

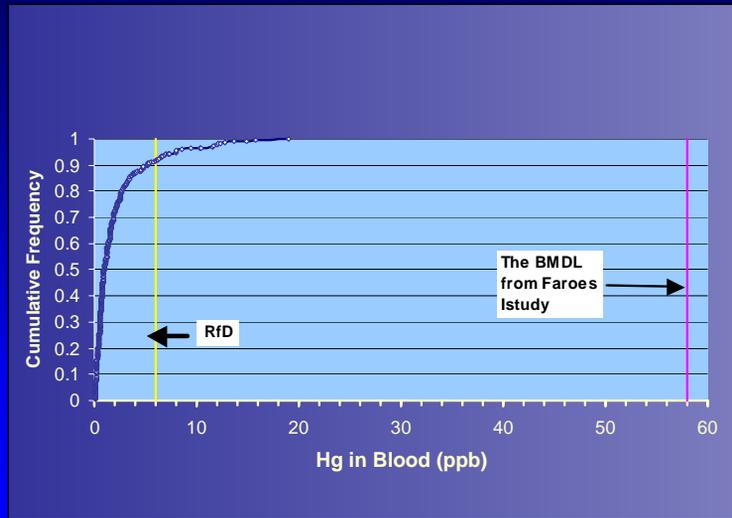
Exposure Assessment: Peer Review and Revisions

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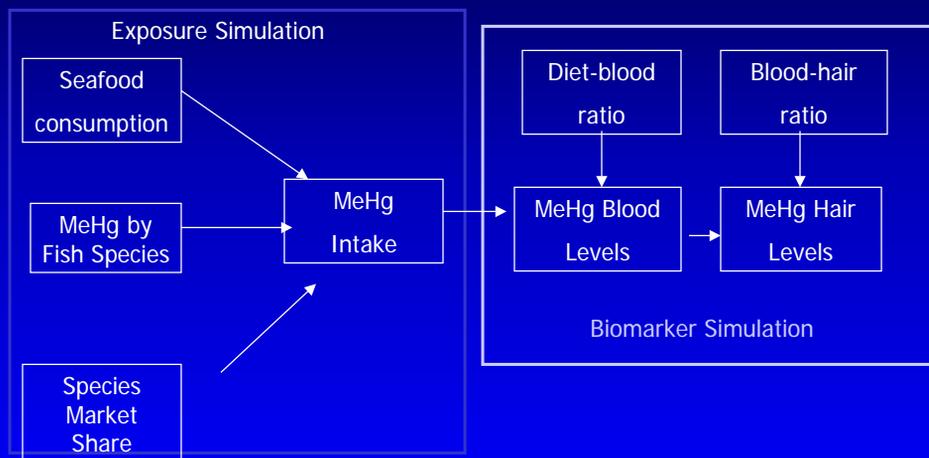
Why was the exposure assessment done?

- Response to 2002 – FDA Food Advisory recommendation on the 2001 fish advice
 - Publish a quantitative exposure assessment used to develop the advisory
 - Develop specific recommendations for canned tuna, based on a detailed analysis of what contribution canned tuna makes to overall methyl mercury levels in women

NHANES – blood mercury levels in women of childbearing age



MeHg Exposure Model Overview



Exposure simulation

- Short term consumption (3 day) – CSFII '89-90
- Long-term purchase diaries (30 day)
- Market share data
 - Shrimp 19.6%
 - Tuna (light) 15.7%
 - Salmon 11.1%
 - Pollock 10.3%
 - Catfish 7.6%
 - Tuna (albacore) 6.5%
 - 70.8%**

Estimation of blood or hair Hg predicated on Scenarios

- Scenarios – weekly levels of fish consumption
 - e.g. No dietary exclusions at all or
 - 12 oz /wk of low mercury fish
- For the scenarios fish were divided into high, medium and low MeHg
 - High: Swordfish, Shark, Tilefish, King Mackerel
 - Medium: e.g. Albacore Tuna, Halibut, Tuna steaks, Rockfish, Haddock, American Lobsters
 - Low: e.g. Light Tuna, Cod, Pollock, Catfish, Shrimp, Salmon, Flatfish, Scallops, Clams, Sardines, Oysters

EPA and FDA use of an exposure assessment

- Considered scenarios and outcomes in formulating bases for revised joint advice
- Discussed FDA / EPA conclusions with Stakeholders at July meetings:
 - The model closely predicts the NHANES data showing population exceeding RfD
 - FDA and EPA believe this will therefore be a useful tool in establishing the scientific background for an advisory
 - FDA and EPA believe the scenarios offer a way to inform the risk management decisions
 - FDA and EPA are submitting this exposure assessment for peer review

What was reviewed?

