

An Intervention Analysis for the Reduction of Exposure to Methylmercury from
the Consumption of Seafood by Women of Child-bearing Age

C D Carrington and P M Bolger.
U.S. Food and Drug Administration
College Park, MD, USA.

Abstract

A previously developed exposure model was used (Risk Analysis 22:689-699, 2002) to assess the effectiveness of various advisory scenarios on minimizing Hg blood levels via the consumption of commercial seafood, both finfish and shellfish. This exposure model was developed to predict levels of mercury (Hg) in blood in women of child-bearing age in the US based on the frequency of seafood consumption, the amount of seafood consumed per serving, and the types of seafood consumed. Steady-state relationships that employed descriptive statistics to account for toxicokinetic variation were used to predict levels of Hg in blood. The model incorporates an uncertainty dimension that is intended to represent the range of plausible interpretations of the data. The predictability of the model was confirmed via the use of NHANES blood Hg data. In the present analysis, the model was used to predict the impact of limitations in the amount or types of seafood consumed on blood Hg levels. Specifically, simulations for various advisory scenarios were developed on the basis of limitations on total consumption of seafood, elimination of the consumption of certain species altogether, and/or a combination of both. In the baseline model, the median (uncertainty) estimates for the 50th, 95th, and 99th per capita population percentiles were 1.25, 8.2, and 16.1 ppb blood Hg, respectively in blood. After restriction of seafood consumption to no more than 12 oz per week, the median (uncertainty) estimates for the 50th, 95th, and 99th per capita population percentiles were 1.22, 6.8, and 10.6 ppb blood Hg, respectively. Elimination of MeHg species, with average concentrations above 0.6 ppm, resulted in very modest decrements in Hg blood levels, in comparison to either the baseline or the reduced consumption scenarios. These results suggest that strategies to reduce MeHg exposure by reducing the amount of fish consumed (e.g., 12 oz/week) are more effective at eliminating the high end of the exposure distribution than are strategies intended to change the types of fish consumed.

Introduction

Methylmercury (MeHg) is a well known environmental toxicant found in the aquatic ecosystem. Inorganic mercury originates from anthropogenic and natural sources. Once in the ecosystem inorganic mercury is converted to methylmercury through bacterial activity and accumulates in fish and other marine species to varying degrees, particularly in long-lived, predators which are at the top of the marine food-chain. Depending on the level of exposure MeHg can cause mild to severe neurological symptoms such as paresthesia, ataxia, dysarthria, hearing defects, visual disturbances and death. Levels of exposure seen in some fish-eating populations have been reported to be associated with developmental delays in children whose mothers were exposed during pregnancy. While high-level poisoning episodes in Minimata and Nigata, Japan and in Iraq demonstrated pronounced MeHg-induced neurological deficits there is also concern that MeHg can cause more subtle developmental delays or other neurological effects at lower levels of exposure more consistent with the usual patterns of fish consumption seen in the U.S.

As part of its efforts to minimize the risks associated with such outcomes the U.S. Food and Drug Administration issued a new advisory in 2002 that provided recommendations concerning the consumption of certain fish species and for fish in general by pregnant women. The FDA advised these women to avoid the consumption of four species of fish; namely King mackerel, shark, swordfish and tile fish. In addition, it was recommended that they include up to 12 oz of a variety of other fish species over the course of a week. In order to better understand and define what a variety of fish means the FDA conducted a series of exposure assessments of various fish consumption scenarios that were constructed to be consistent with the consumption of 12 oz of a variety of fish. The scenarios differed in how “variety” of fish was defined. In these assessments EPA’s reference dose (RfD) was used as a measure of the effectiveness of a variety consumption/exposure scenario was effective in keeping weekly MeHg exposures of women who followed the specific advise scenario below the RfD.

Methodology

The Baseline Model

The model employed in the present analysis is a modified version of a model described previously (Carrington and Bolger, 2002). These modifications are as follows:

- ?? The number of fish categories for which distributions were developed was expanded from 24 to 42. (see Table 1). Tuna was broken into three categories, corresponding to 1) light canned tuna, 2) albacore canned tuna, and 3) fresh/frozen tuna steaks.
- ?? Mercury concentration data was obtained for additional species, which are identified in Table 2. For tuna steaks, this data was used to construct an empirical distribution. For the remaining species for which additional data was obtained, modeled distributions were developed by fitting the distributions to the portions of the cumulative distribution above the

Draft – November 24, 2003

levels of detection. A battery of ten distributions were fit to each data set and the four that provided the best fit were used to construct a probability tree (see Figure 1 for an example and Carrington, 1996 for further description of the methodology).

