

DATA QUALITY ACT CHALLENGE

REQUEST FOR CORRECTION OF FDA'S "ADVICE FOR WOMEN WHO ARE PREGNANT, OR WHO MIGHT BECOME PREGNANT, AND NURSING MOTHERS, ABOUT AVOIDING HARM TO YOUR BABY OR YOUNG CHILD FROM MERCURY IN FISH AND SHELLFISH"

December 22, 2003

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Dr. Acheson:

On behalf of the millions of women of childbearing age and parents of young children who rely on FDA recommendations to guide their food consumption choices, Environmental Working Group respectfully demands a correction of the 2003 FDA Consumption Advisory regarding the risks of mercury contaminated fish and shellfish (hereinafter the "Advisory") pursuant to the Data Quality Act, Section 515 of the Fiscal Year 2001 Treasury and General Government Appropriations Act. The Advisory fails to meet vital information quality guidelines set forth in the Data Quality Act, particularly those requiring federal agencies to maximize the utility and objectivity of influential information. The Advisory falls severely short of the FDA Data Quality Guidelines, which dictate that the FDA produce information that is useful, reproducible, transparent, and that its risk assessment be based on sound scientific practice. See FDA guidelines, www.hhs.gov/infoquality/fda.html (last visited December 10, 2003).

Mercury exposure through consumption of contaminated fish is a major public health concern that according to the Environmental Protection Agency affects an estimated 300,000 children born each year (Mahaffey et. al 2003). If pregnant women and young children follow the Advisory as it is currently drafted, they will substantially increase

their risks associated with mercury exposure from eating contaminated fish. This is unacceptable. The health and safety of millions of Americans is on the line. EWG demands that FDA take immediate action to ensure that the advice that it provides is based on sound science, valid evidence, and provides protective information to women and young children making vital decisions about their health and safety.

Pursuant to the Section 515 of the Fiscal Year 2001 Treasury and General Government Appropriations Act (hereinafter the "Data Quality Act"), Pub. L. No. 106-554, § 515, 114, Stat. 2763A-153 (2000), and the information data quality guidelines promulgated by the Office of Management and Budget (OMB), Health and Human Services (HHS) and the Food and Drug Administration (FDA), 67 Fed. Reg. 36,8452 (Feb. 22, 2003), Environmental Working Group, a nonprofit 501(c)(3) public health watchdog organization, hereby requests that the FDA issue a correction of the agency's recent seafood consumption advisories entitled "Important Message for Pregnant Women, Women Who May Become Pregnant, Nursing Mothers and Young Children About the Risks of Mercury in Fish and Shellfish."

The consumption advisories and the underlying data and analyses fail to meet the requirements with respect to three areas defined in the Act - objectivity, utility, and transparency - and nine specific areas that fall under those criteria.

DETAILED DESCRIPTION OF SPECIFIC MATERIAL TO BE CORRECTED

The specific material to be corrected includes six statements within FDA's final draft advisory entitled "Advice for women who are pregnant, or who might become pregnant, and nursing mothers, about avoiding harm to your baby or young child from mercury in fish and shellfish" (FDA 2003a), and some of the underlying information used to develop those statements. Specifically, these statements include the following:

1. Statements in the draft advisory indicating that four types of seafood - shark, swordfish, king mackerel, and tilefish - should not be consumed in any quantity by pregnant women, women who may become pregnant, nursing mothers, and young children (referred to as the "do not eat" list in this document).
2. Statements in the draft advisory indicating that it is safe to eat a variety of any other kinds of seafood in quantities of up to 12 ounces per week.
3. Statements in the draft advisory indicating that any single type of seafood can be safely consumed at a frequency of up to once a week, barring the four specifically listed for zero consumption.
4. Statements in the draft advisory indicating that children should eat seafood in quantities of less than 12 ounces per week, depending on their size.
5. Statements in the draft advisory concerning canned tuna.

6. Statement in the draft advisory indicating that those following the consumption advice outlined in the advisory will "avoid any developmental problems from mercury in fish."

THE CHALLENGED ADVISORY IS INFLUENTIAL INFORMATION SUBJECT TO THE INFORMATION QUALITY GUIDELINES

The challenged advisory qualifies as influential information disseminated by FDA pursuant to the information quality guidelines of OMB, HHS, and FDA. On December 10, 2003, at a Food Advisory Committee meeting, FDA disseminated its advisory entitled "Advice for Women Who Are Pregnant, or Who Might Become Pregnant, And Nursing Mothers, About Avoiding Harm to Your Baby or Young Child from Mercury in Fish and Shellfish." The advisory provides guidance to women and young children on consumption choices aimed at minimizing risks associated with eating mercury-contaminated seafood. The meeting was a public event, and offered an opportunity for interested members of the public, such as public health and consumer groups and seafood industry representatives, to comment on the advisory. The event was also widely attended and reported on by national media outlets. The advisory clearly meets the definition of influential information, and is subject to information quality standards.

The definition of "information" in the data quality guidelines of both FDA and OMB apply to the advisory. The advisory was disseminated at a public event, conveys FDA's knowledge about mercury risks and seafood consumption, and is intended to inform the public about safe seafood consumption choices in order to minimize risks associated with mercury exposure. FDA's guidelines list, as a type of dissemination method, "oral presentations in public forums sponsored by FDA or outside parties." See FDA guidelines, www.hhs.gov/infoquality/fda.html (last visited December 19, 2003). The Food Advisory Committee meeting qualifies as a forum for public dissemination of information pursuant to the FDA guidelines. The FDA guidelines specifically list a prior version of the advisory in its definition of "information disseminated." See FDA guidelines, www.hhs.gov/infoquality/fda.html (last visited December 19, 2003).

The March 2001 predecessor to the advisory is listed as an example of a type of information disseminated by the FDA, a "public communication about risk," specifically, a "public health and safety alert." See FDA guidelines, www.hhs.gov/infoquality/fda.html (last visited December 19, 2003) (using the 2001 advisory on mercury-contaminated seafood as an example of a public health and safety alert, "An Important Message for Pregnant Women and Women of Childbearing Age About the Risk of Mercury in Fish," March 2001). FDA's definition of information also includes "information on food safety" and "consumer advice," both of which are applicable to the challenged advisory, which is aimed at informing the food safety consumption decisions of women of childbearing age and caregivers of young children who eat seafood. The OMB guidelines define "information" as "any communication or representation of knowledge such as facts or data, in any medium or form, including textual, numerical, graphic, cartographic, narrative, or audiovisual forms." See 67 Fed. Reg. 36,8460 (Feb. 22, 2002). The advisory includes the FDA's knowledge and data

related to mercury-contaminated seafood, and thus falls within the OMB definition of information.

