United States
Environmental Protection
Agency

Office of Water
Washington, DC 20460

EPA–823-R-07-008
September 2007

Proceedings of the 2007 National Forum on Contaminants in Fish

All sections of the 2007 Proceedings are available from our web site at:
http://www.epa.gov/waterscience/fish/forum/2007/

Section II-D
Risk Assessment/Toxicology

Moderator:

Randall Manning, Georgia Department of Natural Resources

Health Risks and Toxicological Effects of Mercury – A Summary from the 2006 International Conference on Mercury as a Global Pollutant

Henry Anderson, Wisconsin Department of Health and Human Services

Australia's Advisory Statement on Methylmercury in Fish

Peter Abbott and Tracy Hambridge, Food Standards Australia New Zealand

Updating Health Canada's Human Health Risk/Benefit Assessment and Risk Management Strategy for Mercury in Retail Fish

Kelly Hislop, Health Canada

IRIS Toxicological Reviews of Several PBDE Congeners

Joyce Donohue and Hend Galal-Gorcheve, Office of Water, Office of Science and Technology, U.S. EPA

[This page intentionally left blank.]

Health Risks and Toxicological Effects of Mercury – A Summary from the 2006 International Conference on Mercury as a Global Pollutant

Henry Anderson, Wisconsin Department of Health and Human Services

Biosketch

Dr. Henry Anderson received his M.D. degree from the University of Wisconsin Medical School in 1972. He is certified by the American Board of Preventive Medicine with a subspecialty in Occupational and Environmental Medicine and is a Fellow of the American College of Epidemiology. Dr. Anderson is Chief Medical Officer and State Environmental and Occupational Disease Epidemiologist with the Wisconsin Department of Health and Family Services. He has adjunct professor appointments in Population Health in the Wisconsin School of Medicine and Public Health and the Gaylord Nelson Institute for Environmental Studies. Over the past 25 years, he has conducted multiple research projects investigating human health hazards of consumption of Great Lakes and other sport fish and developed and evaluated the effectiveness of public health advisories.

Abstract

First convened in 1990, the International Conference on Mercury as a Global Pollutant held its Eighth Conference in Madison, WI, on August 6–11, 2006. Attendees came from 58 countries and presented 1,047 abstracts. A key goal of the conference was to assemble a critical synthesis of existing scientific information. Five synthesis papers were prepared by 40 international experts who began their work in July 2005, a full year before the conference. Each panel presented its findings in a plenary session, and videos of these sessions remain available at www.mercury2006.org. These papers were used to prepare a "Madison Declaration" on mercury pollution. The declaration and the critical synthesis papers have been peer reviewed and published in *AMBIO 36*(1):2-113, February 2007. This presentation will summarize the conclusions of the synthesis paper entitle Methylmercury Exposure and Health Effects in Humans: A Worldwide Concern.

Health Risks and Toxicological Effects of Methylmercury*

Eighth International Conference on Mercury as a Global Pollutant

August 2006, Madison, Wisconsin

Henry A. Anderson, MD

What is the evidence that humans, fish, and wildlife are being adversely affected by exposure to methylmercury?

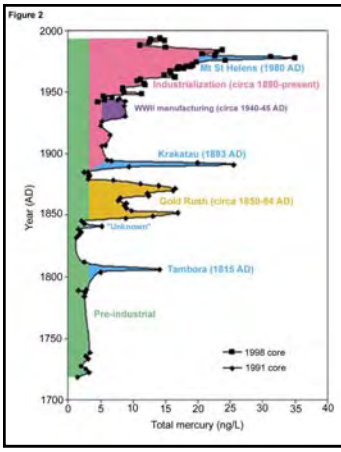
*Mergler D, Anderson HA, Chan LHM, Mahaffey KR, Murray M, Sakamoto M, Stern AH. Methylmercury exposure and health effects in humans: a worldwide concern. Ambio 36:1:3-11, 2007.

Panel members

- **Henry A. Anderson**, Wisconsin Department of Health and Family Services
- **Laurie Hing Man Chan**, University of Northern British Columbia,
- **Michael W. Meyer,** Wisconsin Department of Natural Resources
- **Michael W. Murray**, National Wildlife Federation, Great Lakes Natural Resource Center
- **Donna Mergler (co-chair),** University of Quebec at Montreal
- **Kathryn R. Mahaffey**, Washington, DC
- **Mineshi Sakamoto**, National Institute for Minamata Disease,
- **Mark B. Sandheinrich**, University of Wisconsin – La Crosse
- **Tony M. Scheuhammer (co-chair),** Environment Canada, National Wildlife Research Centre
- **Alan H. Stern**, New Jersey Department of Environmental Protection and New Jersey-School of Public Health

Panel Charge

- **Synthesize current scientific knowledge on methylmercury (MeHg) exposure and its effects in humans and wildlife**
- **Identify unresolved issues**
- **Provide a consensus statement**



A 270-year record

Major atmospheric releases

- **Natural**
  - **Background (42%)**
  - **Volcanic (6%)**
- **Anthropogenic (52%)**
  - **Gold rush**
  - **WWII**
  - **Industrialization**

More significantly
(the take-home message)

The last 100 years
anthropogenic: 70%

The last 10 years
an apparent decline

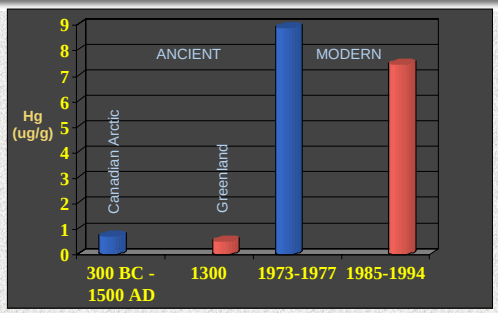
USGS

Relative Rates of Fish Consumption

Organism	Daily consumption of fish g/individual	g/individual/kg
Adult female human (U.S.)[a]		
Median	31	0.6
95th percentile	110	2.2
Common loon[b]		
Chick (first 11 weeks)	400	220-410
Adult	960	190

[a]USDA Continuing Surveys of Food Intake by Individuals (1989-1991).
[b]Barr 1996.

