

INFORMATION QUALITY APPEAL

DOCKET NUMBER 2004P-0004/CP1

EWG APPEAL REQUESTING CORRECTION OF FDA SEAFOOD ADVISORY ENTITLED "WHAT YOU NEED TO KNOW ABOUT MERCURY IN FISH AND SHELLFISH: 2004 FDA AND EPA ADVICE FOR WOMEN WHO MIGHT BECOME PREGNANT, WOMEN WHO ARE PREGNANT, NURSING MOTHERS, YOUNG CHILDREN"

March 15, 2005

VIA FACSIMILE: (301) 436-2605

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Dear Dr. Acheson,

In the interest of protecting the health of women of childbearing age and children who will face serious risks if they follow the March 2004 Environmental Protection Agency (EPA) and Food and Drug Administration (FDA) Advisory on Mercury in Fish and Shellfish, Environmental Working Group (EWG) seeks reconsideration of your response to our December 22, 2003 Information Quality Act Request for Correction. FDA's response to our request fails to address serious deficiencies in the challenged Advisory, and the Advisory in its current form is in violation of Office of Management and Budget (OMB), Health and Human Services (HHS), and Food and Drug Administration data quality guidelines for objectivity and utility (67 Fed. Reg. 36,8452 (Feb. 22, 2002), HHS 2003a,b).

In spite of minor revisions in the final published version, the FDA's mercury seafood

advisory still does not comply with the Data Quality Act's requirements that influential public statements be scientifically sound, accurate, and based on the latest peer-reviewed science.

We argue herein that it is not sound policy and sound scientific practice to recommend fish consumption habits to the American public that if followed will cause the majority of pregnant women to exceed the Agency's safety standard, or reference dose, for their entire pregnancy. We note further, that the Agency did not use the latest peer-reviewed data in developing this advice. In contrast to the exhaustive peer review that accompanied the adopting of the joint EPA/FDA reference dose (RfD), when developing its mercury seafood advisory, the FDA substituted in place of the RfD a standard for safety that has never been subjected to any level of peer review – the standard of “reducing exposure.” FDA then proceeded to state inaccurately on numerous occasions that following the Agency's advice would reduce exposure to mercury, when for the vast majority of women following the Agency's advice would increase exposure substantially.

We are well aware that the FDA does not see the reference dose as a bright line standard that can never be exceeded without risk of harm, and we agree with this view. However, it is also true, and well established across the federal government, that it is not acceptable for exposures to a toxic chemical in food, air or water to exceed the reference dose every single day during the critical period of vulnerability to that toxic compound, in this case the nine months of pregnancy. If the average pregnant woman in America followed FDA's advice to the letter and ate 6 ounces of albacore tuna, her baby would be exposed to mercury at levels greater than the reference dose, *not* just for a single day, *not* just for several days, but for *every day* of the pregnancy. That is not sound science, as required by the Data Quality Act (DQA). If that same woman ate an additional 6 ounces of other seafood, as the FDA recommends, her exposure would be even higher.

Further, the FDA has a duty under the Food Drug and Cosmetic Act (FDCA) to ensure that the food supply is safe, and that exposure to dangerous substances like mercury are kept at levels that are safe, defined as at or below the reference dose, with allowances for occasional excursions above that level. In response to our petition, the FDA implies that its advisory is not constrained by the requirements of the FDCA, but instead that its advice does not violate the DQA because the goal of the advice is not to produce safe mercury exposures, but to reduce mercury exposures. Not only was this goal not met, but as we will show below, the advice if followed would actually *increase* mercury exposures for the vast majority of women. The goal itself is not in compliance with the Agency's statutory obligation under the FDCA, which clearly requires safe, not just reduced, mercury exposure.

Influential public statements encouraging behaviors that are not safe, as defined under the FDCA, are not sound science. Nothing in the Data Quality Act gives the FDA the authority to replace its core safety standards for food contaminants under the FDCA with a vague, never peer-reviewed standard invented under the Data Quality Act that promises reductions in unsafe exposures, that in the end to not produce safe exposures for individual women following the Agency's consumption advice, when measured by the

Agency's traditional yardstick, the reference dose.