- ?? A range of 0.1 to 0.2 ppb was added to blood Hg levels in order to represent contributions from sources other than fish. This range reflected the levels at the low end of the NHANES survey. Since virtually everyone in the NHANES survey had a blood mercury level above zero, yet 10-20% of the NHANES survey population reported no seafood consumption, this suggests that there are contributions to blood Hg levels from other sources (e.g., dental amalgams) other than seafood. Since the present model is intended to represent methylmercury exposure, a range with an uncertainty bound including zero was introduced to acknowledge the possibility of minor exposures from sources other than seafood.
- ?? A correction factor (listed in Table 1) was applied to reflect water loss during food preparation. The values were based on water loss of 11% for fried seafood, 21% for poached or steamed seafood, and 25% for baked or broiled seafood (EPA, 2000). Group-specific correction factors were calculated based on the frequency of use of different food preparation (e.g. baking, steaming, or frying) within each group, based on the CSFII survey. A default value of 0.8 was used for categories not represented in the CSFII survey. These are listed in Table 1. No correction factors were applied for canned-tuna since the MeHg concentration values, expressed as total Hg, were obtained after cooking and draining of water or oil from the can.
- ?? The model parameters used to extrapolate long-term frequency of consumption from short-term records were chosen to be consistent with the 30 day seafood consumption data collected by NHANES (see Figure 2). The percentage of consumers was also changed from 70-90% to 85 to 95% in order to be consistent with the NHANES survey.
- ?? 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. Also, instead of using a range of 20 to 80%, the range of individual repetitiveness was estimated using the NHANES survey, by calculating the fraction of total seafood consumption in the seafood category with the highest number of eating occasions. This produced a range of Repetition Ratios 12 to 100% (see Figure 3)

Scenarios

In order to simulate the impact of consumer seafood advisories for women of child bearing age who become pregnant, several scenarios were developed that are intended to predict the expected impact of the advisory on mercury blood. All the scenarios presumed full compliance with the advisory. Seafood species were divided into three groups, as listed in Table 2.

Using these groups, the following advisory scenarios were modeled:

- ?? *Total Seafood Consumption Limits* (see Table 3). The consumption of seafood is limited to 6, 12, or 18 oz without regard to species.

Draft – November 24, 2003

- ?? *Species Consumption Limits* (see Table 4). There is no limit on how much fish may be consumed. Seafood consumption is limited to either the middle or low groups (No High Hg), or the low group only (Low Hg Only). In either case, seafood from the restricted group(s) is replaced by a random selection from a market-share distribution of low mercury species.
- ?? *Total Seafood and Species Limit Combinations* (see Table 5).
- *12 oz No High* Consumption of seafood is limited to 12 oz per week, high mercury fish are replaced with low mercury fish.
 - *12 oz Variety* (see Table 5). Seafood consumption is limited to 12 oz per week, with no more than 6 oz from the Middle Hg group. High Hg fish (shark, swordfish, and mackerel) and Middle Hg fish in excess of 6 oz are replaced with Low Hg fish.
 - *12 or 6 Albacore* (see Table 5). Same as 12 oz variety. In addition, for the purposes of calculating the 12 oz limit, albacore portions are doubled. As a result, the maximum amount of seafood that may be consumed is reduced by an amount equal to the amount of albacore consumed. For example, if 3 oz of albacore is consumed per week, then the total amount of seafood that may be consumed is 9 oz. As the most extreme example, if 6 oz of albacore is consumed per week, then no additional seafood may be consumed.
 - *12 Low or 6 oz Middle* (see Table 5). Seafood consumption is limited to 12 oz per week, High Hg fish (shark and swordfish) are replaced with Low Hg fish. For the purposes of calculating the 12 oz limit, seafood portions from the Middle group are doubled. As a result, the maximum amount of seafood that may be consumed is reduced by an amount equal to the amount of seafood from the middle group consumed. For example, if 3 oz of Middle Group seafood is consumed per week, then the total amount of seafood that may be consumed is 9 oz. As the most extreme example, if 6 oz of Middle Group seafood is consumed per week, then no additional seafood may be consumed.
 - *12 oz Low* (see Table 5). Seafood consumption is limited to 12 oz, high and mid Hg fish are replaced with low Hg fish.

