements estimated from the group mean data

Comparison of highly chlorinated PCBs in the US population to effect level in the Oswego study

Percentile	1st %	5th %	10th %	25th %	50th %	75th %	90th %	95th %
16-49 yr old women (N=578) (ng/g lipid)	40	54	59	67	80	99	133	170

2nd tertile effect level ≈ 50 ng/g lipid

1st tertile effect level ≈ 10 ng/g lipid

Comparison of effect level in the Dutch study to levels of those congeners in the US population

Percentile	50th %	75th %	90th %	95th %	99th %
16-49 yr old women (ug/L plasma)	0.33	0.61	1.05	1.37	2.58

Cognitive effect level in Dutch study ≈ 1.5-1.99 ug/L

Comparison of levels of congener 153 in the US population and the effect level in the Inuit study

tertile	50th %	75th %	90th %	95th %
women 16-19	20	37	64	81

Data for this group calculated by Mass DOH, January 2007 and reconfirmed by CTDPH from CDC SAS data files.

Otitis media effect level ≈ 77.7 ng/g

Summary of effect levels compared to body burdens in US women

Study	Endpoint	Biomarker	% of NHANES Distribution at Apparent Effect Level
Oswego	various neurodevelopmental effects	highly chlorinated congeners (PCB 170 & above) lipid adjusted, cord vs venous blood	5th
Dutch	several neurodevelopmental endpoints	PCBs 118, 138, 153, 180 in venous blood, wet wt	95th to 99th
Inuit	Otitis media	PCB 153 lipid-adjusted cord blood vs venous blood	90th to 95th

Implications for striped bass and bluefish advisory

- Effects were observed at body burdens well within the range of US women
- Health-protective strategy is to minimize adding to the PCB body burden, at least for women and children
  - Behavioral effects were associated with both *in utero* and postnatal exposure in the Dutch and German studies
- Advise to women and children may depend on levels of PCBs in these fish on a state-wide basis
  - But PCB levels can be very high
  - It seems reasonable to severely restrict intake, or recommend no consumption

Questions and Answers

Q. In the Lanke studies, what types of fish consumption surveys or studies were performed? (Forti)

A. Lanke used visual aids and self-reported fish consumption. We could predict the levels of PCBs in the fish that they ate based on data from New York. In the end, the safest comparison to be made is fish-eaters to non-fish-eaters. Once we have the analyzed PCBs, we will replace our assumptions with actual levels.

Q. How are statements about dose response possible with only three histograms? It is not possible to state differences from the control. (Sekerke)

A. I agree that the current estimates are not optimal; however, there is a very orderly monotonic relationship from the dose response information. The people who perform these studies need to further perform non-linear dose-effect modeling because risk assessment information is not typically available for epidemiological purposes until after one can confirm the quality of the data.