Every day that the FDA fails to correct the Mercury in Seafood Advisory, 800 babies in the United States will be born with elevated mercury exposures that can irreparably impair brain development. EWG's request identifies serious scientific flaws in the Advisory and immediate, irreparable harm that millions of Americans could suffer by following the FDA's erroneous advice. Although the challenged Advisory has been updated since our original request was filed, these errors have not been corrected. Instead of providing guidelines for safe eating choices, FDA's Advisory recommends a level of seafood consumption that could increase pregnant women's and young children's risk of health impacts from exposures to mercury. For an Agency charged with the mission of "protecting the public health by ensuring that foods are safe" and "helping the public get the accurate, science-based information they need to use ... foods to improve their health," correcting this defective Advisory should be an urgent necessity (21 U.S.C.A. § 393(b)(2), FDA 2004).

I. PROCEDURAL HISTORY

On December 22, 2003, EWG submitted a Request for Correction of the December 10, 2003 FDA Mercury in Seafood Advisory. As required by FDA and HHS Data Quality Act Guidelines, EWG's request provided all of the necessary information:

- 1) a detailed description of the specific material to be corrected,
- 1) the specific reasons and supporting documentation for believing that the information does not comply with OMB, HHS and FDA guidelines and is in error,
- 1) the specific recommendations for correcting the information,
- 1) a description of how EWG is affected by the information error, and
- 1) contact information for the individual submitting the request on EWG's behalf (HHS 2003a,b).

The request was sent to the FDA official involved in formulating the challenged Advisory, Dr. David Acheson, as well as the FDA Documents Management Branch, the FDA Office of the Ombudsman, the Director of the office that disseminated the challenged Advisory, the Center for Food Safety and Applied Nutrition, Dr. Robert E. Brackett, and the FDA Commissioner, Dr. Mark B. McClellan. FDA accepted EWG's request, without objection to the format, and without seeking further information from EWG. According to a Certified Mail Domestic Return Receipt, the request was received at the CFSAN on December 23, 2003. FDA subsequently assigned the EWG Request to docket number, 2004P-0004/CP1, on December 31, 2003.

Over the next year, EWG received a series of delay letters, rather than a timely response from the FDA. According to HHS and FDA guidelines, agencies must respond to the merits of Data Quality Act Requests for Correction within 60 calendar days of receipt (HHS 2003a ("The Agency will respond to all requests for correction within 60 calendar days of receipt"), HHS 2003b (FDA "will respond within 60 days, in accordance with the

OMB and HHS Guidelines.”)). The guidelines provide that where an Agency anticipates missing the 60-day deadline, it must notify the requester in a letter stating the reason for the delay and the estimated date for completion (HHS 2003a,b). FDA failed to comply with this requirement, instead issuing six successive delay letters that neither explained the reason for the delay nor provided a reliable estimate of the completion date.

On February 19, 2004, instead of responding to the EWG request, Dr. David Acheson, Chief Medical Officer for FDA's CFSAN, issued a delay letter stating that the request was under review and would be complete by April 20, 2004 (FDA 2004a). This was the first of six delay letters that FDA issued to EWG. After the initial delay letter, on March 19, 2004, FDA released the final version of the challenged draft Advisory, "What You Need to Know About Mercury in Fish and Shellfish, 2004 EPA and FDA Advice for Women Who Might Become Pregnant, Women Who Are Pregnant, Nursing Mothers, Young Children" (HHS & EPA 2004). As discussed below, this version did not cure the fundamental defects identified in the EWG Request for Correction. On April 14, 2004, FDA again failed to respond to the merits of the EWG request and Dr. Acheson issued yet another delay notice, stating that a response would be forthcoming on June 18, 2004 (FDA 2004b). FDA subsequently failed to reply by its own estimated response date, and issued three further delay notices, each setting illusive estimated response dates that FDA consistently failed to honor. The June 16, 2004 delay letter set an estimated response date of August 20, 2004 (FDA 2004c). Two days before this August deadline, FDA issued another delay notice stating that a response would be produced by October 18, 2004 (FDA 2004d). Again on October 15, 2004, FDA issued a fifth delay notice estimating a response date of December 17, 2004 (FDA 2004e). Like clockwork, two days before this illusory response deadline, a sixth delay notice was sent on December 15, 2004 (FDA 2004f).

