Estimated Fish Consumption Rates for the U.S. Population and Selected Subpopulations (NHANES 2003-2010)

Appendix H

EPA Response to External Peer Review of EPA's Draft Document

Fish Consumption Rates

EPA's draft document, *Fish Consumption Rates*, underwent external peer review. The final document, *Estimated Fish Consumption Rates for the U.S. Population and Selected Subpopulations (NHANES 2003-2010)*, incorporates the comments received from the peer review. This appendix provides EPA's response to all peer review comments.

Charge to Reviewers

The following are the questions the reviewers were charged with answering.

1. Is the document logical, clear and concise? Explain. If not, how could the document be improved?

2. Were scientific and statistical assumptions explained and are they appropriate? Explain.

3. Has appropriate literature been cited? Explain. Are there publicly available, peer-reviewed papers that should be included? Explain.

4. Is the methodology as presented and defined in the report scientifically appropriate for meeting the objectives of the project? Additionally and specifically:

    a. Please comment on methods for calculating fish consumption rates.

    b. Please comment on the means for combining fish frequency data.

    c. Please comment on the method used to apportion species.

5. Please comment on appropriateness of the models used for estimating fish consumption rates, focusing on both the "NCI Method" and the "modified EPA Method."

    a. Is the EPA Method clearly described and supported? Explain.

    b. Are uncertainties in the EPA model identified and characterized? Explain.

6. Is the EPA Method adequate for accomplishing the objective? Explain.

7. Specifically in regards to the analysis:

    a. Were sufficient information and explanations given that describes how the data were used and what criteria were used to determine the suitability of the data? Explain.

    b. Were these criteria adequate? Was the methodology appropriate? Explain. If not, how could the methodology could be improved?

8. Are the results presented in the report understandable and appropriate for meeting the objectives of the project? Explain. If not, how could the presentation of the results be improved?

9. Are scientific uncertainties explained and are they appropriate? Explain.

10. The data used in the analysis have been subdivided based on demographic and geographical characteristics of the respondents. Are the subsets of data sufficiently robust to characterize fish consumption within the subgroups for the purposes stated in the report? Please provide your response for each of the major subgroup categories included in the main body of the report.

Summary of Response

Comments

Reviewers reported that overall the report is clear, logical, and concise. They requested more detailed information on the methodology used to process the dietary data and to discuss the limitations of these data (such as the use of standard recipes), and more detailed discussion on the statistical methodologies. One reviewer suggested adding a discussion chapter to discuss the results (such as which subpopulations have higher/lower consumption rates). One reviewer requested repeating the analysis to calculate rates normed to body weight (g fish / kg bodyweight). One reviewer suggested reorganizing Chapter 4 to "improve flow and understanding." One reviewer was not sure that the time savings of the EPA Method outweighed the potential bias of the estimates produced. Some reviewers requested additional references and suggested some. One reviewer noted that the EPA Method is not in the peer-reviewed literature.

EPA Response

In the process of reviewing and responding to the comments and providing additional support for use of the EPA model, we simplified and improved the model while retaining the basic approach and methodology. Thus the model described in the final report is somewhat simpler than the model described in the draft report. The final report has been edited to reflect the final model used and the requests for additional information by reviewers about the EPA Method and the comparison between the NCI and EPA Method have been addressed with respect to the model in the final report. This means that the fish consumption rate estimates in the final report are somewhat different than in the draft report.

We edited the report to expand the discussion of the methodologies, both the processing of the dietary data and the statistical methodologies, to improve clarity and reproducibility. We added a section on the uncertainty associated with use of standard recipes. We added a discussion chapter. We will not repeat the analysis to obtain rates normed to bodyweight at this time. EPA uses the non-normed rates in its water quality standards calculations. Because others may find rates normed to bodyweight useful, this may be an item for future work.

We added references where reviewers thought they were lacking. We reviewed suggested references and included if applicable.

We acknowledge that the EPA Method for estimating fish consumption rates is not in the peer-reviewed literature. Ideally, we would have used the NCI Method as it is validated and peer-reviewed. However, it was not feasible for our needs, as discussed in the following paragraph. We modified it for the purpose of the analyses discussed in the report. We expanded the discussion in the report of why it was necessary to modify the NCI Method.

In the draft report, we did not fully justify the EPA Method by providing specific numbers on the time savings we achieved using it over the NCI Method. While we consider the NCI Method as the preferred method and believe the results to have minimal bias, with large sample sizes and many predictors the computation time required to run the NCI Method and calculate confidence intervals was unacceptable given the schedule and budget for the work. Additionally, our preferred model has more predictors than the NCI Method is set-up to handle. The EPA Method was developed to provide acceptably unbiased estimates within a reasonable computation time. We are using non-publically available data from NHANES that can only be accessed on-site at NCHS. This precludes our use of alternative computing scenarios that might reduce the computation time.

An illustration of the time savings: We ran a simplified model with 4 main effects (age, race/ethnicity, income, and frequency of fish consumption). The NCI Method took 9.5 hours for one run of one fish type. To obtain an estimate of the precision of the estimates we need to run the model 65 times, one for each replicate weight. This gives us an estimated time of over 25 days of continuous computer time for each fish type. There are 18 fish types. Thus, to obtain estimates for all fish types would take 450 days. The EPA Method took 1.5 minutes to run the same model, thus approximately 1.5 hours for each fish type.