Results

Comparison of Baseline Model to NHANES

The results from the blood mercury exposure model were compared to survey mercury blood values from the NHANES survey population between 1999 and 2000 (see Figure 4). The values are in very close agreement.

Intervention Scenarios

The impact of various consumer advisories on mercury blood levels is presented in Tables 3, 4, and 5. In each case, the impact of each advisory is compared to current baseline blood mercury values.

Total Seafood Consumption Limits

Table 3 shows the expected reduction in mercury blood levels following the introduction of consumption limits ranging from 6 to 18 oz per week. While a limit of 18 oz only slightly reduces the level of exposure at the extreme tail (i.e. above the 99th percentile), more aggressive limits reduce exposure for a greater range of consumers and provide a greater reduction at the tail.

Advisories Concerning Specific Species

Table 4 shows the expected reduction in mercury blood levels following the elimination of certain species, with either particularly high mercury levels or any species with above average mercury levels. Although the reductions on mercury exposure are not as dramatic, the reductions in exposure may be noted across the entire distribution

Advisories Combining Limits on Amount and Species

Table 5 shows the expected reduction in blood mercury levels with several different scenarios where the advisory includes some combination of limitation on the amount of seafood consumed with additional limitations on the types of seafood consumed. In the first scenario, which reflects the current FDA advisory avoiding the consumption of high methylmercury species and limiting seafood consumption to no more than 12 oz per week will eliminate the occurrence of blood mercury values that are higher than 5 times the average. The simulations indicate that more aggressive limits on what species are consumed would result in greater reductions across the entire distributions of blood mercury values, but only provide minor, further (in comparison with advisories that only limit the amount of fish consumed) reductions in those consumers with the highest levels of exposure.

CONCLUSIONS

Using the NHANES blood mercury data, the exposure model used to predict blood levels for women of child-bearing age is validated. This does not prove beyond any possible doubt that the model is entirely correct, however, the comparison does indicate that the results of the model are entirely plausible.

An advisory that eliminates consumption of certain species with High Hg levels and limits consumption to 12 oz per week appears to result in the most significant reductions in blood mercury levels. Further restrictions in limiting certain species with Hg levels, exceeding 0.5 ppm Hg, results in minimal further reductions in blood mercury levels.

References

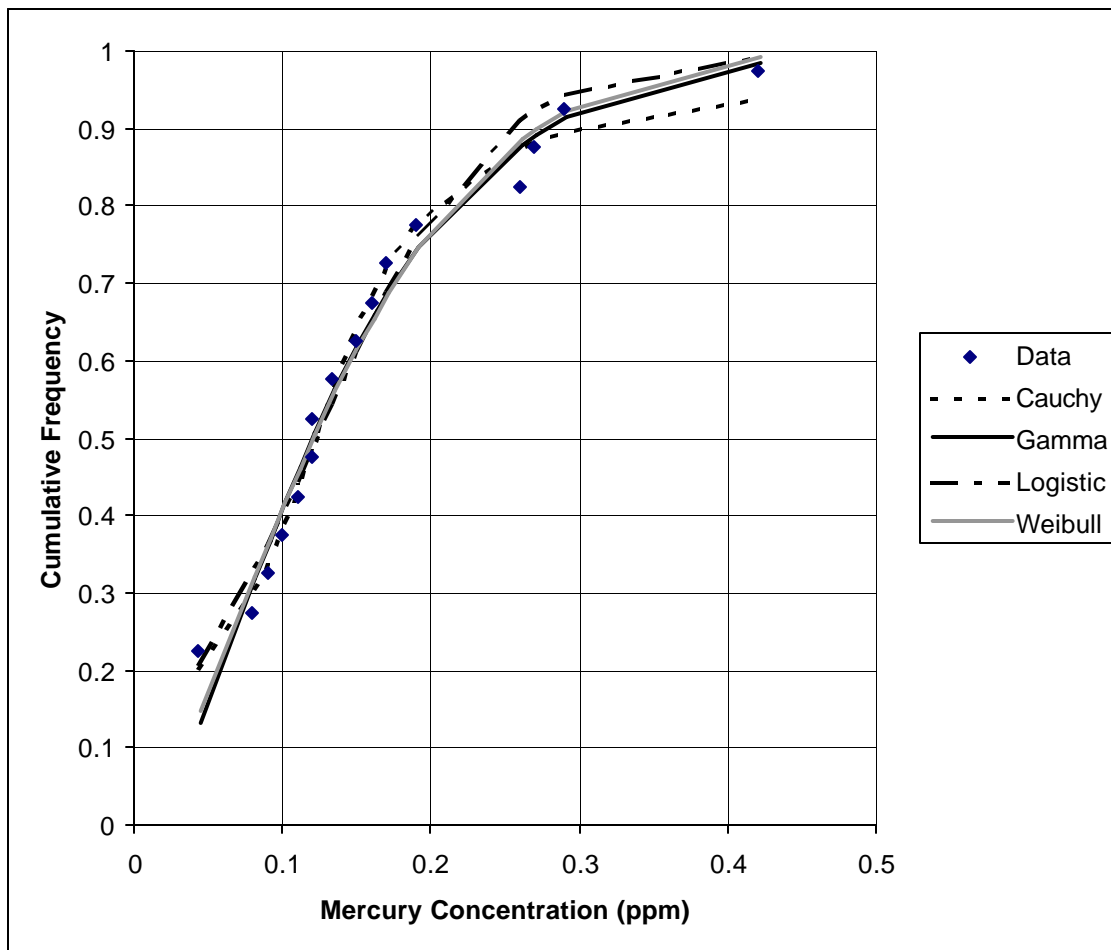
Carrington, CD (1996). Logical Probability and Risk Assessment. *Human Ecology Risk Assessment* 2:62-78.