On February 15, 2005, 421 days after the EWG request was filed, and 360 days after the initial response deadline, FDA replied to the Request for Correction (FDA 2005). FDA did not challenge the categorization of the Advisory as influential scientific information. Stating that it was unnecessary to respond to the specific corrections sought in the EWG request because the Agency considered the request as a comment while it developed the newer advisory, the reply exclusively discussed the recommendations made in the EWG request. The timing of the reply did not comport with this explanation, however, since it came some eleven months after the March 2004 Advisory was published. FDA's response defended the current version of the Advisory without correcting serious errors that the EWG request identified.

II. SPECIFIC REASONS WHY FDA'S RESPONSE IS INADEQUATE

A. Summary of Data Quality Deficiencies

FDA's response is inadequate because the challenged Advisory violates the applicable Information Quality Guidelines:

1. The Advisory's recommendations violate objectivity guidelines. The Advisory's

three recommendations encourage seafood consumption that if followed would cause nearly all women and children to exceed the National Academy of Science's reference dose for a safe level of mercury exposure, in violation of the objectivity guidelines for accuracy and completeness. The extreme and near universal exceedance of the reference dose contradicts longstanding FDA policy that only occasional exposures over the reference dose are deemed safe.

1. The Advisory's statement that following the recommendations will reduce exposures to mercury's effects contradicts existing science, in violation of objectivity guidelines and standards for influential information. The Advisory's claim that following the recommendations will "reduce exposure to the harmful effects of mercury," is confusing and is not supported by latest research on fish consumption trends and mercury contamination, in violation of objectivity guidelines for accuracy and clarity. To the extent that this statement is serving as FDA's safety standard for the purposes of the Advisory, the statement fails to meet guidelines for influential information because it is not based on the best available, peer-reviewed science.
1. The Advisory's guidance regarding children's portions is vague, in violation of utility guidelines. The Advisory's suggestion to feed children "smaller portions," without elaboration, is imprecise and incomplete, in violation of utility guidelines.
1. The Advisory did not undergo a rigorous peer review process, in violation of standards for influential information. FDA did not respond to the majority of the expert panel's comments on the Advisory, and did not ultimately receive approval from the expert panel prior to releasing the Advisory, in violation of transparency standards for influential information.
1. The documentation that FDA has released supporting the Advisory is inadequate and inconsistent with sound scientific practices, in violation of objectivity guidelines, utility guidelines, and requirements for influential information. The documentation that FDA has provided regarding the analyses, testing and data that support the Advisory are grossly insufficient and include unsupportable methods, thus failing to meet the objectivity guidelines for transparency and reproducibility, and sound science standards applicable to influential scientific information.

A. Discussion of Data Quality Deficiencies

1. **The Advisory's recommendations violate objectivity guidelines requiring accuracy and completeness, and comprehensive information on risk.**
 - a. **The Advisory's recommendation to eat up to 12 ounces of a variety of fish and shellfish per week violates standards for**

accuracy, completeness and comprehensiveness because, if followed, it will cause the vast majority of women and children to increase exposure to mercury to the point of exceeding safe levels of mercury exposure.

The statement that eating up to 12 ounces per week of a variety of fish will reduce exposures to mercury is not accurate because the average woman following the advice will actually increase her exposure to mercury to the point where the majority of women exceed the reference dose for the entire length of the pregnancy. This statement fails to meet applicable guidelines for accuracy (67 Fed. Reg. 36,8459 (Feb. 22, 2002), HHS 2003a,b).

As noted in our original petition, 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" or protective of a baby's health. For example, a 140-pound pregnant woman eating a 6-ounce can of albacore tuna every week - a behavior entirely consistent with FDA's Advisory and equivalent to just half the allowable consumption limit - would consume mercury at levels 30 percent in excess of the reference dose (0.1 ug/kg body weight/day) for every week of her pregnancy, assuming an average mercury level in canned albacore tuna consistent with FDA's testing data (0.358 parts per million, or ppm, from FDA (2003b)).

In addition, according to FDA data, the following types of seafood have levels of mercury contamination equal to or higher than albacore tuna; grouper, orange roughy, tuna steaks, freshwater trout, red snapper, and lobster (FDA 2003b, FDA 2001). FDA provides no advice to pregnant women or children on consumption of these species, although to be consistent and objective FDA must at a minimum publish advice for these species similar to that for albacore tuna. As with albacore tuna, if eaten regularly but in accordance with FDA's general advice, these species could also expose a fetus to mercury levels in excess of the reference dose every week of development in the womb.