Historical Increases in Mercury Concentration of Polar Bear Fur



Adapted from Dietz et al (2005)

Human Exposure

Human Exposure: Sources

- Consumption of fish, high on the trophic chain, is the major source of MeHg exposure for humans
- For some populations, marine mammals are also a source of exposure
- Consumption of animals that have been nourished with fish feed may also contribute to body burden
- Recent studies suggest that in some regions, with high Hg contamination, rice may take up MeHg.

MeHg: a Worldwide Concern

- Elevated MeHg in many fish-eating populations throughout the world
- Notably among coastal, island, river and lakeside populations and those living near reservoirs
- Also: persons who eat large quantities of commercially sold high-end predators
- MeHg exposure knows no geographic or social boundaries

Bioindicators of MeHg Exposure

Bioindicators of Exposure

- Hair total Hg
  - generally correlated to consumption of fish, fish-eating waterfowl and marine mammals
  - contains 80-98% MeHg
  - correlated to blood MeHg
  - can provide information on temporal variations
  - high inter- and intra-individual variability
  - short term peaks not well represented
  - recent advances on single strand analyses at micron resolution should yield information on bolus doses

Bioindicators of Exposure

- Blood MeHg
  - Mean T_{50} : 47-70 days
  - On average, cord blood approximately 1.7 x higher than maternal
- Toenail Hg
  - recently used in several studies
  - not established whether it reflects organic or inorganic Hg
- Urinary Hg
  - a good biomarker for inorganic Hg
  - not a good biomarker for MeHg
  - MeHg may contribute to urinary Hg through demethylation

Fish Consumption as a Predictor of MeHg Exposure

- MeHg exposure is generally related to the concentration of MeHg in the fish species, portion size, and frequency of fish consumption.
- But:
  - Recent evidence of inter-ethnic differences (diet? toxicokinetics? genetic?)
  - In the Brazilian Amazon, for similar MeHg intake, those who consume more fruit have lower hair and blood Hg
  - Selenium has been suggested, but reports are inconsistent
- ***Need more research on the factors that modulate MeHg absorption and metabolism***

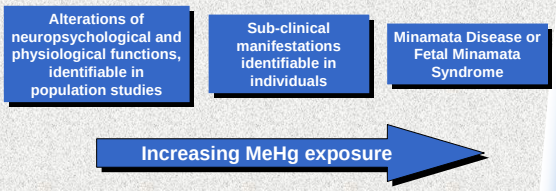
2004 Fish Intake & Hair Hg Level 2,030 WI Residents

# Meals/month	Ave Hg Level in ppm	No (%) > 1 ppm
0	0.09	0/97 = 0%
1-4	0.46	63/570 = 11%
5-8	0.71	140/717 = 18%
>8	1.00	222/703 = 32%

Effects in Humans

From Subtle Alterations to Disease

- A continuum of severity of effects with increasing exposure



Clinical Effects

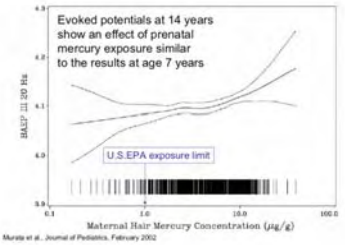
- **Minamata Disease:**
  - Adults: marked by distal sensory disturbances, constriction of visual fields, ataxia, dysarthria, auditory disturbances and tremor
  - Minamata Foetal Syndrome: a debilitating progressive neurologic disease due to *in utero* exposure, even in the absence of symptoms in mothers
- **Today:**
  - Case and anecdotal reports of diffuse and subjective neurologic symptoms in persons with moderately elevated MeHg exposures
  - Need for a formal case description or diagnostic criteria for such effects.

Population Level Effects

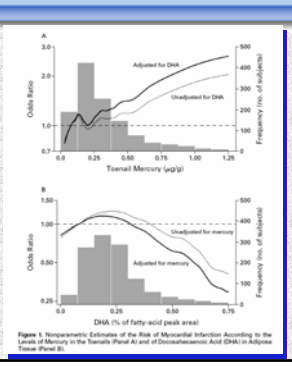
- A growing number of studies on effects of fetal exposure to MeHg.
  - Most demonstrate diminished neurodevelopmental and neurophysiologic functions with increasing MeHg exposure
- Fewer studies performed on adults
  - Exposure associated with reduction of neurobehavioral performance, visual functions and increased cardiovascular disease, particularly myocardial infarction in adult men

Evoked Potential Latency

Data from the Faroe Islands Study



Cardiovascular Effects in Adults



(Guallar et al, 2002)

Conclusions - Humans

- Methylmercury is a developmental neurotoxicant at current environmental levels.
- In adults, neurobehavioral effects are observed at moderately elevated exposures.
- There is a body of evidence indicating elevated risk for cardiovascular disease, especially myocardial infarction.

Conclusions - Humans

- Fish is a nutritious food source, and a dietary mainstay for many populations around the world. All efforts need to be made to reduce and eliminate mercury releases to the environment to protect that food source.

Questions and Answers

Q. It's taken 50 years to increase our understanding of the lower level effects of mercury. Is there any way to increase our learning of effects more quickly? Do you have any different ways to think about mercury effects to help? (Kyle)

A. Continued biomonitoring is very helpful. Other efforts to examine mercury contamination include the observation of seasonal mercury trends (i.e., deposition on leaves in the fall, transfer to dirt in winter). I would suggest that the task of removing mercury from our environment is foremost upon us. The most egregious source of mercury in the environment is not necessarily from burning coal, but from the use of mercury to amalgamate tiny quantities of gold.

Comment: We probably know more about mercury than any other pollutant. It has been said that if we are already seeing contaminant effects in humans, we have failed as risk and toxicology assessors. However, we really don't have the tools to anticipate the effects of toxic substances. I would like to recommend an NRC [National Research Council] report that talks about the need for tools which allow us to go beyond waiting for humans to be exposed or animal testing and the related uncertainties. (Schoeny)

Australia's Advisory Statement on Methylmercury in Fish

Peter Abbott, Science Advisor, and Tracy Hambridge, Food Standards Australia New Zealand

Biosketches

Dr. Peter Abbott is a Science Advisor at Food Standards Australia New Zealand (FSANZ). He held the position of Principal Toxicologist at FSANZ from 1994 to 2006. His primary responsibility is to provide scientific advice to the Authority in relation to food safety, particularly chemicals in food. Recently, he has been documenting FSANZ's approach to risk analysis across a wide range of food-related health risks.