Carrington CD and Bolger PM (2002). An Exposure Assessment for Methylmercury from Seafood for Consumers in the United States. *Risk Anal* 22:689-699.

U. S. Environmental Protection Agency (2002). Estimated Per Capita Fish Consumption in the United States. http://www.epa.gov/waterscience/fish/consumption_report.pdf

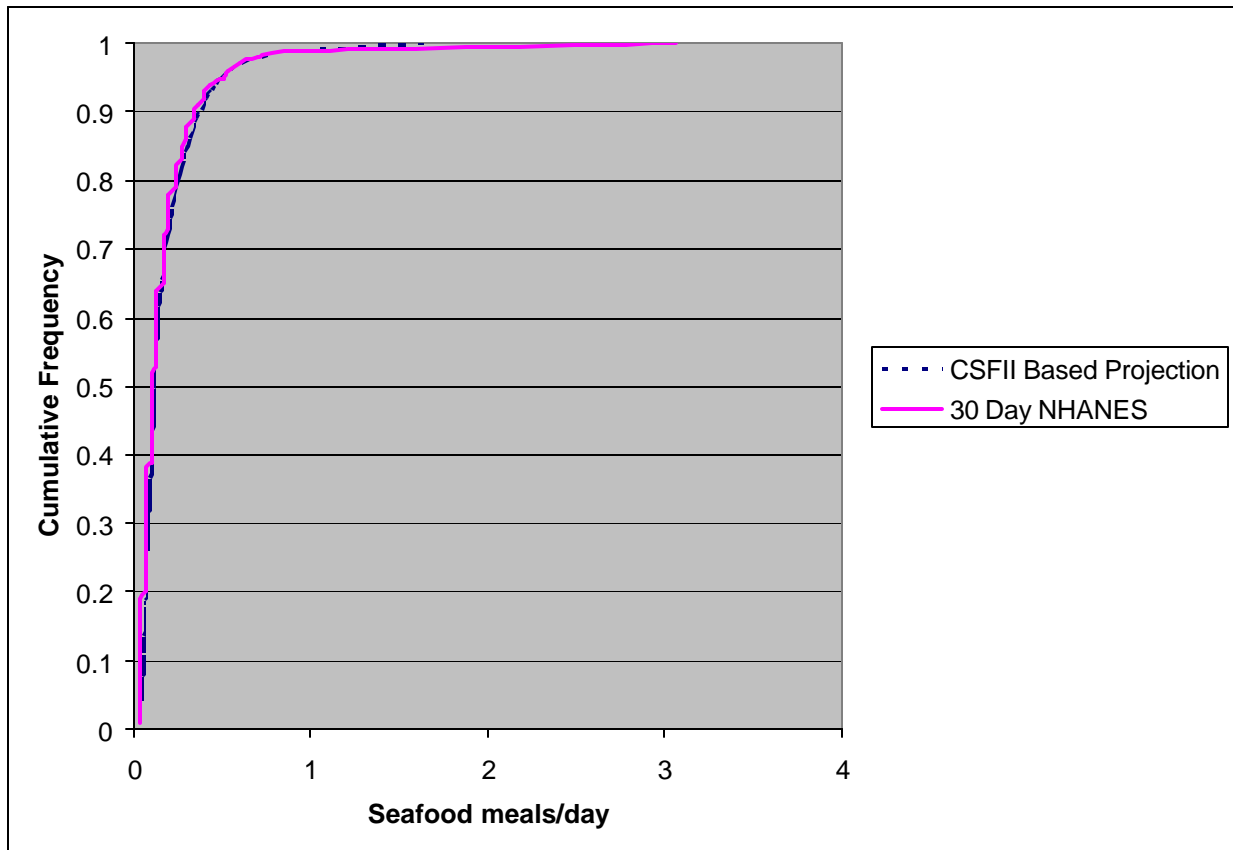
U. S. Food and Drug Administration (2001). Mercury Levels in Seafood Species. <http://www.cfsan.fda.gov/~frf/sea-mehg.html>.