The reference dose for methylmercury, 0.1 micrograms per kilogram of body weight per day, is considered to be a 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.

The FDA argues in its reply to our petition that the reference dose is not a bright line standard that can never be exceeded, and we agree with this view. However, it is also true, and well established across the federal government, that it is not acceptable for exposures to a toxic chemical in food, air or water to exceed the reference dose every

single day during the critical period of vulnerability to that toxic compound, in this case the nine months of pregnancy. But in fact FDA's advice, if followed, would produce exactly that result. If the average pregnant woman in America followed FDA's advice to the letter and ate 6 ounces of albacore tuna and 6 ounces of any other fish each week, her baby would be exposed to mercury at levels greater than the reference dose, *not* just for a single day, *not* just for several days, but for *every day* of the pregnancy. That is not sound science, as required by the Data Quality Act (DQA).

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 just by eating one 6-ounce can of albacore tuna every week, 74 percent of all women would exceed a safe level of mercury exposure. As noted, this is only half of the amount of seafood promoted as safe to eat by the FDA. Assuming consumption is at a rate of more than 6 ounces a week, this model would increase exposures and increase 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 of a question posed to 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, light 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, and black sea bass.

It is not sound science for the FDA to recommend consumption of fish in amounts that its own data indicate would produce mercury exposure above the levels that the Agency deems safe. In addition, this statement is inaccurate, a clear violation of the Data Quality Act.

FDA is also inaccurate in implying that eating up to 6 ounces a week of any type of seafood is safe. FDA's testing data show that average mercury levels in 13 types of seafood exceed the Agency's derived safe limit for mercury contamination by at least a factor of two, and therefore they could not be safely consumed in quantities at or above 6 ounces per week. These species include grouper, tuna (fresh or frozen), canned albacore tuna, northern lobster (American), red snapper, marlin, moonfish, orange roughy, saltwater bass, freshwater trout, bluefish, croaker, and seawater trout (FDA 2003b, 2001).

1. **The Advisory's claim that following the recommendations will reduce exposures to mercury's effects contradicts existing science, in violation of objectivity guidelines and standards for influential information.**

- a. **The claim regarding reduction of exposures to mercury's effects violates objectivity guidelines for accuracy because it makes an unsupported scientific claim and directly contradicts existing data on fish consumption.**

It is not accurate for the FDA to state that following its seafood consumption advice will reduce mercury exposure for women and young children. The Agency's statements to that effect are erroneous and confusing, and fail to meet applicable guidelines for accuracy (67 Fed. Reg. 36,8459 (Feb. 22, 2002), HHS 2003a,b).

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 peer-reviewed science, and that this exposure level is consistent with a blood mercury level of 5.8 parts per billion (ppb) (NAS 2000). Exposure to levels higher than this for any extended period of time presents potentially significant risks and is considered in excess of the reference dose.

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 study showing that the principal 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,b), the Agency shows that if heavy seafood consumers follow the FDA's advice and eat less of certain contaminated species, the estimated fraction of women exposed to mercury at levels over the reference dose will decline. But nowhere in the modeling exercise, nor in any other publicly available document, does the Agency ever discuss the fact that for women who are not heavy seafood consumers, following FDA's advice would dramatically increase their exposure to mercury. This omission is critical because just nine percent of women of childbearing age eat seafood even once a week, suggesting that large numbers of women are infrequent fish consumers who could increase their mercury exposure significantly by following FDA's advice. Notably, the nine percent figure corresponds roughly with the percentage of women, 7.8 percent, with mercury in their blood at levels above those equivalent to the reference dose (5.9 parts per billion) according to the National Academy of Sciences.

Instead of analyzing the full impact of its public advice to eat up to 12 ounces of a variety of seafood per week, the FDA simply constructed "intervention scenarios" where they assume 100 percent of heavy seafood consumers eat no more than 12 ounces of seafood a week, and that they avoid fish on the "do not eat" list. In this scenario FDA predicts a decline in the number of heavy seafood consumers who exceed the mercury reference dose.