- Poster presentation by CD Carrington and PM Bolger, presented at 2003 meeting of the Society of Toxicology (abstract published in *The Toxicologist*)
 - Devised fish consumption scenarios and predicted blood and hair mercury for women of child-bearing age and children
 - Baseline scenario expected to reflect NHANES data

How was review done?

- “Letter” review done through existing EPA peer review contract (Contract No. 68-C-02-091, Versar)
 - EPA /FDA described required reviewer expertise
 - Contractor selected 3 reviewers
 - EPA approved listed reviewers as having the requisite credentials
 - Contractor provided all materials to reviewers, collected written comments from reviewers, compiled peer review report

EPA /FDA wrote the charge to the reviewers -- 1

- 1. Is the document **logical, clear and concise**? Are the arguments presented in an understandable manner?
- 2. Has the **appropriate literature** been cited? Are there publically available, peer-reviewed papers that should be included? Please provide copies of any papers or reports for consideration.
- 3. Is the **model clearly described**? Are modifications supportable by existing data? Modifications include these: expansion of fish categories from 24 to 28; fitted distributions in place of analogues for some species; addition of 0.1 to 2 ppb mercury to blood levels to account for sources other than fish.

EPA /FDA wrote the charge to the reviewers -- 2

- 4. Data from the **Continuing Study of Food Intake** by Individuals (CSFII) from 1989-1991 were the basis for distributions of fish consumption. These data were from three days of survey information vs. two days for the later data (CSFII 94-96). Comment on this choice. Comment on the adjustments made to compensate for likely under-reporting of fish consumption by the low consumption portion of the population.
- 5. In this paper women of child-bearing age are defined as those between **18 and 45 years** of age; children are defined as of **2 to 5 years** old. Are these the appropriate ranges?

EPA /FDA wrote the charge to the reviewers -- 3

- 6. Are the **fish consumption scenarios** logically described, clear and supportable? Comment on the identification of 0.5 ppm mercury or greater as “high mercury fish.”
- 7. For purposes of applying the scenarios in the exposure assessment, the following boundaries were set for **High, Medium and Low** mercury contamination of fish species: High, swordfish, shark, tilefish, king mackerel; medium greater than 0.13 ppm; low less than or equal to 0.13 ppm. Comment on these choices. Note and comment on the following: 0.12 ppm is a level of mercury contamination that would permit 12 oz. fish/week without exceeding the RfD.

Response to reviewers

- Written response by EPA / FDA available on Web. (www.cfsan.fda.gov, www.epa.gov/ost/fish)
- This describes
 - Revisions to assessment,
 - Differences of scientific opinion,
 - Review comments considered outside the scope of the current analyses,
 - Areas for future work

The exposure assessment has been revised and expanded

Some changes in response to review

- More categories of fish added; new data on [Hg]
- Correction for water lost from food preparation
- Parameters in consumption frequency chosen to reflect NHANES
- Slight increase in number of consumers
- Variation in consumer fish choice (changed to individual variable from population variable)
- Scenarios changed to reflect limit on amount of fish consumed, type of fish consumed and limits on both
- Body weight scaling changed

Model Changes: Mercury Concentration

- The number of fish categories for which distributions were developed was expanded from 24 to 42.
- Mercury concentration data was obtained for additional species.
- More data collected on canned tuna
- A correction factor was applied to reflect water loss during food preparation.

Model Changes: Consumption Frequency

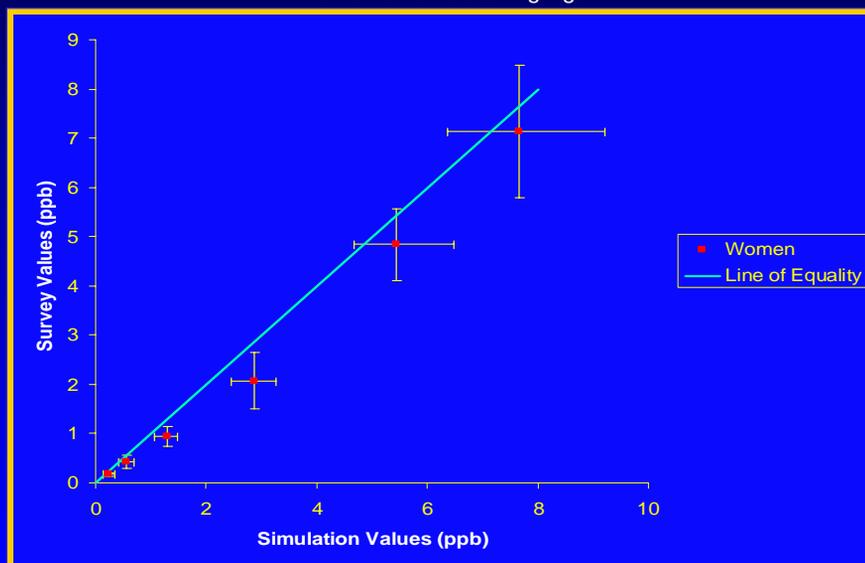
- The model parameters used to extrapolate long-term frequency of consumption from short-term records were optimized to be consistent with the 30 day NHANES survey.
- The percentage of consumers was also changed from 70-90% to 85 to 95% in order to be consistent with the NHANES survey.