Dr. Abbott's academic training and research background is in the area of chemically induced cancer. He has a B.Sc. and an M.Sc. from the University of Queensland and a PhD from the University of Manchester. Following a research career, he moved to government employment in 1985. His work within the public sector has been largely in providing advice on the public health aspects of exposure to chemicals in food and in the environment. Dr. Abbott has also participated as a technical expert for the World Health Organization (WHO) on the Joint U.N. Food and Agriculture Organization (FAO)/WHO Expert Committee on Food Additives (JECFA) since 1996.

Ms. Tracy Hambridge joined FSANZ in 1998 and currently holds the position of Team Leader, Dietary Modelling. She overseas all the dietary exposure assessment work for FSANZ. This covers a range of food chemicals, including food additives, contaminants, agricultural and veterinary chemical residues, nutrients, and food ingredients, for a range of purposes, such as standards development, total diet surveys, and other risk assessments. Ms. Hambridge has also participated as a technical expert and member for the WHO on the JECFA. She has also been involved in teaching how to perform dietary exposure assessments for many international risk analysis training courses, particularly to participants from the Asia Pacific region. Ms. Hambridge received a bachelor's degree in Nutrition at the University of Canberra, ACT, in 1995, and she earned a masters degree in Nutrition and Dietetics at Deakin University, Victoria, in 1997.

Abstract

The regulatory approaches in Australia and New Zealand to the potential risks associated with mercury (Hg) in fish have been, firstly, to establish maximum levels for Hg in fish to remove high Hg fish from the market and, secondly, to advise pregnant women and women planning pregnancy to limit their consumption of certain types of fish. Both of these approaches have limitations—the advisory statement was first established in 2001 and revised in 2004; and the maximum levels will be reviewed in the near future. This presentation will briefly examine the issues that impacted on the revision of the advisory statement, including the toxicity of Hg, the target population, data on the levels of Hg in fish, data on dietary exposure to various fish species, and the need to maintain an adequate consumption of fish for all groups in the population. Maintaining a focused, balanced and simple message was a major consideration in the revised advisory statement.

Australia's Advisory Statement on Methylmercury in Fish

Peter Abbott and Tracy Hambridge

EPA Fish Forum

July 2007

1 © FSANZ 2007

Discussion Topics

- Regulation of contaminants
- Safety concerns with methylmercury
- Survey data on methylmercury
- Dietary exposure estimations
- Advisory statement

2 © FSANZ 2007

Food Standards Australia New Zealand

Functions

- Developing, varying and reviewing food standards
- Coordinating food surveillance and recalls
- Limited public education role

Objectives

- Protection of public health and safety
- Provision of adequate information to enable consumers to make informed choices
- Prevention of misleading or deceptive conduct

3 © FSANZ 2007

FSANZ's Role in Role in Relation to Food-related Health Risk

- Getting the science right
  - Adequate data / rigorous assessment procedures / evidence-based decisions
  - Addressing real and potential risks
- Building public support
  - Addressing public concerns
  - Seeking support from recognised experts
  - Having a cautious approach to risk
  - Identifying an acceptable level of risk
  - Meeting community expectations

4 © FSANZ 2007

Regulation of Contaminants

5 © FSANZ 2007

1999 Review of Contaminants

1. **Potential public health risk**
   - Nature and severity of risk, particularly in susceptible population groups
   - Frequency of contamination
   - Importance of the food in the total diet
2. **Potential risk management options**
   - Regulatory (maximum levels)
   - Non-regulatory (guidelines, dietary advice)

6 © FSANZ 2007

Contaminants Review Outcome

- Removal of number of MLs for contaminants
- Use of guideline levels ('generally expected levels' or 'GELs')
- Retain the MLs for mercury
- Advisory statement for mercury

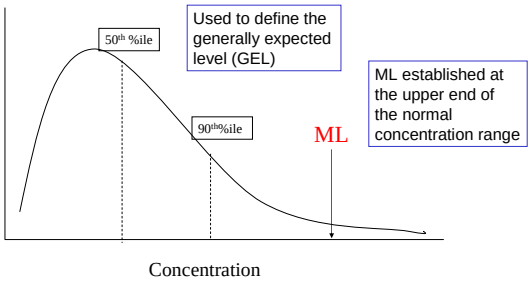
7 © FSANZ 2007

2001 Regulatory Approach to Mercury

- ML of 1 mg/kg for high mercury fish (swordfish, southern bluefin tuna, barramundi, ling, orange roughy, shark)
- ML of 0.5 mg/kg for all other species
- Advisory statement for pregnant women and women intending to become pregnant

8 © FSANZ 2007

ML for Contaminants



9 © FSANZ 2007

2001 Advisory on Mercury in Fish

- Recommended pregnant women (and those intending to become pregnant) to limit their consumption of specified types of fish to four portions per week (4 x 150g)
- No limit on consumption of other types of fish
- Based on PTWI of 2.8 µg/kg bw for pregnant women (Seychelles study) and 5 µg/kg bw for general population
- Based on consumption data from the Australian National Nutrition Survey and survey data

10 © FSANZ 2007

2003 Review of the Mercury Advisory Statement

Basis for the review:

- New analytical data on Hg in fish available
- Further information on the benefits of consuming fish
- WHO/FAO revised recommended weekly intake for mercury (PTWI)

11 © FSANZ 2007

Safety Concerns with Methylmercury

12 © FSANZ 2007

Safety Concerns

- **Neurological effects in adults**
  - Data from outbreaks in Japan (contaminated fish) and Iraq (contaminated grain)
  - Symptoms: peripheral neuropathy, paraesthesia, fatigue, blurred vision
- **Neurobehavioral development in children**
  - Early link between maternal hair mercury and delayed development in children
  - Longitudinal epidemiological studies in the Seychelles and in the Faroe Islands

13 © FSANZ 2007

Epidemiological Studies

Faroe Island study & Seychelles Child Development Study (SCDS)

Studied effects in children following prenatal exposure

- Faroe Island study:
  - Decreased scores on neurobehavioural tests at 7 yrs (fine motor skills, attention, language, memory)
- Seychelles study:
  - No changes observed at 0.5, 2.5, 5.5 & 8 yrs