But the Agency never analyzed what would happen to the vast majority of women of childbearing age who are moderate to low seafood consumers if they followed the Agency's advice and ate up to 12 ounces a week of a variety of fish, including 6 ounces of albacore tuna. Indeed, although Agency scientists have produced risk mitigation models showing that consuming 12 ounces of seafood a week is an infrequent behavior (Carrington and Bolger, 2003a,b), the model has never been used to understand whether or not this is a safe behavior. It is not scientifically sound to recommend as "safe" an individual behavior that the Agency's analyses have never been shown to be safe. To the contrary, as shown above, if the average woman of childbearing age ate albacore tuna alone in quantities recommended as "safe" by the FDA, her baby would be exposed to mercury levels above the reference dose for the entire 40-week duration of pregnancy.

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 6 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. **To the extent that this statement is serving as FDA's safety standard for the purposes of the Advisory, the statement fails to meet guidelines for influential information because it is not based on the best available, peer-reviewed science.**

In the FDA reply to EWG's request, the Agency rejects the use of the mercury reference dose as the basis for determining the safety of the Advisory's recommendations, asserting instead that the applicable standard is whether the advice helps consumers reduce exposure to mercury (FDA 2005). FDA, however, fails to identify a scientific basis for relying on this standard as the safety measure for this seafood advisory, while rejecting the best available, peer-reviewed science on safe exposures to mercury, the reference dose. This violates the data quality guidelines for influential information, which, according to OMB standards, must "use ... the best available, peer reviewed science and supporting studies conducted in accordance with sound and objective scientific practices" (67 Fed. Reg. 36,8457). FDA, in its reply, acknowledges that the established reference dose for mercury sets a level of exposure "that a person can experience every day for a lifetime without appreciable risk of harm" (FDA 2005). Nonetheless, FDA rejects the use of this reference dose as the applicable safety measure for the purposes of the seafood advisory in favor of the standard of helping consumers to reduce exposures, a standard with no identifiable safety measure whatsoever. While we agree with FDA's characterization of a reference dose as something that "is not a bright line just above which there is a likelihood, much less certainty of an adverse effect," (FDA 2005), to recommend behavior that will cause pregnant women and young children to exceed the reference dose on a daily basis for what is in essence a "lifetime," – in this case the nine months of gestation – is wholly unsupported by the best available, peer-reviewed science by the Agency's own admission. The standard that FDA has employed, of helping to reduce exposures, has no comparison to scientific measures of safety, is not even

followed in its own recommendations, and is a profoundly irresponsible measure to use when formulating an advisory regarding a dangerous chemical that can cause permanent harm to the most vulnerable of populations, unborn babies and young children.

c. **Recommended correction.**

To address the deficiencies in this statement, FDA should revise the Advisory to provide recommendations that will help women to maintain a level of mercury exposure from fish that is below the established reference dose for mercury. If this is done, then the Advisory can legitimately claim that women and children can safely follow the recommendations without appreciable risk of harm from mercury in seafood.

2. **The Advisory's guidance regarding children's portions is vague, in violation of utility guidelines.**

The Advisory's only recommendation that is specific to young children is to serve children smaller portions. Without further detail on safe consumption amounts for children, this is not useful, and fails to meet information quality standards for utility (HHS 2003a,b, 67 Fed. Reg. 36,8459 (Feb. 22, 2002)). FDA argues that because focus groups following the Advisory fed children less than 12 ounces of seafood, that the advice is useful. FDA does not, however, explain the utility of an Advisory aimed at women and young children that only provides specific consumption amounts for adults. A consumer following the guidance will not have information on how much seafood is safe to feed young children, and how much seafood consumption will pose an appreciable risk of adverse health effects in the child. The vague language that the FDA has chosen leaves consumers to guess what might be a safe amount to feed a child.

In order to correct this deficiency, FDA must issue specific guidance on a safe quantity of seafood that young children could eat regularly without exceeding the reference dose for safe levels of mercury exposure.

3. **The Advisory did not undergo a rigorous peer review process, in violation of standards for influential information.**

FDA's response does not address the matter of its failure to subject the Advisory to a rigorous peer review process. FDA guidelines require peer reviews when appropriate for reviewing influential information (HHS 2003b). FDA's response to the EWG request does not question the appropriateness of a peer review for the Advisory. The Advisory is a plain-language translation of technical findings of the exposure assessment, intended to influence the behavior of individuals in ways that may significantly impact public health, thus warranting an external peer review to ensure the objectivity of the Advisory, and to meet the transparency standards for influential information.