Figure 1: Fitted Distributions for Hg in Cod



An example of a fitted distribution. 10 different distributions were fit to the sample Hg data for Cod. The four best models were used to create a probability tree that describes the frequency distribution with a representation of model uncertainty.

Figure 2: Long-Term Frequency Extrapolation for Consumption



The CSFII based projection employed the exponential function described in Carrington and Bolger (2002b), using values of 0.696 and 0.356 for the alpha and beta parameters, respectively.

Figure 3: Repetition Ratio Distribution

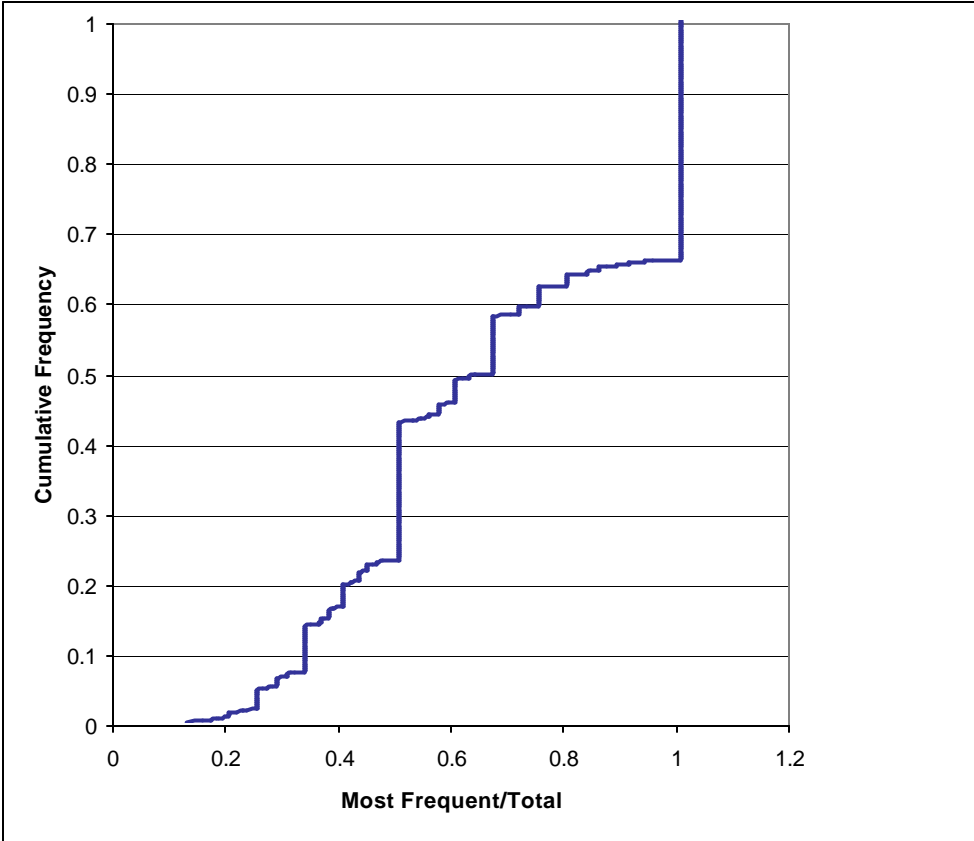


Figure 4: Quantile-Quantile Comparison of Simulation and Survey Blood Hg Values

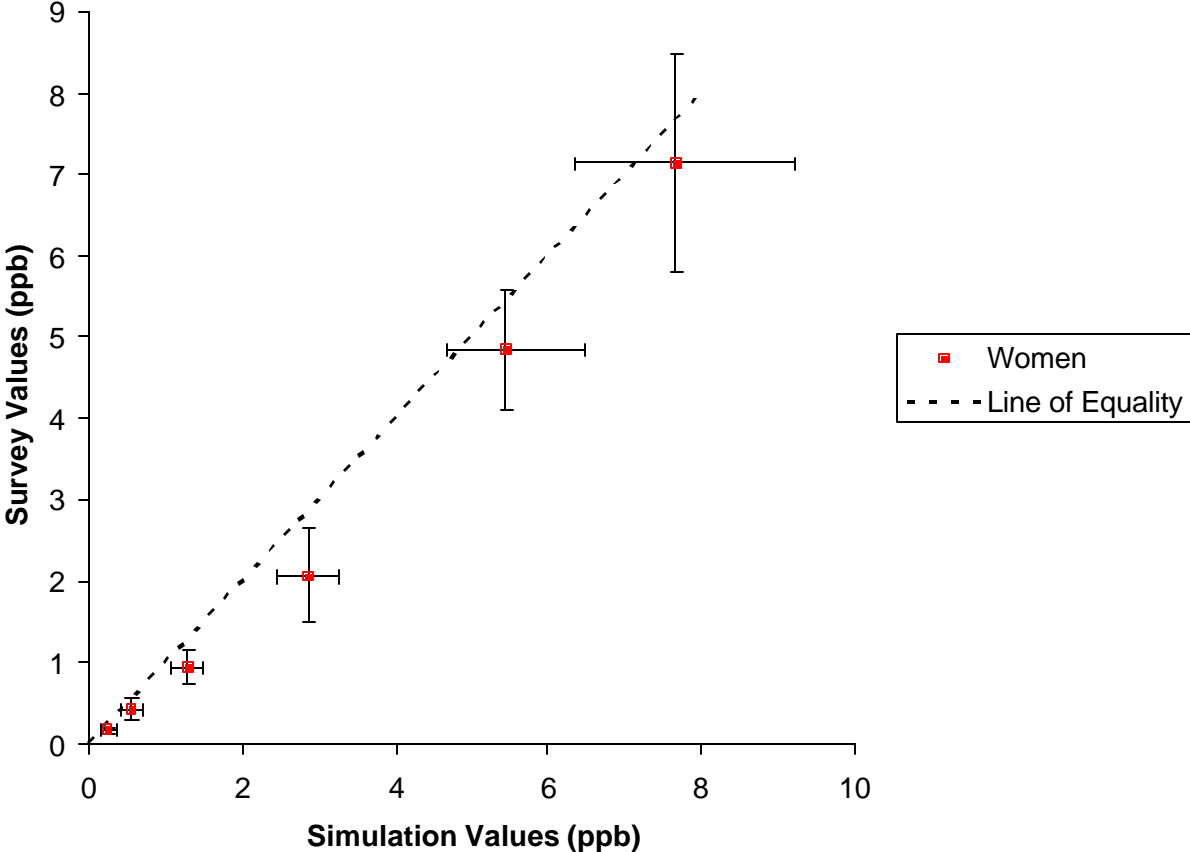