Model Changes: Species Selection

- The fraction of the annual seafood diet estimated from the individual dietary survey, as opposed to market share, was treated as an individual variable rather than as a population uncertainty.
- Instead of using a range of 20 to 80%, the range of individual repetitiveness was estimated using the NHANES survey.

Blood MeHg: Simulation vs. NHANES

Women of Childbearing Age



Hg Concentration Groups

High	Medium		Low	
Swordfish	Grouper	Sablefish	Blue crabs	Catfish
Shark	Orange Roughy	Halibut	Snow crab	Whitefish
King Mackerel	Tuna, Albacore	Rockfish	Cod	Croaker
	Trout, Saltwater	Haddock	Tuna, Light	Scallops
	Tuna, Steaks	Snapper	Sea Bass	Flatfish
	Spiny Lobster	Bluefish	Trout, freshw.	Crawfish
	Dungeness Crab	Lobster	Perch, freshw.	Salmon
			King Crab	Shrimp
			Blue Crab	Clams
			Ocean Perch	Tilapia
			Oysters	Sardines

Advisory Scenarios

- Limit Total Seafood Consumption
 - 6, 12, or 18 oz per week without regard to species.
- Restrict Species Consumed
 - No limit on amount of fish consumed.
 - Consumption limited to either middle or low groups (No High), or low group (Low Only).
 - Where seafood from the restricted group(s) is specified, the serving is replaced by a random selection from a market-share distribution of low mercury species.
- Restrict Both Amount and Species

Advisory Scenario Simulations: Total Consumption Limits

	Baseline	18 oz/week	12 oz/week	6 oz/week
Average	2.3 (2.1, 2.6)	2.2 (2.0, 2.5)	2.1 (1.9, 2.3)	1.7 (1.5, 1.8)
Median	1.3 (1.1, 1.5)	1.3 (1.1, 1.5)	1.3 (1.1, 1.5)	1.2 (1.0, 1.4)
90th Percentile	5.5 (4.7, 6.5)	5.4 (4.6, 6.4)	5.1 (4.4, 5.7)	3.5 (3.3, 3.8)
95th Percentile	7.7 (6.4, 9.2)	7.4 (6.2, 8.9)	6.5 (5.7, 7.2)	4.2 (3.9, 4.5)
99th Percentile	13.6 (10.8, 20.2)	11.7 (10.2, 14.4)	9.5 (8.4, 11.3)	6.2 (5.3, 8.2)
99.5th Percentile	16.4 (13.1, 25.9)	13.7 (11.4, 17.1)	11.5 (9.4, 14.8)	7.9 (6.4, 10.6)
99.9th Percentile	26.3 (17.5, 52.0)	20.7 (14.1, 35.4)	18.8 (12.8, 24.9)	12.2 (8.5, 15.1)
% > RfD	8.8 (6.4, 12.0)	8.5 (6.3, 11.4)	7.1 (4.8, 9.4)	1.3 (0.8, 2.2)

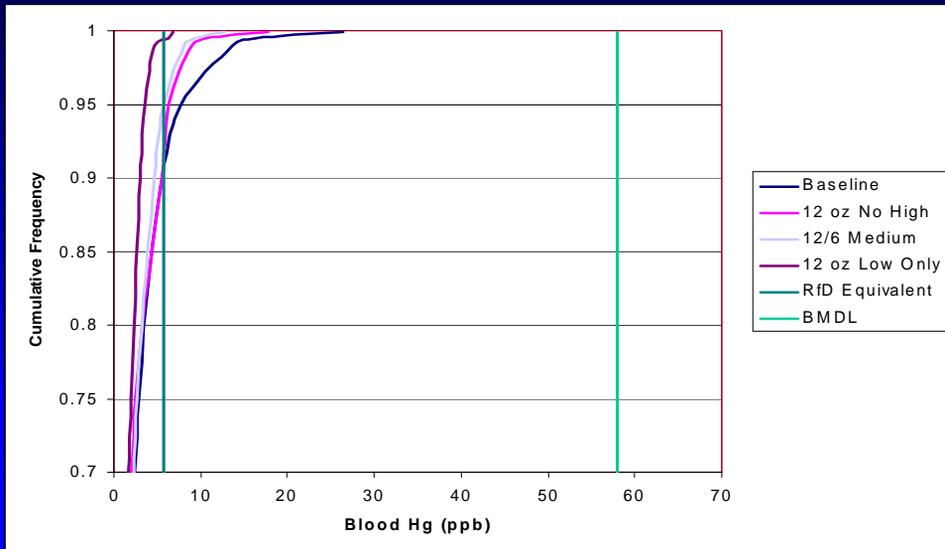
All units are ppb, with confidence limits in parentheses