We find no documentation that the FDA Advisory has undergone peer review to consider the potential effectiveness of the document. Although FDA presented the draft advisory to its Food Advisory Committee, the Agency did not request guidance and input from the

Committee (FDA 2003). FDA's response to EWG's request does not attempt to claim that the request for the Committee members to "concur" with the Agency constitutes a call for comments on the draft Advisory (FDA 2003). Nor did the response counter the FDA official's claim, made prior to the December 10-11, 2003 meeting of the Committee, that the Agency intends to "stand by [the] advisory" (Kay 2003). The Agency appears to have carried out this intention, failing to address several key comments made at the December meeting:

- Whether the message, in being made comprehensible, has been simplified beyond meaning and science.
- The possibility of issuing a list of fish believed to be safe based on current data.
- Specifications regarding bodyweight, especially for children.
- The need for better data and continuous testing, particularly more species and more samples of each species.
- The need for objective criteria to define high-, mid-, and low-mercury fish[.]
- The possibility of the FDA hiring communication experts to work on the advisory.

(FDA 2003a).

With respect to the 12 ounce consumption recommendation, one panelist commented that FDA's advice would cause women and children to experience unsafe exposure to mercury, stating, "I think it was quite clear that you actually, for 98 percent of the population, can achieve the desired exposure only if you eat 12 ounces of low mercury fish, and it won't work if you are mixing it up with middle mercury fish" (FDA 2003b). During a discussion of this problem, a panelist suggested a change in the language of the advisory that would make the 12 ounce consumption guidance safe:

Now, I took a look at the low mercury list that he was working with and compared it to the fish that are consumed by the public, and if you take the top 10 fish that are being eaten by the public, they are all on the list of low mercury fish except for albacore tuna. So, you could easily construct an advisory, just change a few words in what has been written here, and significantly change the import of it. Instead of saying you can safely eat 12 ounces, say you can safely eat 12 ounces of low mercury fish, which include--and then list the top 10 or even the top 5 - shrimp, salmon, pollock, catfish, cod, to take the top 5, and add shellfish, and you pretty much have it.

(FDA 2003b).

Panelists also expressed concerns regarding the incomplete "do not eat" list. Specifically, panelists were concerned about the exclusion of albacore tuna from the list, since it has higher levels of mercury than certain species on the list. One panelist explained, "we have pretty much confirmed that albacore tuna is high and grouper and orange roughy aren't looking very good ... [t]hey appear to be higher than the tilefish" (FDA 2003b). Panelists also suggested creating a uniform standard for deciding what should go on the high mercury level or "do not eat" list and on the low mercury level list, stating, in one instance, "there would need to be a reason for selecting the cutoff, and some uniformity about what was on the list" (FDA 2003b). FDA did not incorporate this recommendation into the final Advisory.

The panelists also commented that the advice for children was not clear. One panelist suggested that FDA clarify the advice regarding portion sizes for children:

The issue of the children is given very short shrift in the present advisory. The statement is, 'Follow these same rules when feeding fish and shellfish to your young child, but the serving sizes should be smaller.' The young child can vary from 20 pounds to 80 pounds, and we don't have any clarity in terms of what the serving size is, certainly not what the serving size is for children.'

(FDA 2003b). FDA rejected this comment, and included the very same flawed advice in the final version.

One panelist commented that FDA had failed to "get it right" with respect to the consumption guidelines in the Advisory. The panelist questioned whether albacore should be on the "do not eat" list, noted that FDA's delivery of the information in the Advisory needed improvement, and also stated that FDA's advice on light tuna and portion size was inadequate:

... you made a stab at tuna, but we don't think you quite got that right, so let's put light tuna into that lower [consumption] group... I think the other place that we thought the Agency didn't quite get it right had to do with portion size, not only for the adult, but for children.

(FDA 2003b). FDA rejected these comments as well, and included the very same flawed advice in the final version.

There is no documentation of a subsequent meeting of the Committee, although the final Advisory was released in March 2004. One advisory Committee member, outraged at the content of the Advisory and the failure to distribute the final Advisory to the Committee, resigned in protest (Stauffer 2004).