The information is "influential" because the FDA can "reasonably determine that dissemination of the information will have or does have a clear and substantial impact on important public policies or important private sector decisions." See 67 Fed. Reg. 36,8460 (Feb. 22, 2002); www.hhs.gov/infoquality/fda.html. The FDA defines "influential information" as "disseminated information that results from or is used in support of agency actions that are expected to have an annual effect on the economy of \$100 million or more or will adversely affect in a material way, the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, or tribal governments or communities." See FDA guidelines, www.hhs.gov/infoquality/fda.html (last visited December 19, 2003). The definition only "applies to 'information' itself, not to decision that the information may support." Id.

The advisory sets an unsafe standard for women and parents trying to make health-conscious seafood consumption choices for themselves and their young children. The advisory recommends a level of seafood consumption that puts women and children at risk from potentially harmful levels of mercury exposure. According to a study performed by the National Academy of Sciences (NAS) Committee on Toxicological Effects of Methylmercury, "Chronic, low-dose prenatal [methylmercury] exposure from maternal consumption of fish has been associated with ... neurotoxicity in children ... includ[ing] poor performance on neurobehavioral tests, particularly on tests of attention, fine motor function, language, visual-spatial abilities (e.g. drawing) and verbal memory." (NAS 2000). Children exposed to methylmercury in the womb, according to the NAS study, will potentially face serious difficulty learning, and may require special remedial education. Citing major epidemiological studies of populations in the Faroe Islands and New Zealand, where prenatal methylmercury exposures were within the range of some U.S. exposures, NAS found numerous indications of learning deficits in children exposed to methylmercury in the womb:

The [methylmercury]-associated performance decrements on neuropsychological tests administered in the Faroe Islands and New Zealand studies suggest that prenatal [methylmercury] exposure is likely to be associated with poorer school performance. In the Faroe Islands sample, [methylmercury]-related deficits were seen across a broad range of specific domains, including vocabulary, verbal learning, visuospatial attention, and neuromotor function. Deficits of the magnitude reported in these studies are likely to be associated with increases in the number of children who have to struggle to keep up in a normal classroom or who might require remedial classes or special education.

The scientists who conducted the Faroe Islands study predict that the statistically significant developmental delays seen in the study could affect society as a whole, "Such decrements in average cognitive function, especially if permanent, could well be of societal significance in the populations affected." (Grandjean et. al 1997).

At risk is the public health and safety of some four million pregnant women each year, and the developing babies that face prenatal exposure to methylmercury. In order to

effectively address the serious problem posed by methylmercury in seafood, FDA must adequately inform women of childbearing age of the implications of their consumption of seafood, and must provide advice that minimizes mercury exposures. The FDA must issue a correction of the advisory and the underlying analyses and data that form the basis of the currently inadequate seafood consumption advisory.

SPECIFIC REASONS WHY THE INFORMATION DOES NOT MEET THE APPLICABLE OMB, HHS, OR FDA GUIDELINES, IS IN ERROR, AND SUPPORTING DOCUMENTATION

SUMMARY

1. FDA's consumption advice is not "Accurate." FDA's statements that women and young children can safely eat up to 12 ounces of a variety of seafood each week barring four fish on a "do not eat" list, and can safely eat up to one serving of a particular type of seafood each week, are not accurate. Following this advice could put a woman or child at high risk for exceeding a safe dose of mercury. We present below an example in which we show that an average woman following this advice and eating six ounces of canned albacore tuna each week would exceed a safe dose of mercury (the reference dose) by 30 percent, and that 74 percent of all women under this scenario would exceed the reference dose for the duration of pregnancy. It follows that the statement in which the agency asserts that by following the consumption advice a woman could "avoid any developmental problems from mercury in fish" is also inaccurate.
2. FDA's advisory fails to meet the "Transparency" requirements of data quality guidelines. FDA has not provided adequate documentation of analyses and data underlying the advisory needed to achieve transparency.
3. FDA's advisory fails to meet the "Reproducibility" and "High Degree of Transparency" requirements of "Influential" FDA information. By providing inadequate documentation of analyses and data key to the development of FDA's exposure and risk models and the consumer advisory, FDA has failed to meet requirements for transparency and reproducibility that apply to influential information under data quality guidelines.
4. FDA's advisory fails to meet the requirements for "Sound Scientific Practices." FDA has failed to meet the standards for sound scientific practices with respect to the testing, analysis, and documentation that form the basis of the risk and exposure assessments and the advisory.
5. FDA fails guidance for objectivity with respect to "Peer Review." FDA has not met data quality guidelines with respect to peer review by failing to adequately address the concerns of peer reviewers with respect to the agency's exposure assessments, and by failing to obtain peer review of the advisory.
6. FDA information fails to meet guidance on providing "Comprehensive Information on Risk." In its advisory FDA fails to provide the target population with

comprehensive information on risk through its failure to disclose that eating some types of seafood regularly but in accordance with the advisory would cause a woman or child to consume mercury in excess of safe levels, and by providing vague advice with respect to canned tuna consumption and safe consumption levels for children.

7. FDA information fails to meet guidance with respect to "Completeness." FDA has not provided complete information in its "do not eat" list, in its documentation of testing programs and other analyses, and in its information on canned tuna and safe exposures for children.

8. FDA information fails to meet guidance with respect to "Utility." The vague and implicit advice FDA provides in its advisory with respect to canned tuna and safe consumption levels for children fails data quality guidelines on utility.

9. FDA information fails to meet guidance with respect to "Clarity." FDA has failed to provide clear advice in a number of important areas covered by the advisory.

DETAILED OUTLINE OF CRITERIA AND FDA'S FAILURE TO SATISFY THE APPLICABLE INFORMATION QUALITY STANDARDS

1. FDA's consumption advice is not "Accurate." The consumption advice comprised of Statements 1, 2, and 3 above fails the data quality guidelines for accuracy specified in 67 Fed. Reg. 36,8459 (Feb 22, 2002) and HHS (2002). The claim that eating seafood in accordance with the advice is without risk also fails the guidelines for accuracy.

a. Recommended "Safe" consumption patterns. In its consumer advisory FDA informs the target population that a "safe" consumption pattern would consist of the following: i) avoid four specific kinds of fish; ii) eat up to 12 ounces per week of all other species; and iii) do not eat the same type of seafood more than once a week. FDA states that this advice will "protect your baby," and is "safe" (FDA 2003a).