14 © FSANZ 2007

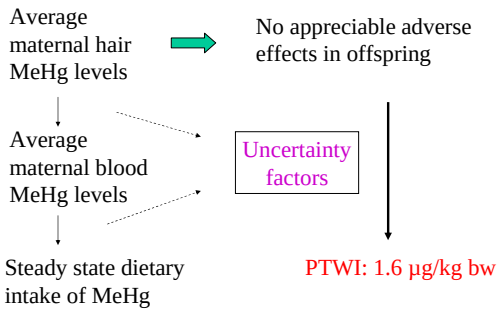
JECFA Review 2003

1. Reviewed recent animal studies & epidemiology studies
2. Reviewed results at 8 years of Seychelles Study
3. Assessed dose-response relationship for neurotoxicity following *in utero* exposure

PTWI: 3.3 µg/kg bw → 1.6 µg/kg bw

15 © FSANZ 2007

Establishing the PTWI



16 © FSANZ 2007

FSANZ Position on Safe Level of Intake

- **New PTWI of 1.6 µg/kg bw for foetus**
  - Based on delayed neurobehavioural development
  - Special risk management strategy for those women considering pregnancy
- **PTWI of 3.3 µg/kg bw for adults and children**
  - Based on general neurological effects
  - Young children may be at slightly higher risk due to lower bodyweight
- **Review dietary advice, particularly for women considering pregnancy and for young children**

17 © FSANZ 2007

Methylmercury Risk Management

General Population

- Maintain the MLs for methylmercury in fish
- Provide dietary advice for young children and the general population

Foetus

- Revise the dietary advice for pregnant women and women considering pregnancy

18 © FSANZ 2007

Mercury in Fish

Maximum levels established consistent with responsible fishing practices

+

Advise on limiting consumption of certain fish

Fish safe for general population

Fish safe for susceptible population (foetus and young children)

19 © FSANZ 2007

Survey Data for Methylmercury

20 © FSANZ 2007

Mercury Survey Data

- 15,300 data points for all foods
- 9,600 data points for seafoods
- Median concentrations were used for exposure assessment

21 © FSANZ 2007

Survey Data for Methylmercury

Food	Median conc. (mg/kg)	No. of Samples
Catfish	0.37	187
Perch	0.15	120
Gemfish	0.33	143
Billfish	0.90	36
Orange roughy	0.54	233
Shark	0.40	506

22 © FSANZ 2007

Dietary Exposure Estimations

23 © FSANZ 2007

Dietary Exposure

Dietary Exposure = Food consumption x Food chemical concentration

- Exposure calculated for each individual
- Summed for all foods
- Adjusted for bodyweight
- Compared to reference health standard

24 © FSANZ 2007

Mercury PTWI

Two separate PTWIs:

1. General population: 3.3 µg/kg bw/wk
2. Females 16-44 years: 1.6 µg/kg bw/wk

25 © FSANZ 2007

Population Groups

Three groups:

1. Whole population
2. Women of child bearing age 16-44 years
3. Children up to 6 years

- Women of child bearing age identified as vulnerable group as a 'proxy' for the foetus.

26 © FSANZ 2007

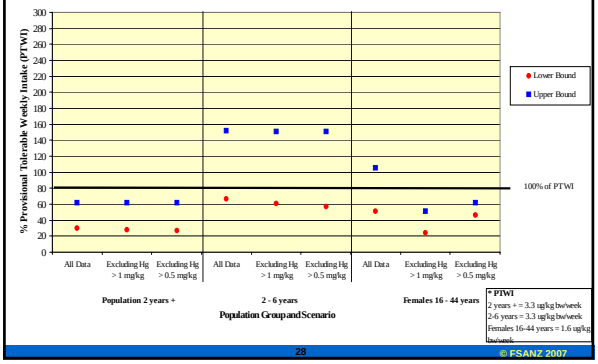
Mercury Exposure

Estimated exposures from all foods
(Range ND = 0 to ND = LOR)

Australian population group	Mean dietary exposure (% PTWI)	High exposure (95th percentile) (% PTWI)
2 years +	30 - 60	110 - 160
2-6 years	65 - 150	270 - 270
F 16-44 years	50 - 110	200 - 230

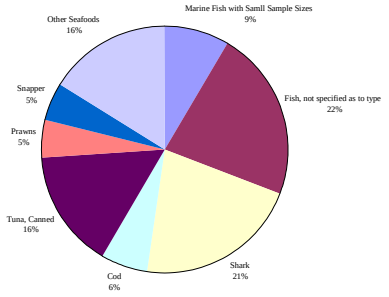
27 © FSANZ 2007

Mean weekly dietary exposure to Methylmercury



28 © FSANZ 2007

Major Contributors to Mercury Exposure in Australian Population



29 © FSANZ 2007

Determination of fish to include in the advice statement

PTWI – Hg exposure from all other foods = consumption x concentration / body weight

e.g Orange Roughy

0.106* – 0.0001 mg/week = consumption x 0.54 mg/kg

= 194 grams/week

= 1 x 150g serve/week

* PTWI x BW of 66kg females 16-44 yrs

30 © FSANZ 2007

Advisory Statement for Methylmercury

www.foodstandards.gov.au/foodmatters/mercuryinfish.cfm

Risk – Benefit Considerations

Benefits

- Fish are source of essential omega-3 fatty acids, iodine and some vitamins
- Reduced risk of primary cardiac arrest
- Possible reduced risk of several cancers, especially digestive tract

Risks

- Delayed neurobehavioural development in children

Recommended Fish Consumption

Pregnant women/ women planning pregnancy or children up to 6 years	The rest of the population
2-3 serves per week of any fish not listed below; or	2-3 serves per week of any fish not listed below; or
1 serve orange roughy, catfish; or	1 serve per week shark or billfish
1 serve per fortnight of shark or billfish.	