To correct the deficiency of the failure to subject the Advisory to a rigorous peer review process, FDA must enlist qualified experts from outside the Agency, with expertise in toxicology and risk assessment, and create an Advisory that meets the expert panel's

approval.

4. **The documentation that FDA has released supporting the Advisory is inadequate and inconsistent with sound scientific practices, in violation of objectivity guidelines, utility guidelines, and requirements for influential information.**

a. **The analyses and data supporting the recommendations in the Advisory fail to meet objectivity and utility guidelines for transparency.**

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. Data quality guidelines for utility and objectivity requiring transparency demand the release of this information (67 Fed. Reg. 36,8459 (Feb. 22, 2002), HHS 2003b). FDA's response to the EWG request fails to identify this missing data. FDA presents no analyses or data to support that it is "safe" for an individual woman to eat canned albacore tuna at a rate of 6 ounces per week. 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 final Advisory implies that it is. FDA must provide this supporting documentation in order to comply with the applicable guidelines.

b. **FDA failed to use sound scientific practices required for influential scientific information in its risk mitigation scenarios, use of analog data, assumption of exposure time and documentation of sampling and analysis plans.**

i. **FDA's risk modeling relies on unsound assumptions regarding compliance.**

FDA's risk mitigation modeling scenarios (Carrington and Bolger 2003a,b) suggest that the recommendations will reduce the number of women overexposed to mercury by making the inappropriate assumption of 100 percent compliance. This assumption is scientifically unsound, and therefore violates the information quality guidelines for influential scientific information (HHS 2003b, 67 Fed. Reg. 36,8460 (Feb. 22, 2002), 42 U.S.C. § 300g-1(b)(3)(A) and (B)). FDA's reply to the EWG request does not counter this finding. In the risk mitigation modeling scenarios presented in FDA (Carrington and Bolger 2003a,b), 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. By enforcing an artificial 100 percent compliance with the Agency's advice in the population of heavy fish consumers, FDA predicts a decline in the number of women who are overexposed to mercury. To cure this deficiency, FDA must reanalyze the risk mitigation modeling scenarios use a scientifically sound compliance rate.

ii. **FDA's use of analog mercury distributions in place of further testing is not scientifically sound.**

FDA uses "analog" mercury distributions derived from shark, swordfish, and tuna data in the model documentation 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). This method does not comport with scientifically sound practices, and violates the data quality guidelines for influential scientific information (HHS 2003b, 67 Fed. Reg. 36,8460 (Feb. 22, 2002), 42 U.S.C. § 300g-1(b)(3)(A) and (B)). FDA does not claim, in its response to the EWG request, that this method is sound. 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. In order to cure this data deficiency, FDA must conduct further mercury testing of species for which mercury levels are not well-characterized.

iii. **FDA's assumption of exposure time corresponding to the reference dose does not comport with scientifically sound practices.**

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, and violates data quality guidelines for influential scientific information (HHS 2003b, 67 Fed. Reg. 36,8460 (Feb. 22, 2002), 42 U.S.C. § 300g-1(b)(3)(A) and (B)). FDA did not defend this practice in its reply to EWG's request for corrections.

In its latest assessment of the reference dose that underlies FDA's Advisory, the National Academy of Sciences (NAS) 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 NAS 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 blood mercury concentrations of shorter duration 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).

B. FDA's Legal Duty to Ensure Food Safety

The fundamental problem with the Advisory in its current form is that by recommending that women and children eat up to 12 ounces of fish per week, including one can of albacore tuna, the FDA has issued advice to pregnant women, that if followed, would guarantee unsafe exposures to millions of unborn babies each year. In this respect, the Advisory directly contradicts the Food and Drug Administration's duty to protect Americans from unsafe foods and substances that can render food dangerous to eat. Mercury has been identified by the Agency as a substance that is serious enough to justify the creation of an expert panel and advisory devoted to mercury in seafood. In undertaking this vitally important effort, the FDA must adhere to its clear statutory mandate to protect the public from the unsafe exposures to dangerous substances in food by ensuring that the resulting guidance is safe according to the best available science regarding mercury in seafood.