These statements are not accurate. A woman could follow FDA's advice to the letter and still face a substantial risk of chronic mercury exposures in excess of the reference dose, which would not be "safe," "all right," or protective of a baby's health. For example, a 140-pound woman eating a six-ounce can of albacore tuna each week – a behavior entirely consistent with FDA's advisory and equivalent to just half the allowable consumption limit - would consume mercury in excess of the reference dose (0.1 ug/kg body weight/day) by 30 percent, assuming an average mercury level in canned albacore tuna consistent with FDA's testing data (0.358 parts per million, or ppm).¹ According to FDA data, other types of seafood with similar or higher levels of

¹ Assumptions and calculations: Body weight: 140 pounds (64 kilograms); Weekly serving size: 6 ounces (170 grams); Daily serving size: 0.86 ounces (24 grams); Mercury concentration in tuna (average): 0.358 ug/g (ppm); Mercury ingested each day = (Daily serving size) x (Mercury concentration in tuna) = (24 grams tuna) x (0.358 ug Hg/g tuna) = 8.6 ug mercury/day; Dose adjusted by body weight = total mercury dose / body weight = 8.6 ug mercury/day /64 kilograms = 0.13 ug mercury/kg body weight/day; (Reference dose = 0.10 ug mercury/kg body weight/day).

mercury include grouper, orange roughy, tuna steaks, and lobster (FDA 2003b, FDA 2001). If eaten regularly but in accordance with FDA's advice, these species could also expose a woman to mercury at levels that place her fetus at potential risk.

The reference dose for methylmercury, 0.1 micrograms per kilogram of body weight per day, is considered to be daily exposure that is not likely to cause harmful effects. The reference dose is also expressed as 5.8 parts per billion (ppb) of methylmercury in blood, consistent with findings of the National Academy of Sciences (NAS 2000). In its most recent assessment of methylmercury toxicity, the NAS found that the current reference dose for methylmercury is consistent with the most recent science, and that it most closely corresponds to exposures during the last seven weeks of pregnancy (NAS 2000). As shown by the calculations above, by following FDA's consumption advice, a woman of average size would exceed the reference dose not only for the last seven weeks of pregnancy, but throughout the entire 40-week duration of pregnancy, on average.

A more detailed assessment that incorporates "Monte Carlo" style random combinations of measured body weights for women of childbearing age (CDC 2000) coupled with measured concentrations of mercury in canned albacore tuna (FDA 2003c), shows that by eating one six-ounce can of albacore tuna every week, 74 percent of all women would exceed a safe level of mercury exposure (Figure 1)². This is only half of the amount of seafood promoted as safe to eat by the FDA. Assuming consumption at a rate of more than six ounces a week in this model would increase exposures and the fraction of women who exceed the reference dose for the duration of pregnancy.

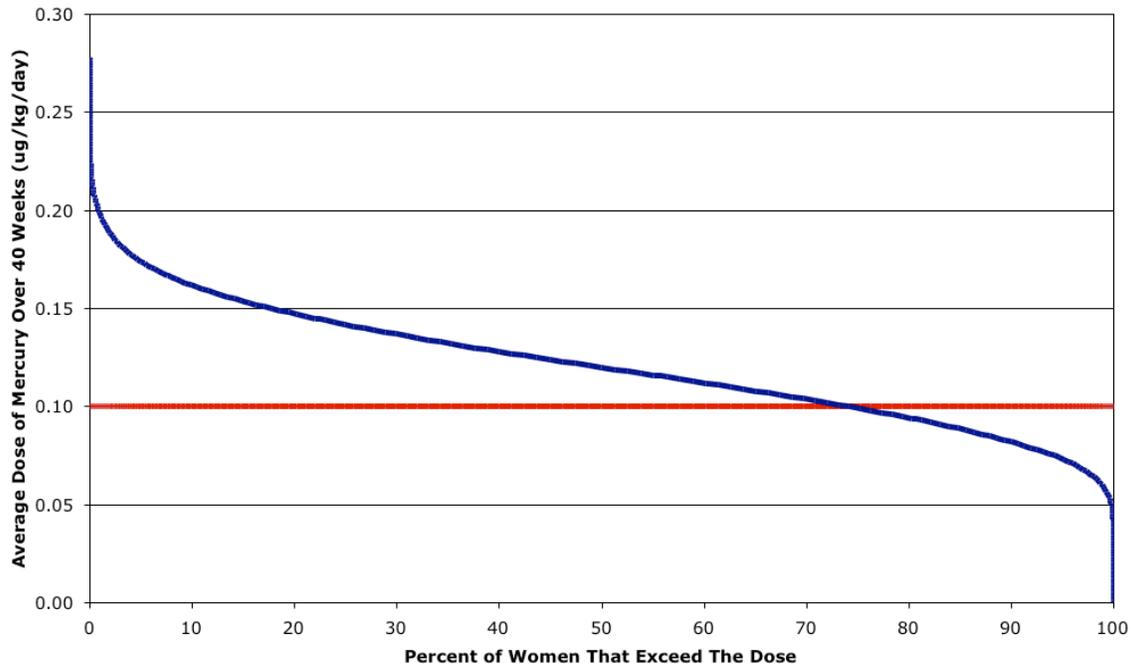
FDA's translation of a reference dose into a "safe" level of mercury in fish can be found in a single sentence in a question posed of three peer reviewers charged with assessing the agency's exposure assessment: "Note and comment on the following: 0.12 ppm is a level of mercury contamination that would permit 12 oz. fish/week without exceeding the RfD" (FDA 2003d). Although the derivation of this number is not presented, FDA's testing data (FDA 2003b, 2001) show that this concentration is exceeded, on average, in 28 types of seafood: grouper, canned albacore tuna, tuna (fresh or frozen), northern lobster (American), halibut, sablefish, Pollock, canned tuna, blue crab, Dungeness crab, tanner crab, red snapper, marlin, moonfish, orange roughy, saltwater bass, freshwater trout, bluefish, croaker, seawater trout, cod (Atlantic), mahi mahi, ocean perch, haddock (Atlantic), whitefish, herring, spiny lobster, black sea bass. Since each of these species exceeds FDA's derived limit, on average, it follows that combinations of these fish could not be safely consumed by the target population of the advisory.