One serve 7 years and above = 150g; One serve children 0-6 years = 75g

Cautious Approach

- ✓ Provide information to the public regarding the potential risks and benefits of fish consumption
- ✓ Promote the benefits of fish consumption, even during pregnancy
- ✓ Discourage heavy consumption of fish during pregnancy
- ✓ Provide dietary advice to maintain consumption below the PTWI for all
- ✓ Make the advisory statement available widely in the community through health care outlets

Conclusions

- The heath risk associated with mercury in fish remains uncertain
- On the basis of current data, a cautious approach to the potential risk is required
- MLs for mercury may not be an effective for managing risk
- Advice on reducing fish consumption for susceptible population groups is appropriate


FOOD STANDARDS
Australia New Zealand
Copyright
© Food standards Australia New Zealand 2007
This work is copyright. You may download, display, print and reproduce this material in unaltered for only (retaining this notice) for your personal, non commercial use or use within your organisation. Apart from any other use as permitted under the Copyright Act 1968, all other rights are reserved. Requests for further authorisation should be directed to info@foodstandards.gov.au
37
© FSANZ 2007

Questions and Answers

Q. There have been positive results from the Seychelles study. Are you going to revisit your advice since the Seychelles population is healthy? (Mahaffey)

A. We do not have current plans to do so. We intend to be cautious and follow the most current research.

Q. Do you think the general public is aware of the selective species consumption concept (i.e., if an individual eats orange roughy, they should limit their intake of other fish species for a specific period of time)? Also, do you have any plans to address the risks of mercury versus the benefits of omega-3's in your advisory? (Kyle)

A. Some individuals may be aware of selective species consumption. We do not have plans to address the risks and benefits of mercury and omega-3's, respectively, at this time.

Q. Do you have plans for additional studies using biomonitoring as an exposure assessment and validation technique?

A. We do not currently plan to biomonitor individuals as a validation of the mercury advisory.

[This page intentionally left blank.]

Updating Health Canada's Human Health Risk/Benefit Assessment and Risk Management Strategy for Mercury in Retail Fish

Kelly Hislop, Health Canada

Biosketch

Dr. Kelly Hislop is head of the Food Additives and Contaminants Section of the Bureau of Chemical Safety, Food Directorate, Health Canada. Dr. Hislop received her Ph.D. in Environmental Chemistry from the University of Western Ontario in London, Ontario, Canada. She soon joined Health Canada's Bureau of Chemical Safety as a Scientific Evaluator. In this capacity, she was involved in the development of human health risk assessments of a variety of chemical contaminants in food, including the update to the Canadian risk assessment of methylmercury in retail fish. Dr. Hislop's current position covers not only food contaminants, but also the pre-market evaluation of additives in retail foods in Canada.

Abstract

In Canada, there are two federal departments that are involved in regulating retail fish sold in Canada. Health Canada is responsible for setting food safety standards related to human health. The Canadian Food Inspection Agency is responsible for enforcing compliance with those standards, as well as any other non-health-related standards. In support of its health-related standard-setting responsibilities, Health Canada recently completed a comprehensive re-evaluation of its human health risk assessment of mercury (Hg) in retail fish, with the collaboration of various other federal government departments. Fish intake data specific to the Canadian population and occurrence data for total Hg levels in retail fish available in Canada were considered. In addition, a revised tolerable intake designed to protect the developing fetus from neurodevelopmental effects of methylmercury was used. This tolerable intake was applied to women who may become pregnant, pregnant women, nursing mothers, and young children. The updated risk assessment forms the basis of Health Canada's revised risk management strategy, released in March 2007, which comprises both fish consumption advice and a two-tiered standard for total Hg in retail fish.

Updating Health Canada's Human Health Risk / Benefit Assessment and Risk Management Strategy for Mercury in Retail Fish

July 24, 2007
Bureau of Chemical Safety
Food Directorate
Health Products and Food Branch

Health Canada

Health Products and Food Branch

"policies, standards and programs relating to the health determinants, benefits, and risks associated with **products that are ingested or put into the human body**."

Health Canada

Health Products and Food Branch Mandate

- "minimizing health risk factors to Canadians while maximizing the safety provided by the regulatory system for health products and food"
- "promoting conditions that enable Canadians to make healthy choices and providing information so that they can make informed decisions about their health"

Canada Food and Drugs Act, Part I, section 4

No person shall sell an article of food that:

(a) has in or on it any poisonous or harmful substance;
(b) is unfit for human consumption;
(c) consists in whole or in part of any filthy, putrid, disgusting, rotten, decomposed or diseased animal or vegetable substance;
(d) is adulterated; or
(e) was manufactured, prepared, preserved, packaged or stored under, unsanitary conditions.

Retail fish in Canada

Santé Canada Health Canada

CFIA • ACIA

"Non-retail" fish in Canada

First Nations Inuit Health Branch Health Canada
- First Nations and Inuit communities

Provincial/territorial authorities
- inland lakes and rivers

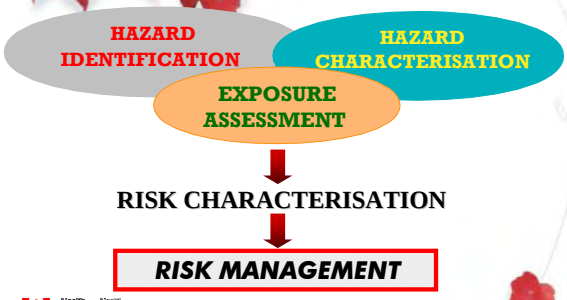
Parks Canada
- within national parks

Fisheries and Oceans Canada
- Fisheries Act Authorisations

Retail fish - past risk management decisions

1970	0.5 ppm guideline (standard) for all retail fish
1979	swordfish exempted
1990	shark exempted
1997	fresh and frozen tuna exempted; lower pTDI set by BCS
(2003)	(JECFA set a lower pTWI)
2004	various countries issue or update advice

Risk Assessment Paradigm



Risk Assessment Science Team

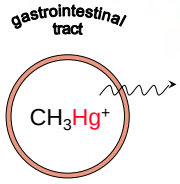
- Health Canada
  - HPFB (Bureau of Chemical Safety)
    (Bureau of Nutritional Sciences)
    (Office of Nutrition Policy and Promotion)
  - Healthy Environments and Consumer Safety Branch
- Canadian Food Inspection Agency (Fish, Seafood and Production Division)
- Environment Canada
- Fisheries and Oceans Canada

Health Benefits

The Science Team did not quantitatively assess the benefits of fish consumption against the risks of mercury exposure.

The Science and Policy Teams did recognise the importance of providing information on the health benefits of fish consumption in any communications.