The standard for safety that FDA is advocating in its reply, "help[ing] [consumers] reduce exposure," is unprecedented and violates FDA's statutory duty. The Agency argues that adherence to the RfD is unnecessary because "most RfDs have a degree of uncertainty (of conservatism) built into them" (FDA 2005). According to the Food Drug and Cosmetic Act, "[t]he Administration shall ... promote the public health by ensuring that [] foods are safe, wholesome, sanitary and properly labeled" (21 U.S.C. § 393(b)(2)). Indeed, the RfD, as FDA indicates, "is an exposure that a person can experience every day for a lifetime without appreciable risk of harm ... not a bright line, just above which there is a likelihood, much less certainty of an adverse effect" (FDA 2005). We agree. However, the level of exposure that FDA recommends in the challenged Advisory would cause the average pregnant woman to exceed the reference dose every day for the duration of her pregnancy, the critical period of exposure for mercury toxicity. This is in clear contradiction to the Agency's description of the meaning of the RfD.

If FDA seeks to deviate from the accepted standard of safety for mercury exposure in this seafood advisory, according to its own practices, the Agency must prove that its chosen alternative is either as reliable as or more reliable than the RfD at ensuring consumer safety. In the context of food additives, FDA requires that regulated entities seeking to deviate from accepted scientific procedures prove that the alternative is as reliable as or more reliable than those used by the National Academy of Sciences (21 CFR 170.20(a)). The only identifiable standard that the Agency has put forth in its reply is that of "help[ing] [consumers] to reduce exposure to methylmercury" (FDA 2005). This provides no reference to safety whatsoever. Reduction of exposure is simply not proof of safety, and is in no way reliable, particularly not in comparison to the scientifically-derived, peer-reviewed reference dose.

This rejection of the use of the reference dose as the controlling safety standard in favor of a standard that involves no safety assessment whatsoever, clearly fails to satisfy the standard set forth in the Food Drug and Cosmetic Act. FDA's role, as defined by this statute, is to ensure that foods are safe, not to help consumers reduce exposures without any reference to safety. Nothing in the Data Quality Act or any other law exempts the Agency from compliance with this statutory mandate. FDA is therefore acting outside of its authority in issuing an advisory that suggests consumption levels that will substantially exceed the reference dose and refusing to use any measure of safety to support the mercury Advisory.

FDA has provided no justification for deviating from this Agency-wide use of scientific assessments of safety in the context of the seafood Advisory. The danger that mercury poses to pregnant women and young children is just as serious as the dangers posed by drug residue or food additives, and requires the same degree of scientific rigor in the development of an advisory on consumption of seafood contaminated with the chemical.

FDA's Advisory and response to EWG's request acknowledges the scientific legitimacy of the reference dose, but departs from longstanding precedent in deciding to reject adherence to the reference dose as the standard for defining safety for the purposes of the challenged seafood Advisory. Instead, FDA argues that essentially no safety standard at all should apply to the Advisory, without reference to any precedent or justification for doing so. This is a clear departure from FDA's history of defining safety in terms of scientific determinations of health risks, legislative determinations of FDA's duty to protect the public health from food safety threats, and exceeds FDA's authority by violating its mission as a federal Agency. The Agency must, according to the legal duties set forth in the Federal Food Drug and Cosmetic Act, correct the Advisory to provide accurate information on safe consumption of seafood that is based on the accepted scientific measure of mercury safety, the mercury reference dose. If the FDA prefers to use an alternative standard, it must provide proof that the alternative is as reliable as or more reliable than the mercury reference dose.

III. CONCLUSION

To address the public health threat posed by the defective Advisory, for the reasons set forth above, EWG now appeals FDA's response to our December 22, 2003 Data Quality Act Request for Corrections, and requests that FDA amend its March 2004 Advisory on Mercury in Fish and Shellfish to ensure that it is safe, and meets the standards for objectivity and utility required by the applicable Information Quality Guidelines (67 Fed. Reg. 36,8452 (Feb. 22, 2002), HHS 2003a,b).

We reserve the right to seek administrative relief if a response is not provided within 60 calendar days of receipt of this appeal, as required by HHS Information Quality Guidelines (HHS 2003a). We further reserve the right to seek administrative relief if a substantive response to this appeal is not provided within 120 calendar days of receipt of this appeal.

Respectfully Submitted,

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December 22, 2003 Environmental Working Group Data Quality Act Challenge
February 15, 2005 Letter from David Acheson to Jane Houlihan

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