² Monte Carlo analysis methodology: The model generates 10 million hypothetical exposure scenarios, each representing the exposure corresponding to a particular women of childbearing age eating six ounces of canned albacore tuna each week through a 40 week pregnancy. The weight of each woman is randomly assigned from measured body weights of the 1767 women of childbearing age (16-49) examined during CDC's National Health and Nutrition Examination Survey (CDC 2001). The model then randomly selects 40 samples of canned albacore tuna from the 170 samples recently tested by FDA (FDA 2003c), and assumes these samples represent the woman's mercury exposures through pregnancy of a 280 day duration (40 weeks). Exposure is calculated as the average daily mercury dose over the course of the entire 280 day exposure period. Population statistics are generated by compositing all realizations of exposure (hypothetical women) produced during the simulation.

FIGURE 1

**Average Mercury Dose for Women of Childbearing Age Eating
6oz Canned Albacore Tuna Weekly**

74 percent of women exceed the reference dose for the duration of pregnancy, on average.



Source: EWG analysis of data from CDC (2000) and FDA (2003c)

Clearly, the FDA is inaccurate in stating that eating up to 12 ounces a week of a variety of fish besides the four on the “do not eat” list is safe and protective of a baby’s health.

FDA is also inaccurate in implying that eating up to six ounces a week of any particular type of seafood is safe. FDA’s testing data show that eight types of seafood exceed the agency’s derived limit by at least a factor of two, and therefore could not be safely consumed in quantities at or above six ounces per week. These species include grouper, canned albacore tuna, northern lobster (American), bluefish, croaker, orange roughy, freshwater trout, and seawater trout (FDA 2003b, 2001).

b. *FDA’s assurances that women can avoid “any” developmental problems from mercury in fish.* As noted in Statement 6 above, FDA informs the target population of its seafood consumption advisory that by following the advice embedded in the advisory, “you will... avoid any developmental problems from mercury in fish.” This statement is inaccurate. The reference dose upon which FDA’s consumption advice is purportedly based is derived from a benchmark dose limit that is not associated with a zero risk level, as noted by the National Academy of Sciences, and as summarized in

comments provided to FDA's Food Advisory Committee by the Harvard School of Public Health's Dr. Philippe Grandjean, (NAS 2000, Grandjean 2003). Instead, this limit is derived from a level associated with a doubling in risk that children exposed to mercury in the womb will, later in childhood, fall in the bottom fifth percentile of certain intelligence tests. Dr. Grandjean states that "Adverse effects at exposures at or below the large-study [benchmark dose limit] may therefore still be significant" (Grandjean 2003). Given the continuum of risk associated with exposures to methylmercury in seafood, and the fact that the reference dose is not based on a "no effects" level, it is inaccurate for FDA to assert that any level of exposure is without risk.

2. FDA's advisory fails to meet the "Transparency" requirements of data quality guidelines. The consumption advice comprised of Statements 1, 2, and 3 above, and the data underlying these analyses, fail the data quality guidelines for transparency as required under the criteria of Utility and Objectivity specified in 67 Fed. Reg. 36,8459 (Feb 22, 2002).

a. *Key underlying analyses and data.* FDA has not disclosed the analyses and data used to develop Statements 1, 2, and 3 referenced above. Specifically, FDA has not released analyses and data to support statements that it is safe for a person in the Agency's target population to follow the Agency's consumption advice - to eat up to 12 ounces of seafood each week, and to eat up to one serving of a particular type of seafood each week, barring the four fish on the agency's "do not eat" list provided in Statement 1. For example, under FDA's advice a woman could eat six ounces of canned albacore tuna each week. FDA presents no analyses or data to support that it is "safe" for an individual woman to eat canned albacore tuna in that quantity. FDA's Food Advisory Committee was given no documentation in their December 10th and 11th 2003 deliberations of the consumption advisory showing that eating canned albacore tuna in that quantity is safe, even though the advisory implies that it is.

b. *Key underlying mercury testing results.* FDA has not disclosed mercury testing results used as a basis for its exposure and risk models, the basic summary statistical information on these mercury tests (including, at a minimum, mean, standard deviation, range, number of tests, and species tested), or information on the modeled distributions of mercury concentrations in various types of seafood as used in the agency's exposure assessment and risk mitigation scenarios. EWG was forced to request testing data under the provisions of the Freedom of Information Act (EWG 2003), since these data are not publicly available. The lack of transparency in regard to these critical data that underlie the model fails the requirements of the data quality guidelines. A more detailed description of this failure to disclose is provided under the criteria below.

3. FDA's advisory fails to meet the "Reproducibility" and "High Degree of Transparency" requirements of "influential" FDA information. FDA's disclosure of the testing data and assumed distributions of mercury in various types of seafood that underlie the risk mitigation models (Carrington and Bolger, 2003a and 2003b) and consumption advice (FDA 2003a) fails to meet the standard for "high degree of transparency" and "reproducibility" as required of influential information, as specified in 67 Fed. Reg. 36,8459 (Feb 22, 2002).

a. *Consumption advice.* As noted above, FDA has not disclosed the analyses and data used to develop Statements 1, 2, and 3, which together indicate that it is safe for a person in the Agency's target population to eat up to 12 ounces of a variety of seafood each week, and to eat up to one serving of a particular type of seafood each week, barring the four fish on the agency's "do not eat" list provided in Statement 1. This conclusion is not reproducible because the underlying analyses and data have not been provided (and are, therefore, also not transparent).

b. *Mercury testing data.* FDA presents mercury testing data in three partial listings of fish testing results published at various times during the agency's assessment. (FDA 2001, FDA 2003b, Carrington and Bolger 2003a – Table 1). None provide the detailed data. None give a basic statistical description of the data that would include, at a minimum, the mean, standard deviation, range, and number of samples for the various species tested. None allow an independent party to reproduce FDA's analyses.

In a 2001 publication of mercury levels in seafood, FDA presents the mean, range, and number of samples for various types of seafood compiled from "FDA database FY 85-99," from EPA's Mercury Study Report to Congress 1997, and from 1976 and 1978 reports issued by the National Marine Fisheries Service on samples from the Gulf of Mexico (FDA 2001). In a December 2003 publication FDA provides the mean, range, and number of samples from "old data" as well as "new" data that FDA characterizes as derived from "recent further measurements of mercury in different types of fish" (FDA 2003b). In yet another publication, FDA presents a table entitled "Seafood Hg data" that shows the range of mercury detected and number of samples tested for various species, including 13 species designated as "New data obtained since Carrington and Bolger (2000)." (Carrington and Bolger 2003a).