Hazard Characterisation



Toxicity of Methylmercury

- *Distributed to various tissues*
- *Central and peripheral nervous systems.*
- *Range of effects observed in humans.*
- *Most subtle effects are neurobehavioural.*
- *The developing central nervous system considered most susceptible.*

Hazard Characterisation

- Approximate threshold of 10 ppm methylmercury in maternal hair for neuropsychological dysfunctions
- Converted to a dietary intake of 60 µg/day
- 5-fold Uncertainty Factor applied
- pTDI of 12 µg for reproductive age women or 0.2 µg/kg bw/day for a 60 kg woman

pTDI – provisional Tolerable Daily Intake

Hazard Characterisation

Health Canada provisional TDI values for MeHg:

Adults: 0.47 ug/kg bw/day
Women (Childbearing Age): 0.2 ug/kg bw/day
Children: 0.2 ug/kg bw/day

Occurrence data

Levels of total mercury in pre-retail samples

CH_3Hg^+

Hg + Hg + …

Hg^{2+}

"Total Mercury"

Occurrence data – Mercury levels influenced by…

…where the fish lived (Hg levels in the water and in the fish's food);

… whether it is herbivorous or piscivorous; high or low on the food chain;

…the fish's age.

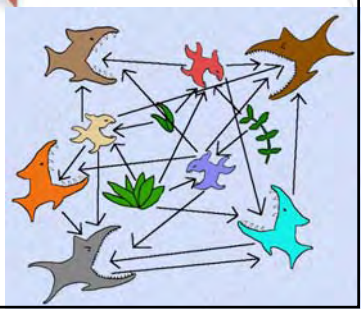


Diagram used with permission from web-posted essay entitled "Food Chains and Food Webs" by Lynn J. Fancher, College of DuPage, Glen Ellyn, IL

Mercury speciation in fish

Fish	Sample size (N)	Percent MeHg	Source
Sablefish	4	81 - 95	CFIA, 2003
Tuna (various species)	1* - 30 *(composite of 7)	60 – 77 (avg's)	Yamashita *et al.*, 2005
	50	61 - 94	Forsyth *et al.*, 2004
Swordfish	10	43 - 76	Forsyth *et al.*, 2004
Swordfish	7	72 (avg)	Yamashita *et al.*, 2005
Marlin	3	51 - 63	Forsyth *et al.*, 2004
Blue Marlin	7	43 (avg)	Yamashita *et al.*, 2005

Fish intake data used in Health Canada's assessment

Dietary survey of Canadians

- consumption a function of meal size and frequency of meal consumption
- monthly diaries (covering three months) of 3,815 respondents to a 1991 survey
- Average consumption of fish per day of the month was: 22 grams for adults
  14 grams for children 6-12 years of age
  10 grams for children 1-5 years of age

Exposure Assessment

Deterministic Exposure Scenario: only one type of fish ever eaten to the exclusion of all other types of fish

PDI values for each individual type of fish calculated for each population group using…

- average fish consumption per day of the month
- average body weights
- average total mercury concentrations

Risk Assessment

Initial screening for fish requiring further scrutiny and risk management beyond the 0.5 ppm standard

$$\frac{\text{PDI}}{\text{pTDI}} \times 100\% = \%\text{pTDI}$$

%pTDI values used as an indicator.

Risk Assessment

Fish identified for further scrutiny upon initial screening:

Barracuda	Sauger
Cusk	Sea bass
Escolar	Shark
Grouper	Swordfish
Halibut	Tuna, fresh/frozen
Marlin	Wahoo
Orange Roughy	Walleye

Previous Risk Management Strategy

0.5 ppm total mercury standard for most retail fish

Exceptions: shark, swordfish, fresh/frozen tuna

Consumer advisory for shark, swordfish, fresh/frozen tuna

General public	Women of child-bearing age and young children
↓	↓
one meal per week	one meal per month

Previous Risk Management Strategy

Previous consumer advisory

Not protective when total mercury > 1 ppm

Range of average total mercury levels; recent data

Swordfish	0.50 – 1.82 ppm
Shark	0.86 – 1.63 ppm
Dogfish	0.46 – 0.67 ppm
Fresh/frozen tuna	0.25 – 1.27 ppm

Risk Management

Criteria for subjecting fish to a 1 ppm standard

Does a high percentage of samples of the particular fish exceed the 0.5 ppm standard?

Is the particular fish a type that could be considered an infrequently consumed variety? What is the likelihood that it is frequently consumed?

Risk Management

Specific fish identified for risk management strategy:

Barracuda	Sauger
Cusk	Sea bass
Escolar	Shark
Grouper	Swordfish
Halibut	Tuna, fresh/frozen
Marlin	Wahoo
Orange Roughy	Walleye

Risk Management

Are there any fish containing less than 0.5 ppm that could require additional risk management attention?

Canned tuna is consistently identified as a popular fish choice that is consumed by some at rates greater than 22 g per day of the month.

Previous Risk Management Strategy

Canned tuna: subject to 0.5 ppm standard; no consumer advice.

Canned albacore (white) tuna	*0.26 to 0.43 ppm*
Canned light tuna	*0.05 to 0.12 ppm*

Updated strategy

A second standard

and

Updated advisory

The Updated Risk Management Strategy

0.5 ppm	1.0 ppm	advisory
All retail fish with certain exceptions	➢ Tuna (fresh and frozen) ➢ Swordfish ➢ Shark ➢ Marlin ➢ Escolar ➢ Orange Roughy	➢ Tuna, canned albacore ➢ Tuna (fresh, frozen) ➢ Swordfish ➢ Shark ➢ Marlin ➢ Escolar ➢ Orange Roughy

The Updated Risk Management Strategy

- Media and major stakeholders notified and information published on Health Canada's website (March 2007):
  - Human Health Risk Assessment of Mercury in Fish and Health Benefits of Fish Consumption
  - Updating the Existing Risk Management Strategy of Mercury in Retail Fish
  - Fish Consumption Advice

http://hc-sc.gc.ca/fn-an/securit/chem-chim/mercur/index_e.html

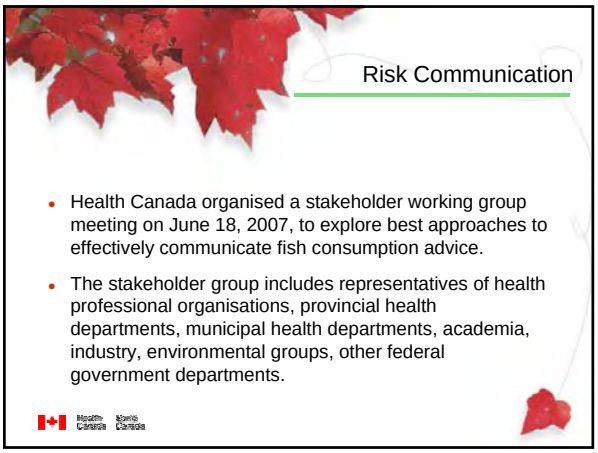
- The 1 ppm standard came into force July 11, 2007.