Advisory Scenario Simulations: Species Consumption Limits

	Baseline	No High	Low Only
Average	2.3 (2.1, 2.6)	2.3 (2.0, 2.5)	1.7 (1.5, 1.9)
Median	1.3 (1.1, 1.5)	1.3 (1.1, 1.5)	1.0 (0.8, 1.2)
90th Percentile	5.5 (4.7, 6.5)	5.3 (4.6, 6.2)	3.8 (3.3, 4.4)
95th Percentile	7.7 (6.4, 9.2)	7.4 (6.3, 9.4)	5.4 (4.4, 6.7)
99th Percentile	13.6 (10.8, 20.2)	13.1 (10.5, 20.3)	8.8 (7.0, 14.3)
99.5th Percentile	16.4 (13.1, 25.9)	16.1 (11.8, 27.1)	10.4 (8.0, 16.7)
99.9th Percentile	26.3 (17.5, 52.0)	26.6 (17.9, 49.6)	14.4 (10.1, 24.7)
% > RfD	8.8 (6.4, 12.0)	8.5 (6.3, 11.4)	4.2 (2.3, 6.5)

All units are ppb, with confidence limits in parentheses

Scenario Comparison



Summary

- Many revisions have been made to the exposure assessment
- For women of childbearing age the model now generates slightly higher values than the NHANES survey, rather than slightly lower values
- Lowering seafood consumption by either **limiting the amount consumed and/or the species consumed** can be expected to reduce higher levels of exposure to mercury from seafood encountered in the U.S. population

Advisory Scenarios: Limit Combinations

Scenario	High	Middle	Low	Total
12 oz No High	None	12 oz/wk	12 oz/wk	12 oz/wk
12 oz Variety	None	6 oz/wk	12 oz/wk	12 oz/wk
12/6 Albacore	None	6 oz/wk	12 oz/wk	12 – Albacore oz/wk
12/6 Medium	None	6 oz/wk	12 oz/wk	12 – Medium oz/wk
12 oz Low Only	None	None	12 oz/wk	12 oz/wk

Advisory Scenario Simulations: Limit Combinations

	Baseline	12 oz No High	12 oz Variety	12/ 6 Albacore	12/ 6 Medium	12 oz Low Only
Average	2.3 (2.1, 2.6)	2.0 (1.8, 2.2)	2.0 (1.8, 2.2)	2.0 (1.8, 2.2)	1.9 (1.7, 2.1)	1.5 (1.3, 1.7)
Median	1.3 (1.1, 1.5)	1.3 (1.1, 1.5)	1.3 (1.0, 1.5)	1.2 (1.1, 1.5)	1.3 (1.1, 1.5)	0.5 (0.4, 0.6)
90th Percentile	5.5 (4.7, 6.5)	4.9 (4.4, 5.5)	4.9 (4.3, 5.6)	4.8 (4.3, 5.4)	4.7 (4.2, 5.2)	2.0 (1.8, 2.3)
95th Percentile	7.7 (6.4, 9.2)	6.3 (5.7, 7.0)	6.2 (5.5, 6.9)	6.0 (5.5, 6.7)	5.7 (5.1, 6.5)	3.6 (3.1, 4.0)
99th Percentile	13.6 (10.8, 20.2)	9.0 (8.0, 11.2)	9.1 (8.0, 10.7)	8.8 (7.4, 11.3)	8.0 (6.9, 9.4)	4.6 (4.0, 5.3)
99.5th Percentile	16.4 (13.1, 25.9)	10.6 (9.1, 13.7)	10.7 (9.1, 12.8)	10.6 (8.4, 14.1)	9.3 (7.7, 11.3)	6.3 (5.4, 8.2)
99.9th Percentile	26.3 (17.5, 52.0)	17.8 (12.4, 25.7)	15.3 (12.0, 18.1)	17.8 (12.0, 23.9)	12.7 (9.7, 15.2)	6.9 (5.8, 8.8)
% > RfD	8.8 (6.4, 12.0)	6.7 (4.8, 8.8)	6.2 (4.2, 9.0)	5.9 (3.9, 8.2)	4.8 (3.0, 7.4)	1.9 (0.5, 3.7)

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