Table 1: Seafood Hg data

Species	Range (ppm)	Samples
Bluefish ¹	0.14 - 0.63	23
Catfish	ND - 0.31	29
Cod	ND - 0.42	20
Crawfish ¹	0.01 – 0.05	20
Croaker, Atlantic ¹	0.01 - 0.10	20
Croaker, Other	0.18 - 0.41	15
Flounder (Flatfish)	ND - 0.18	17
Grouper ¹	0.07 – 1.21	18
Halibut	ND - 1.52	31
Lobster, Spiny	ND - 0.27	8
Orange Roughy	0.01 – 0.76	23
Oysters	ND - 0.25	34
Pollock	ND - 0.78	38
Red Snapper ¹	0.08 – 0.44	13
Sardines ¹	0.00 – 0.04	21
Salmon	ND - 0.19	57
Sea Bass, Black ¹	0.06 – 0.35	20
Shark	ND - 4.21	240
Shrimp	ND - 0.5	25
Swordfish	0.05 - 2.98	280
Tilefish ¹	0.06 – 1.12	13
Trout, Sea ¹	0.02 – 0.88	13
Trout, Freshwater ¹	0.02 – 0.66	17
Tuna, Albacore Canned ¹	0.02 - 0.85	175
Tuna, Fresh	0.01 - 1.13	181
Tuna, Light Canned ¹	0.01 - 0.75	225
Whitefish ¹	0.03 – 0.14	14