None of these sources lists the standard deviation of mercury levels for the species tested. One source does not even list the mean mercury level. None of these sources represents a complete characterization of the data used to construct the mercury distributions that underlies FDA's risk mitigation scenarios. The presentation of the summary statistics on mercury testing data in a fragmented and incomplete format, and the failure of the agency to disclose the detailed testing data, precludes the public from reproducing the basic analyses that underlie the agency's risk mitigation scenarios (Carrington and Bolger 2003a and 2003b).

c. *Modeled mercury distributions.* FDA has failed to provide information on the modeled distributions of mercury levels in various seafood species used in the agency's exposure assessment and risk mitigation scenarios (Carrington and Bolger 2003a and 2003b). FDA's model documentation notes that "analog" or "modeled" distributions were constructed for 34 of 39 types of seafood included in the agency's analyses, but provides no details on the forms of these distributions. The failure of FDA to provide this information precludes an independent reproduction and assessment of FDA's analyses.

4. FDA's advisory fails to meet the requirements for Sound Scientific Practices. The OMB guidelines state that information "with regard to analysis of risks to human health, safety, and the environment maintained or disseminated by agencies, agencies shall either adopt or adapt the quality principles applied by Congress to risk

information used and disseminated pursuant to the Safe Drinking Water Act Amendments of 1996 (42 U.S.C. § 300g-1(b)(3)(A) and (B)). These principles first require that the agency use the “best available, peer-reviewed science and supporting studies conducted in accordance with sound and objective scientific practices.” (www.hhs.gov/infoquality/fda.html)(42 U.S.C. § 300g-1(b)(3)(A(i)). FDA fails to meet the requirement for the use of sound scientific practices on a number of counts, described below.

a. Risk Mitigation Scenarios. In 2000 the National Academy of Sciences found that the reference dose for methylmercury, 0.1 micrograms per kilogram of body weight per day, is supported by the most recent science, and that this is consistent with a blood mercury level of 5.8 parts per billion (ppb) (NAS 2000). Exposure levels higher than this are of potential risk. In 2002, the Centers for Disease Control and Prevention reported that 7.8 percent of American women of childbearing age had mercury levels in their blood above this 5.8 ug/liter safe level (Schober et. al 2003). In the spring of 2003, FDA's scientists published a peer-reviewed paper showing that the principle cause of elevated mercury levels in the American public is seafood consumption (Schober et. al 2003). Recent studies show that the reference dose may not provide adequate protection from health harm, and that a lower value may be appropriate (Grandjean 2003, Stern 2003).

In the risk mitigation modeling scenarios presented in FDA (Carrington and Bolger 2003a, 2003b), the agency shows that by forcing shifts in consumption patterns among heavy seafood consumers, the Agency can reduce the estimated fraction of women exposed to mercury at levels over the reference dose

The Agency model achieves these risk reductions by first constructing a “baseline” modeled population that consumes seafood consistent with current estimated consumption patterns, and then by constructing “intervention scenarios” that involve forcing 100 percent of heavy seafood consumers in the model to eat no more than 12 ounces of seafood a week, and to avoid fish on the “do not eat” list of Statement 1. By enforcing an artificial 100 percent compliance with the Agency's advice in the population of heavy fish consumers, FDA predicts a significant decline in the number of women who are overexposed to mercury.

The agency's risk mitigation model shows that consuming 12 ounces of seafood a week is an *infrequent* behavior (Carrington and Bolger, 2003a, 2003b). The model has not been used, however, to understand if this is a *safe* behavior. It is not scientifically sound to recommend as “safe” for an individual a behavior that the agency's analyses merely show is infrequent. To the contrary, as shown above, if women of childbearing age eat albacore tuna in levels just half the amount recommended as “safe” by the FDA, three-quarters of these women will be exposed to mercury levels above the reference dose for the entire 40-week duration of pregnancy, on average.

If other data or analyses in the FDA's possession support the agency's statement that it is safe for an individual to eat up to 12 ounces of seafood a week, and up to six ounces of any particular type of seafood, this information has not been provided to the public, as noted in the comments on “Transparency” and “Reproducibility” above.

b. Mercury testing data. FDA's mercury testing data do not adequately characterize the levels of mercury in seafood consumed by the target population. The use of these data in FDA's risk mitigation models and the Agency's development of Statements 1, 2, and 3 is not consistent with the data quality guidelines for sound scientific practices.

Commercial seafood consumed in the US is landed in 29 states, harvested from farms across the world, and imported from more than 100 countries (NMFS 2002a,b). Mercury levels in the environment vary dramatically at regional and local scales (EPA 1997). The capacity of various species of fish and shellfish to accumulate mercury varies widely, even within a particular genus (EPA 1997). We find no documentation from FDA on attempts to discern the influence of geographic variation in mercury pollution on levels of mercury in the US seafood supply. We find no documentation from FDA showing that the data used in its models to develop mercury distributions in the domestic, commercial seafood supply are representative of the specific species and concomitant geographic sources that account for the vast majority of what is consumed in the US. This documentation and accompanying analyses would be required of a scientifically sound, transparent, reproducible, and accurate risk mitigation policy aimed at substantially protecting public health.

According to agency records, FDA has tested more than 100 samples of just three of the top 10 most popular types of seafood in the US - canned tuna, crab, and pollock. FDA documents fewer than 30 mercury analyses for six of the remaining seven most popular types of seafood (FDA 2000a, 2003b, Carrington and Bolger 2003b) - shrimp, catfish, cod, clams, tilapia, and flatfish (flounder and sole). FDA has relied on 52 samples of salmon, the 3rd most popular fish in the US, lumping all data together regardless of the particular species, the source (farmed or wild), or the country of origin. It is not a scientifically sound practice to base major public health policies on sparse sampling data that fail to adequately characterize the distribution of contamination.

By way of contrast, in a recent exposure and risk analysis of similarly high import to public health as FDA's mercury advisory, the Environmental Protection Agency relied on tests of 673 samples of broccoli, 275 samples of cherries; and 1467 samples of cucumbers for the organophosphate pesticide dimethoate (EPA 2002), just one of the approximately 50 pesticides included in the assessment. Notably, dimethoate was detected on between about only one to three percent of the samples. Defining even low rates of detections for contaminants in food is critical for assessments in which aggressive public health protection goals are set.

FDA's testing data show that not only does the Agency fail to test adequate numbers of fish, but also that the Agency focuses the bulk of its testing on species with high mercury levels well established with existing data, particularly some of those that fall on the "do not eat" list. It is not sound scientific practice for FDA to fail in thoroughly characterizing mercury concentrations in all types of seafood, even those with relatively low rates of detection, as these are the very fish that FDA's target population should likely be advised to consume in increased amounts.

Described below are some examples of the inadequacy of FDA's testing data in light of the requirement that FDA's information be based on scientifically sound principles.