Risk Assessment – the future

Future reassessments can consider:

- any new data that becomes available or that helps to address uncertainties (consumption patterns; changes to mercury levels in fish; changes to pTDI; etc.)
- other quantitative methods that refine the risk assessment (e.g. probabilistic exposure assessment); depends on quality of consumption data)
- quantitative methods that consider both risks and nutritional benefits


Risk Communication
• Ensure that those who need to be (vulnerable groups; those who may eat a lot of retail fish) are aware of and understand Health Canada's advice.
• Balance existing mercury in fish advice with the message that fish can be part of a healthy balanced diet, as set out in Canada's Food Guide.
• Stakeholders are involved in the process.


Risk Communication
• Health Canada organised a stakeholder working group meeting on June 18, 2007, to explore best approaches to effectively communicate fish consumption advice.
• The stakeholder group includes representatives of health professional organisations, provincial health departments, municipal health departments, academia, industry, environmental groups, other federal government departments.

Questions and Answers

Q. Will the survey information and data regarding canned tuna be publicly available? (Sheeshka)

A. Yes, and the result will most likely be in a PR [public relations] journal.

Q. How do you enforce that the correct fish in the market have been tested (i.e., fish can be marketed under different names)? (Forti)

A. The Canadian Food Inspection Agency would be better able to provide information on this subject.

Q. Do you have any plans to do urban biomonitoring? (Mahaffey)

A. There are plans to do biomonitoring, but not specifically looking at urban populations.

IRIS Toxicological Reviews of Several PBDE Congeners

Joyce Donohue and Hend Galal-Gorcheve, Office of Water, Office of Science and Technology, U.S. EPA

Biosketches

Dr. Joyce Morrissey Donohue (Ph.D., R.D.) is a Lead Environmental Protection Specialist in the Health and Ecological Criteria Division in EPA's Office of Science and Technology, Office of Water. She has a background in biochemistry and nutrition and more than 20 years of experience in dealing with the toxicological properties of contaminants in drinking water. During her career she has written toxicological profiles of chemicals for EPA, NSF International, the U.S. Department of Agriculture (USDA), the Agency for Toxic Substances and Disease Registry (ATSDR), and the Department of the U.S. Army. She has taught courses in organic chemistry, biochemistry, nutrition, and nutrition sciences at Virginia Tech, Northern Virginia Community College, Framingham State College, the National Institute of Health (NIH), and the University of Pristina in Kosovo as a full-time, adjunct, or visiting Associate Professor.

Dr. Hend Galal-Gorchev (Ph.D.) is a Scientist in the Senior Environmental Employment (SEE) Program of EPA's Office of Water, Health and Ecological Criteria Division, in Washington, DC. Her main area of interest is the health assessment of environmental chemicals. She received her M.S. degree and Ph.D. in Environmental Sciences from Harvard University, Cambridge, MA. She worked for EPA's Office of Research and Development in Washington, DC, where she managed the drinking water research program before moving to the WHO in Geneva, Switzerland. At WHO, she was in charge of the Global Environment Monitoring System for Food (*GEMS/Food*), the development of WHO *Guidelines for Drinking-Water Quality* and *Environmental Health Criteria Monographs* on several chemicals (polybrominated biphenyls; polybrominated dioxins and furans; and disinfectants and disinfectant by-products). She was the WHO representative to several FAO/WHO Expert Groups on Pesticide Residues, Food Additives and Contaminants, Marine Pollution, and Codex Committees, all involved in the health assessment of chemicals (mercury, cadmium, lead, pesticides) and the development of international standards and guidelines for chemical contaminants in food, including fish. Upon her retirement from WHO, she rejoined EPA where her main duties included the "Six-Year Review of Drinking Water Contaminants" mandated by the Safe Drinking Water Act, health assessment of chemicals in biosolids, and the preparation of Integrated Risk Information System (IRIS) Toxicological Reviews of polybrominated diphenyl ethers (PBDEs).

Abstract

Polybrominated diphenyl ethers (PBDEs) have been found in human biological media and in several environmental compartments, such as air, dust, biosolids, and food, including fish. The need for a peer-reviewed Integrated Risk Information System (IRIS) health assessment of PBDEs and the possible derivation of reference doses (RfDs) became apparent to the Office of Water when PBDEs were found in fish and biosolids. It was decided from the onset that the IRIS assessments will deal with individual PBDE congeners and not with the commercial mixtures pentaBDEs, octaBDEs, and decaBDEs of varying congener's composition and contaminants' content. Production of the pentaBDE and octaBDE commercial products ceased in the United States in 2004, and the current decaBDE commercial products consist of >97% decaBDE-209.

IRIS Toxicological Reviews have been prepared by the Office of Water for tetraBDE-47, pentaBDE-99, hexaBDE-153, and decaBDE-209 congeners. These four congeners are those for which toxicological studies suitable for dose-response assessments were available and are the ones most commonly found in the environment and human biological media. The Toxicological Reviews underwent internal Agency

review by EPA's offices and regions, the Office of Management and Budget (OMB), and other interagency reviews (the Agency for Toxic Substances and Disease Registry, the National Institute of Environmental Health Sciences, and the Consumer Product Safety Commission), public review and external peer review by a panel of experts. An electronic version of the draft Toxicological Reviews, charges to the expert panel of external peer reviewers and their comments, and public comments are available at the following Web site: http://cfpub.epa.gov/ncea/cfm/nceawhatnew.cfm. At present, the Office of Water is addressing the external peer review and public comments and revising the Toxicological Reviews as appropriate. After an additional Agency-wide review and OMB and further interagency reviews, it is planned to post the final documents on the IRIS Web site during 2007.