1- New data obtained since Carrington and Bolger (2000)

Table 2: Methylmercury (as total Hg) Distributions for Various Species

Species	Market Share ¹	Mean Hg (ppm)	Distribution Type	Concentration Factor	Advisory Group
Swordfish	0.0042	0.988	Empirical	0.750	High
Shark	0.0013	0.982	Empirical	0.767	High
King Mackerel	0.0047	0.730	Analog	0.800	High
Grouper	0.0017	0.552	Modeled	0.800	Middle
Orange Roughy	0.0020	0.485	Modeled	0.800	Middle
Tuna, Albacore Canned	0.0529	0.351	Empirical	1.000	Middle
Trout, Saltwater	0.0006	0.340	Modeled	0.800	Middle
Tuna, Fresh	0.0179	0.324	Empirical	0.798	Middle
Bluefish	0.0009	0.318	Modeled	0.800	Middle
Lobsters, American	0.0129	0.310	Analog	0.765	Middle
Sablefish	0.0025	0.273	Modeled	0.823	Middle
Halibut	0.0090	0.217	Modeled	0.750	Middle
Rockfish	0.0039	0.204	Modeled	0.791	Middle
Crabs, Dungeness	0.0038	0.170	Analog	0.766	Middle
Haddock	0.0062	0.170	Modeled	0.793	Middle
Lobsters, Spiny	0.0082	0.165	Modeled	0.765	Middle
Snapper	0.0046	0.154	Modeled	0.800	Middle
Crabs, Blue	0.0159	0.150	Analog	0.766	Low
Crabs, Snow	0.0177	0.148	Analog	0.766	Low
Cod	0.0471	0.143	Modeled	0.806	Low
Tuna, Light Canned	0.1335	0.135	Empirical	1.000	Low
Sea Bass	0.0004	0.127	Modeled ⁴	0.791	Low
Trout, Freshwater	0.0069	0.126	Modeled ⁴	0.800	Low
Perch, Freshwater	0.0004	0.110	Modeled	0.785	Low
Crabs, King	0.0040	0.092	Analog	0.766	Low
Pollock	0.1105	0.071	Modeled	0.820	Low
Catfish	0.0477	0.070	Modeled	0.870	Low
Whitefish	0.0022	0.068	Modeled	0.800	Low
Perch, Ocean	0.0049	0.056	Analog	0.785	Low
Croaker	0.0030	0.054	Modeled ⁴	0.876	Low
Scallops	0.0080	0.050	Modeled	0.793	Low
Flatfish	0.0361	0.046	Modeled	0.756	Low
Crawfish	0.0056	0.028	Modeled	0.773	Low
Salmon	0.1067	0.025	Modeled	0.758	Low
Shrimp	0.1514	0.025	Modeled	0.773	Low
Clams	0.0169	0.020	Modeled	0.754	Low
Tilapia	0.0187	0.019	Modeled	0.800	Low
Oysters	0.0079	0.017	Analog	0.793	Low
Sardines	0.0123	0.016	Modeled	0.795	Low

1 – As a result of species not included in the list, the sum of the market share values is about 90%.

2 - *Empirical* – Direct sampling of data set, used for large data sets with very few values below the limit of detection. *Fitted* – Modeled distribution with uncertainty about model form (see text for additional explanation). Used for data sets with a limited number of observations, often with many values below the level of detection.

Draft – November 24, 2003

Analog – Two distributional forms (lognormal or gamma) - mean value from 1978 National Marine Fisheries Survey, shape parameter by analogy (see Carrington and Bolger, 2002 for additional explanation). Used when only mean values are available.

3 – These values reflect weight after food preparation as a percentage of initial weight. Mercury concentrations for seafood as eaten were calculated by dividing initial concentration by the correction factor. No correction factor was applied for canned tuna, since the mercury measurements were made after cooking. .

4 - Croaker, Sea Bass, and Freshwater Trout all had bimodal distributions that were described with two different distributions. The Croaker and Sea Bass data subsets corresponded to surveys taken at different times and may reflect different species with the same common name.