- *Shrimp - #1 seafood in the US (NFI 2003)*. Based on a reading of FDA's model documentation, it appears that the agency has incorporated into its assessments 25 tests for mercury in shrimp (FDA 2001, FDA 2003x). Shrimp is the most popular seafood in the United States. According to the National Fisheries Institute, Americans ate a per capita average of 3.7 pounds of shrimp in 2002 (NFI 2003). According to the National Marine Fisheries Service, in 2002 shrimp were landed commercially in 20 states and were imported from 81 countries (NMFS 2003a,b). If FDA has information showing that their 25 shrimp samples provide a scientifically and statistically sound representation of mercury levels in the one billion pounds of shrimp eaten in the US annually, the agency has not disclosed these data. In the absence of this proof, it is clear that the use of these data in an influential public health analysis does not meet basic standards of statistical rigor or scientific quality. It is plainly poor scientific practice to assume that 25 shrimp samples adequately characterize multiple species of shrimp and multiple shrimp-based processed products consumed in the US, from shrimp landed in 20 states, imported from 81 countries, and harvested from shrimp farms around the world.

- *Tilapia – 9th most popular seafood in the US (NFI 2003)*. In a summary published by FDA in 2001, the agency notes that it has tested eight samples of tilapia, the 9th most popular fish in the US (FDA 2001). Subsequent documents on additional mercury testing programs do not indicate that additional tilapia samples were tested. It appears from a reading of these documents that in its exposure and risk analyses FDA used these eight tilapia tests to develop a representation of the potential distribution of mercury in this popular fish. National Marine Fisheries Service data show that in 2002 tilapia was imported from 27 countries (NMFS 2003b), caught commercially in two states, and harvested from farms around the world. In light of these facts, eight samples is not a scientifically sound or defensible sample size.

- *Clams – 6th most popular seafood in the US (NFI 2003)*. According to FDA documents, the agency has tested six clams, the 6th most popular seafood in the US (FDA 2001). Apparently these six samples are used to represent the potential distribution of mercury levels in clams for the entire domestic supply of clams consumed in the US, as no additional clam tests are listed in subsequent documents (FDA 2003b, Carrington and Bolger 2003b). National Marine Fisheries Services lists "clams and bivalves" as being harvested from nine states in 2002 and lists clams as being imported from 30 countries (NMFS 2003a,b). Given the diversity of potential sources and the high consumption rate of clams in the US, developing public health recommendations based on a sample size of six is not scientifically sound or defensible.

- *Tilefish – One of four types of seafood listed on FDA's "do not eat" list (FDA 2003a)*. In newly-available tests of 20 samples of "golden tilefish," FDA records finding an average mercury level of 0.208 ppm (FDA 2003b), a value seven times lower than the levels of mercury in tilefish of unknown variety from an older sampling program that drove FDA to include tilefish on its "do not eat" list in the consumption advisory (FDA 2001). FDA informed its Food Advisory Committee during its December 10th and 11th, 2003 meetings that the differences between the two sampling programs may derive from differences in geographic origin or even species between the two groups of fish tested, information that is not available from the older sampling program. FDA was not able to provide its Food Advisory Committee with information on the types of tilefish generally eaten by the public, and the market names under which it

might appear in the store. We also find no documentation from FDA on the source and dates of sampling associated with the older program.

It is generally not sound scientific practice to base a major public health recommendation on a sampling program for which the geographic origin of the fish and the species of the fish are unknown. It is not scientifically sound practice to fail to reconcile substantial discrepancies between sampling programs before moving forward with a major public health recommendation. The National Marine Fisheries Service tracks the status of stocks of golden tilefish in the Mid Atlantic and South Atlantic; bluefin and sand tilefish in the South Atlantic; goldface, anchor, bluefin, and blackfin tilefish in the Gulf of Mexico; and blackfin and sand tilefish in the Caribbean (NMFS 2003c). Given the potential diversity of geographic origin and species of tilefish, sound scientific practice would involve assessing what of this supply people eat, and then testing a statistically significant number of representative samples from that supply.

The deficiencies in FDA's testing data are manifested in the agency's exposure and risk analyses by the agency's development of modeled distributions to approximate mercury levels in various types of seafood included in the model. Of the 39 types of seafood listed as being included in FDA's assessments, for only five did the agency develop testing data in sufficient quantity that the data were used directly in the model (noted as "empirical" distributions in FDA's documentation (Carrington and Bolger 2003b)). For the remaining 34 types of seafood, FDA either fit a statistical distribution to the data (a "modeled" distribution), or substituted distributions from alternate species to represent mercury concentrations (an "analog" distribution). FDA lacked sufficient data for 9 of the top 10 most popular types of seafood in the US (Carrington and Bolger 2003b, NFI 2003). It is not a scientifically sound practice to approximate, estimate, and even invent much of the basic data underlying an influential public health assessment.

c. Use of analog data. FDA notes in model documentation that "analog" mercury distributions derived from shark, swordfish, and tuna data were used in the model to represent mercury distributions in king mackerel, American lobster, dungeness crabs, blue crabs, snow crabs, king crabs, ocean perch, and oysters (Carrington and Bolger 2003b). We find no documentation supporting the validity of this assumption. Given the known and well-documented differences in the distributions of mercury levels among various types of seafood and in the absence of other documentation to the contrary, it is not scientifically sound to substitute analog distributions for species for which mercury levels are not well characterized. The standard, scientifically sound practice to address such a data deficiency would involve further mercury testing of species for which mercury levels are not well characterized.

d. Assumption of exposure time corresponding to reference dose. As a basis for its new advisory, FDA has calculated steady-state mercury exposures corresponding to long-term mercury ingestion for various model scenarios, and compared these steady-state exposures to the reference dose. This practice is not supported by the science. In its latest assessment of the reference dose that underlies FDA's advisory, the National Academy of Sciences determined that the cord blood measurements that underlie the reference dose are best interpreted as corresponding to fetal exposures

over about three half-lives (150 days) prior to delivery, or the last half of the second trimester and the third trimester. The Committee also determined that the cord blood concentrations would be most heavily influenced by exposures during the most recent half-life, or about the last half of the third trimester (NAS 2000).

It is not a scientifically sound practice to use an inappropriate dose metric for exposure and risk analyses. FDA has compared long-term exposures from a model to shorter-term exposures from epidemiological data, and has used these comparisons to assert safety and set major policy health policies. FDA's calculations implicitly assume that exposures throughout a large part of pregnancy could exceed the reference dose without potential health implications, and that average exposures alone dictate health concerns. In contrast, the National Academy of Science determined that the data supported considering periods as short as the last seven weeks of pregnancy (the last half of the third trimester) as corresponding to the cord blood mercury levels on which the reference dose is grounded.