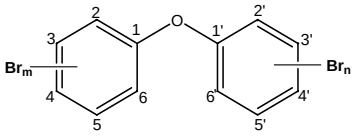
Draft RfDs have been proposed for tetraBDE-47 (0.1 µg/kg-day), pentaBDE-99 (0.1 µg/kg-day), hexaBDE-153 (0.2 µg/kg-day) and decaBDE-209 (7 µg/kg-day), on the basis of neurodevelopmental effects observed in adult rodents after exposure to PBDE congeners during the neonatal period. For various reasons, the overall confidence in each of the four RfD assessments is considered "low." There was inadequate information to assess the carcinogenic potential of tetraBDE-47, pentaBDE-99, or hexaBDE-153. There was "suggestive evidence of carcinogenic potential" for decaBDE-209. The draft proposed oral cancer slope factor derived on the basis of chronic carcinogenicity studies of decaBDE-209 in rats and mice, conducted by the National Toxicology Program, is 7×10^{-7} per µg/kg-day. Based on this cancer slope factor, the dose associated with an excess cancer risk of 10^{-5} is 14 µg/kg-day (i.e., greater than the RfD of 7 µg/kg-day for decaBDE). The proposed RfDs and cancer slope factor should be considered drafts until the documents are finalized by the Agency.

* NOTE: Although this work was reviewed by EPA and approved for publication, it may not necessarily reflect official Agency policy.

Polybrominated Diphenyl Ethers

Joyce M Donohue and Hend Galal-Gorchev
U. S. EPA Office of Water
Fish Forum
Portland, Maine
July 24, 2007

Chemical Structure



- Number of Bromines defines congener grouping
  - Mono- through deca-
- Positions of Bromines vary within a congener grouping
  - Substitution at the 2, 2' and the 2,2',6, 6' positions cause the congeners to be nonplanar
  - Congeners with substitution at the other positions are more planar

Background

- Synthetic organic chemicals
- First manufactured in Germany in the 1970s
- Used as flame retardants
  - Electronic Equipment
  - Polyurethane foam
  - Textiles
- Environmentally Persistent
  - Human and animal tissues
  - Food including fish
  - Ambient air (particulate matter)
  - Ambient waters
  - Sediments, biosolids

USEPA Integrated Risk Information System (IRIS) Assessment

- Four Congeners
  - BDE-47 – 4 bromines
  - BDE-99 – 5 bromines
  - BDE-153 – 6 bromines
  - BDE 209 – 10 bromines
- Available as pre-peer review drafts
  - http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=161970
  - Peer Review held February 22, 2007
- Post-peer review drafts nearly complete

Toxicokinetics: Oral Absorption

- Humans
  - No human data
- Animal data
  - >80 % BDE-47
  - 60-90% BDE-99
  - 70% BDE-153
  - 7-26% BDE-209

Distribution

- Humans
  - Found in sera (adult, children, maternal, fetal), adipose tissue, liver, cord blood
  - Found in maternal milk
- Animals
  - Mice and rats
    - Radiolabel experiments – no differentiation between parent and metabolites
    - Highest levels in adipose tissue, muscle and skin
    - Moderate levels in liver and kidney
    - Crosses blood brain barrier
  - Fish
    - Di- to deca- congeners

Metabolism

- Humans
  - No data
- Animals (mice and rats)
  - Data incomplete
  - Monohydroxylated metabolites
  - Debrominated monohydoxylated metabolites
    - Possible glutathione conjugates
  - Brominated phenols (rats)
    - Sulfate and glucuronate conjugates
  - Debromination in the absence of hydroxylation only observed for BDE-209
    - Lowest congener observed was hepta-BDE

Excretion

- Humans
  - No data
- Animals (mice and rats)
  - Fecal excretion is the major route
    - Unabsorbed parent
    - Metabolites via bile
  - Urinary excretion greater in mice than rats
    - Mostly metabolites
  - Intestinal or microbial metabolism may occur for BDE-209

Toxicity Database – BDE-47 and BDE-153

- No conventional, acute, short-term, or long-term studies
- Neurodevelopmental studies by one laboratory
- Studies of thyroid hormone homeostasis
- Studies of interactions with the aryl hydrocarbon, estrogen, and androgen receptors
  - No to weak interactions

Toxicity Database – BDE-99

- No conventional acute, short-term or long-term studies
- Neurodevelopmental studies from several laboratories
- Examination of reproductive organs and function
- Studies of thyroid hormone homeostasis
- Mechanistic neurotoxicity studies
- Studies of Ah, estrogen and androgen receptors
  - No to weak interactions

Toxicity Database – BDE-209

- Short-term, subchronic and chronic studies by NTP
- Reproductive and neurodevelopmental studies by several laboratories
- Studies of thyroid hormone homeostasis
- Studies of interactions with the aryl hydrocarbon, estrogen, androgen receptors
  - No to weak interactions

Critical Studies and Effects

- Critical effects: Neurodevelopmental impact on motor behavior and habituation in young adults after a single postnatal dose
  - pnd 10: BDE-47, BDE-99, BDE-153
  - pnd 3: BDE-209
- Critical studies – University of Uppsala, Sweden
  - Eriksson and Viberg Research Group

Reference Dose (RfD)

- BDE – 47 (UF 3000)
  - 0.0001 mg/kg-day
- BDE – 99 (UF 3000)
  - 0.0001 mg/kg-day
- BDE-153 (UF 3000)
  - 0.0002 mg/kg-day
- BDE – 209 (UF 300)
  - 0.007 mg/kg-day
- All RfD values are considered as having low confidence

Cancer Weight of Evidence

- BDE-47, BDE-99 and BDE-153
  - No chronic bioassays
  - Genotoxicity data: primarily negative
- ***Inadequate Information to Assess Carcinogenic Potential***
- BDE-209
  - Chronic bioassays in F-344 rats and B6C3F1 mice
  - Significant increase in hepatic neoplastic nodules and carcinomas in male rats
  - Genotoxicity negative
- ***Suggestive evidence of carcinogenicity***

Cancer Dose-Response

- Quantification based on hepatic neoplastic nodules and carcinomas combined in male rats
  - Classification of liver lesions has changed since the completion of the NTP (1986) bioassay
  - Some of the neoplastic nodules may have been nonneoplastic hyperplasia.
  - Classification change introduces some uncertainty in the dose-response quantification
- Risk Specific dose at 1×10^{-5} = 0.01 mg/kg-day

Questions and Answers

Q. Can you briefly describe some of the main comments you received on the IRIS profiles? (Laflamme)

A. The bulk of comments have noted the unusual study design and the decision not to use a full battery of neurodevelopmental tests. In some cases, only one animal per litter was observed. Some data presented are not modeled and are only presented in graphs. Other comments referenced neoplastic modeling or adenomas.

Q. Deborah Rice is also looking at Diphenyl Ethers. Did she comment on the IRIS Review? (Frohmberg)

A. We addressed her study and have included it in the IRIS.