Table 3: Effect of Advisories Based on Seafood Consumption Limits on Estimated Hg Blood Levels

Scenario	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)
Perc 0.10	0.2 (0.1, 0.3)	0.2 (0.1, 0.4)	0.2 (0.1, 0.4)	0.2 (0.1, 0.3)
Perc 0.25	0.6 (0.4, 0.7)	0.6 (0.4, 0.7)	0.5 (0.4, 0.7)	0.6 (0.4, 0.7)
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)
Perc 0.75	2.9 (2.5, 3.3)	2.8 (2.4, 3.2)	2.8 (2.5, 3.2)	2.7 (2.4, 3.1)
Perc 0.90	5.5 (4.7, 6.5)	5.4 (4.6, 6.4)	5.1 (4.4, 5.7)	5.5 (4.9, 6.2)
Perc 0.95	7.7 (6.4, 9.2)	7.4 (6.2, 8.9)	6.5 (5.7, 7.2)	7.9 (7.1, 8.9)
Perc 0.99	13.6 (10.8, 20.2)	11.7 (10.2, 14.4)	9.5 (8.4, 11.3)	13.0 (11.1, 16.4)
Perc 0.995	16.4 (13.1, 25.9)	13.7 (11.4, 17.1)	11.5 (9.4, 14.8)	16.2 (12.9, 25.6)
Perc 0.999	26.3 (17.5, 52.0)	20.7 (14.1, 35.4)	18.8 (12.8, 24.9)	23.8 (16.0, 37.8)

All units are $\mu\text{g Hg/L}$ in blood with uncertainty bounds expressed as 5th and 95th confidence limits in parentheses .

Table 4: Effect of Advisories Based on Species Selection on Estimated Hg Blood levels

Scenario	Baseline	No High	Low Only
Average	2.3 (2.1, 2.6)	2.3 (2.0, 2.5)	1.7 (1.5, 1.9)
Perc 0.10	0.2 (0.1, 0.3)	0.2 (0.2, 0.3)	0.2 (0.1, 0.3)
Perc 0.25	0.6 (0.4, 0.7)	0.5 (0.4, 0.7)	0.5 (0.3, 0.6)
Median	1.3 (1.1, 1.5)	1.3 (1.1, 1.5)	1.0 (0.8, 1.2)
Perc 0.75	2.9 (2.5, 3.3)	2.8 (2.3, 3.2)	2.1 (1.7, 2.3)
Perc 0.90	5.5 (4.7, 6.5)	5.3 (4.6, 6.2)	3.8 (3.3, 4.4)
Perc 0.95	7.7 (6.4, 9.2)	7.4 (6.3, 9.4)	5.4 (4.4, 6.7)
Perc 0.99	13.6 (10.8, 20.2)	13.1 (10.5, 20.3)	8.8 (7.0, 14.3)
Perc 0.995	16.4 (13.1, 25.9)	16.1 (11.8, 27.1)	10.4 (8.0, 16.7)
Perc 0.999	26.3 (17.5, 52.0)	26.6 (17.9, 49.6)	14.4 (10.1, 24.7)

All units are $\mu\text{g Hg/L}$ in blood with uncertainty bounds expressed as 5th and 95th confidence limits in parentheses .

Table 5: Effect of Advisories with Species and Consumption Limits on Estimated Hg Blood Levels

Scenario	Baseline	12 oz No High	12 oz Variety	12 or 6 Albacore	12 or 6 Medium	12 oz Low
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)
Perc 0.10	0.2 (0.1, 0.3)	0.2 (0.1, 0.4)	0.2 (0.1, 0.4)	0.2 (0.2, 0.4)	0.2 (0.1, 0.4)	0.2 (0.1, 0.2)
Perc 0.25	0.6 (0.4, 0.7)	0.6 (0.4, 0.7)	0.5 (0.4, 0.7)	0.5 (0.4, 0.7)	0.5 (0.4, 0.7)	0.2 (0.1, 0.3)
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)
Perc 0.75	2.9 (2.5, 3.3)	2.8 (2.3, 3.2)	2.8 (2.4, 3.2)	2.8 (2.3, 3.1)	2.7 (2.3, 3.1)	1.0 (0.8, 1.1)
Perc 0.90	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)
Perc 0.95	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)
Perc 0.99	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)
Perc 0.995	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)
Perc 0.999	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)

All units are $\mu\text{g Hg/L}$ in blood with uncertainty bounds expressed as 5th and 95th confidence limits in parentheses.