Notably, one of the three experts who reviewed FDA's model scenarios recommended that FDA calculate transient blood mercury concentrations as opposed to the steady-state exposures selected by FDA (FDA 2003d), and use these levels for comparison against the reference dose. FDA declined, and responded that "most toxicological analyses" for methylmercury make the assumption that "chronic exposure is the relevant dose metric," which is not, in fact, the case (NAS 2000).

e. Documentation of sampling and analysis plans. FDA has failed to adhere to sound scientific practices in documenting the testing programs that underlie the consumer advisories. We find no sampling and analysis plan documenting the testing program rationale, methodology and results. Such a plan is the standard method of scientific documentation for sampling programs such as those that underlie FDA's consumption advisory. Most government agencies that engage in environmental monitoring make such plans available for public review and comment before sampling is initiated. In the case of FDA's most recent testing program (FDA 2003b), the Agency declined to disclose even the basic types of fish being tested when pressed for this detail by stakeholder groups in meetings held in July 2003.

It appears that the results of FDA's 2003 sampling program of more than 200 samples of 14 types of seafood and are documented on a single piece of paper entitled "Mercury Levels in Various Fish" that provides the mean, range, and sample number for various types of seafood, listing both "old data" and "new data" (FDA 2003b). In meetings of December 10th and 11th, 2003, a member of FDA's Food Advisory Committee commented that this level of documentation would be unacceptable had it come from a student at his institution.

5. FDA fails guidance for objectivity with respect to peer review. The OMB guidelines state that information that has been subjected to formal, independent, external peer review is generally regarded as presumptively objective, although this presumption is rebuttable (67 Fed. Reg. 36,8454 (Feb 22, 2002)). FDA fails to meet the requirements for objectivity with respect to peer review by failing to respond to

important comments from its peer reviewers on the exposure assessment and by failing to subject the consumer advisory to peer review by qualified experts.

a. *Exposure assessment.* FDA's exposure assessment has been subjected to a peer review process, according to documentation provided by FDA (FDA 2003d). Our analysis of the FDA summary document, however, shows that the agency rejected or dismissed 16 of the 23 comments listed. For three of the 23 comments FDA indicated it was already integrating new analyses that would partially address the concerns of the reviewer. FDA accepted just four of the 23 comments received, two of which involved suggested edits to the exposure assessment documentation. Notably, one of the three peer reviewers suggested that using a population-based model to set consumption advice for individuals was inappropriate, and requested that FDA instead consider telling the public how much of each species is safe to eat, a suggestion that calls into question the entire mathematical structure on which FDA has based its consumer advisory. This comment was dismissed (FDA 2003d). While the categorizations into which we have placed responses are arguably subjective, it would be difficult under any accounting scheme to find that FDA had done other than reject or dismiss the majority of comments outlined. It is doubtful that such a high rate of dismissal and rejection of review comments constitutes a legitimate peer review.

b. *Consumer advisory.* We find no documentation indicating that the Agency's consumer advisory has undergone peer review. As a plain-language translation of the technical findings of the exposure assessment, intended to influence the behavior of individuals in ways that may significantly impact public health, an external peer review of this influential advisory is warranted.

The potential effectiveness of this advisory in protecting public health has not undergone peer review. The inherent safety of the advice FDA provides in the consumer advisory has not undergone peer review. Although FDA presented the consumer advisory to its Food Advisory Committee, the agency did not request guidance or input on the advisory (FDA 2003e). FDA's document entitled "Questions" for the Food Advisory Committee is devoid of questions, and does not seek a review of the advisory, but instead asks only that the Committee "concur" with the agency: "We believe that [improving the scientific basis of the advisory] is best conducted concurrently with an outreach and educational program that in the interests of public health should commence as soon as possible. We therefore seek the Committee's concurrence" (FDA 2003e).

Statements made by a top FDA official in the press prior to the Agency's presentation of the advisory to the Food Advisory Committee also indicate the agency did not intend to seek a substantive peer review of the advisory from the Committee: "We're going to stand by our advisory... We believe that if people follow what's written in the advisory, there will be a significant level of protection." (Kay 2003). Notably, the Food Advisory Committee is largely not comprised of individuals with expertise in toxicology, exposure and risk assessment, making difficult an informed assessment of the adequacy of the advisory.

6. FDA information fails to meet guidance with respect to providing comprehensive information on risk. Under the data quality guidelines, the agency is required to

“ensure that the presentation of information about risk effects is comprehensive, informative, and understandable.” (www.hhs.gov/infoquality/fda.html) (42 U.S.C. § 300g-1(b)(3)(B)).

a. *FDA's consumption advice.* FDA fails to meet data quality guidelines by failing to disclose that eating some types of seafood regularly but in accordance with the guidance would cause a women or child to consume mercury in quantities in excess of the reference dose, in some cases substantially in excess. FDA's failure to disclose risk associated with frequent consumption endangers public health given that (Kris-Etherton et. al 2002)

Both the American Heart Association and the American Dietetic Association recommend eating seafood twice a week to reduce risk of cardiovascular disease (Kris-Etherton et. al 2002, ADA 2003). By failing to provide women with comprehensive information on risks association with consuming seafood in accordance with the agency's own advisory, as well as the advice of other health experts, FDA fails to meet the data quality guidelines with respect to providing comprehensive information on risk.

b. *Vague advice.* FDA fails to provide comprehensive information on risk through its use of implicit and non-specific advice in Statements 4 and 5 on safe levels of canned tuna consumption, and safe levels of seafood consumption for children. See 8(a) and 8(b) below for further discussion.

7. FDA information fails to meet guidance with respect to completeness.

On a number of counts, FDA's consumer advisory fails to meet the criteria for completeness outlined in data quality guidelines.

a. *The “do not eat” list.* Given the agency's apparent attempt to provide advice that tells consumers how to eat up to 12 ounces of fish per week without appreciable risk, the four fish listed in FDA's consumer advisory do not comprise complete information. As noted previously, an average woman following FDA's advice and eating six ounces of canned albacore tuna each week would exceed a safe dose of mercury (the reference dose) by 30 percent, and that 74 percent of all women under this scenario would exceed the reference dose for the duration of pregnancy. And as noted in Section 1(a) of this document, FDA's safety criteria and testing results show that 28 types of seafood are unsafe to eat in quantities of 12 ounces per week, and the eight types of seafood are unsafe to eat in quantities of 6 ounces per week. The “do not eat” list comprised by Statement 1 is not complete with respect to the types of seafood for which consumption must be restricted to less than 6 or 12 ounces per week if a women or young child is to avoid being overexposed to mercury.

The “do not eat” list is also incomplete with respect to providing advice that would protect women who are following consumption recommendations issued by the American Heart Association and the American Dietetic Association, both of which recommend eating seafood twice a week to reduce risk of cardiovascular disease (Kris-Etherton et. al 2002, ADA 2003). FDA's “do not eat” list fails to include species that, if eaten regularly in accordance with FDA's advisory as well as the advice of other health organizations, would expose women to unsafe levels of mercury.

b. *Documentation of fish testing programs and results.* Information provided by FDA on its fish testing programs, including study design, methods, and results, is incomplete. See Sections 3(b) and 4(e) for details.

c. *Documentation of analyses on safety of advisory.* Information provided by FDA to the public is incomplete with respect to documenting the validity of the agency's claim that eating 12 ounces of seafood per week except for fish on the "do not eat" list, and six ounces of any particular type of seafood per week, is a safe behavior and will not expose a person to levels of mercury above the reference dose. FDA labels this consumption scenario "safe" in the advisory. We find incomplete documentation to support this assertion. In fact, it appears that the documentation needed to support this realization of FDA's advice has not been released in any form to the public.

d. *Information on safe consumption of canned tuna and safe consumption levels for young children.* Information with respect to safe levels of consumption of canned tuna and safe levels of seafood consumption for young children is incomplete. See Sections 8(a) and 8(b) below for further discussion.

8. FDA's Advisory fails the guidelines with regards to Utility. The consumption advice comprised of Statements 4 and 5 above require fail the data quality guidelines for utility specified in [67 Fed. Reg. 36,8459] (Feb 22, 2002).

a. *Canned tuna advice.* In Statement 4, FDA provides the following information about tuna that fails to meet the utility standard: "Tuna is one of the most frequently consumed fish in the United States in the United States. Mercury levels in tuna vary. Tuna steaks and canned albacore tuna generally contain higher levels of mercury than canned light tuna. You can safely include tuna as part of your weekly fish consumption." Reading this advice, a woman cannot be sure if she should eat or avoid types of tuna with higher levels of mercury, or if the types of tuna that have higher levels of mercury are among those "you can safely include...as part of your weekly consumption."

In the media FDA officials have argued against more specificity, asserting that consumers will "self-limit" their consumption (see "FDA says tuna warning needn't be spelled out", Anon 2003), and that specific safe amounts of canned tuna are "implicit" in the advisory as falling between four and six ounces per week (Pianin 2003). To understand that this is meant to be the safe quantity of tuna, a woman must read the 7th and 8th sentences of the advisory, and then divide two numbers into 12 ounces to derive the "safe" range of consumption. Implied advice given in the hope that women will calculate safe quantities and self-limit consumption lacks utility.

b. *Advice for children.* In Statement 4 FDA informs the public to "follow these same rules when feeding fish and shellfish to your young child, but the serving sizes should be smaller" (FDA 2003a). Taken literally, this advice implies that children can safely eat 12 ounces of seafood per week if it is eaten in smaller, more frequent servings than those for adults. Alternatively, if a person interprets the advice as meaning that children should eat less seafood overall than adults, they are provided no information on the specific amounts that might be safe. Again, the Agency's desire for

a simply-worded advisory has left consumers with stripped-down, vague language that lacks utility and that forces consumers to guess what might be a safe amount for a given child.

9. FDA's Advisory fails the guidelines with regards to Clarity. The consumption advice comprised of Statements 4 and 5 above require fail the data quality guidelines for clarity specified in [67 Fed. Reg. 36,8459] (Feb 22, 2002).

a. *Advice on canned tuna consumption and advice for young children.* FDA fails to provide clear information on safe levels of canned tuna consumption, and safe levels of seafood consumption for children in Statements 4 and 5. See 8(a) and 8(b) above for further discussion.

b. *Advisory title.* The title of the advisory is unclear. It reads as though it applies to young children only if their mother is planning a pregnancy, pregnant, or nursing. We assume that all parents or other caregivers of young children are an intended target audience for this advisory.

SPECIFIC EWG RECOMMENDATIONS FOR CORRECTING THE INFORMATION

EWG recommends the following actions to correct the information:

1. Conduct an updated, comprehensive sampling program for seafood, to inform an accurate, scientifically sound advisory. The sampling program should be guided by a detailed assessment of what people eat, parsed by geographic origin of the seafood and individual species of seafood consumed. The sampling program should aim to adequately define the distribution of mercury levels in species that represent the vast majority of the fish people eat.
2. Provide consumption advice that can be followed to the letter without appreciable risk to health. This includes an advisory for which the maximum limit of recommended consumption is safe. This of necessity must include a list of fish known to be very low in mercury that can be consumed with negligible risk of exceeding the reference dose for mercury. The advisory should be designed to ensure that at most, one percent of the population of women who consume 12 ounces of seafood a week would be expected to exceed the reference dose for mercury.
3. Provide specific advice on canned tuna, based on assessments of the amount of various types of canned tuna that can be consumed with negligible risk of exceeding the reference dose for mercury.
4. Provide specific advice for how much seafood can be safely consumed by young children.
5. Base calculations of risk on exceedences of the reference dose for the last half of the third trimester of pregnancy, consistent with interpretations of the National Academy of Sciences (NAS 2001).
6. Develop and make public comprehensive and scientifically defensible documentation of scientific assessments conducted in correcting the advisory.

DESCRIPTION OF HOW EWG IS AFFECTED BY THE INFORMATION ERROR

EWG is affected by the information error because we are a public health watchdog organization. For the past seven years, EWG scientists have researched the public health issue of mercury in seafood. We have issued two reports, Brainfood and Focus Pocus, which detail the FDA's apparent inability to collect appropriate data to monitor mercury levels in fish. EWG is also concerned that women of childbearing age are not adequately informed about the dangers of mercury-contaminated seafood to the developing fetus. EWG is affected by the information error because over four million women may unknowingly expose their fetuses to unsafe levels of mercury by following FDA's advice.

EWG has conducted analyses showing that a women following the advise provided by FDA in all its various versions of consumer advisories could face a high risk of being exposed to excessive amounts of mercury that could place a baby at risk for developmental harm (see, for example, EWG 2001, and analyses presented in this legal challenge).

ENVIRONMENTAL IMPACT

No environmental impact statement is included because it is not applicable to this request.

CERTIFICATION

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

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