We added detailed information to the report about the trade-offs that were made and why the EPA Method is best for this purpose. We also added more comparisons of results obtained using the two methods.

Response to General Impressions

Reviewer 1

Overall, I find the report readable, stays on topic and comprehensive. There are very few areas needing major revision and the writing is clear and concise with very, very few spelling errors.

EPA Response: No response needed.

This said, I do see an alternate way of reorganizing the information in Chapter 4 to improve flow and understanding (see responses to charge questions 1 and 3 specifically).

EPA Response: No response needed – organization comments are addressed below.

Reviewer 2

In general, the methods and procedures should be clear enough so that they could be independently produced; this is not the case for how the dietary data were handled.

EPA Response: In the report text we added more detailed descriptions of the procedures and methods for handling the dietary data and included an example working through the steps. We also added additional details to Appendix B.

It is not possible to judge the accuracy of the information presented because it is impossible to know exactly what types of fish and the exact amounts of fish that were consumed by the survey participants. One must assume that the reports of 24-hour dietary intake were accurate, precise, and unbiased; and this should be stated in the report.

EPA Response: We added a discussion about the assumption that the 24-hour data are unbiased reports of respondents' consumption.

The limitations of the standardized recipes used for mixed dishes were not mentioned. This probably is not an important factor because most fish are probably not consumed as part of a mixed dish; however, it should be mentioned.

EPA Response: We added a discussion about the standardized recipes for mixed dishes and the limitations associated with this.

It is not stated anywhere that the amounts presented in the tables are uncooked amounts of fish. How the cooked amounts reported by survey participants were converted to uncooked amounts is unclear. It is also unclear if the uncooked amounts are for the edible portion of fish or for the entire fish.

EPA Response: We clarified this issue by adding "raw weight, edible portion" to the tables and added details concerning the methodology for conversion to uncooked weight.

I leave it to the statisticians to decide if the statistical methods used are clear and sound; however, it does seem that the modified NCI Method yielded results that are fit for use in terms of how close they are to estimates from the original NCI Method.

EPA Response: No response needed.

Reviewer 3

This is a very good piece of work, applying very sophisticated statistical methods to the available data. However, it could be improved by adding a discussion chapter that analyzes and summarizes the findings relevant to risk assessment. I have done some preliminary analysis of geometric means and geometric standard deviations for total fish consumption from probability plots of the percentile information (see table on the next page.) Using this kind of analysis, the reader could be informed, for example that among racial groups, the "other race" category stands out as having higher overall fish consumption than other races. I assume this is due to the inclusion of Native Americans in that group, some of whom are subsistence fishers and are particularly at risk for high consumption of locally-caught fish and shellfish. It is also of interest that women of child-bearing age have slightly smaller geometric mean consumption but a greater apparent inter-individual variability in consumption than other age/sex groups.

EPA Response: We have added a discussion chapter to discuss and summarize the results.

Another aspect that could be improved would be to provide an additional set of data tables in which the dependent variable was not raw grams consumed per day per person, but grams consumed per kilogram of body weight. This could be readily done using the same methodology because the NHANES data include individual body weights.

EPA Response: This is an item for future work.

Finally, I think it would be helpful to show calculations of geometric standard deviations by the various breakdowns in the detailed tables so that the reader could appreciate (1) which groups have more or less variability in fish consumption and (2) so that comparisons could be made to long-term biomarkers of fish consumption, such as methylmercury and PCB blood concentration distributions. These latter statistics may be in part available from other measurements in the NHANES data. In addition, I published some older data on these variables:

Hattis, D. and Burmaster, D. E. "Assessment of Variability and Uncertainty Distributions for Practical Risk Analyses" Risk Analysis, Vol. 14, pp. 713-730, 1994.

EPA Response: The discussion has been modified to note that the geometric standard deviations are around 2. However, as implemented, the NCI and EPA models assume the same variance components (in the transformed units) for all subpopulations. Thus, the differences in geometric mean and standard deviations shown in the table below are not particularly informative and reflect, in part, differences in the geometric mean and small differences between the lognormal and Box-Cox transformation.

Table of results of lognormal fitting to the consumption percentiles for all fish (Based on Data from Table 6a)

Group	Geom Mean (g/day)	Geom. Std Dev.
All adults	14.61	2.247
Males	17.02	2.216
Females	13.03	2.216
Women 13-49	9.66	2.512
21-35	11.56	2.498
35 - < 50	14.62	2.172
50-<65	20.33	2.025
65+ yrs	13.21	2.218
Non-Hisp White	13.67	2.231
Non-His Black	16.78	2.090
Other Race	27.39	2.044

Reviewer 4

I found the layout of this report to be presented in a logical, clear, and concise manner. The classification of the fish groupings from the 24-hour recall data appeared to be done appropriately using the NHANES data as well as other sources. Being able to obtain the information from NHANES on geographical region is a strength. The tables are clearly presented and are provided for a broad range of fish type and subgroup. The document demonstrated a sound understanding of the NCI Method.

EPA Response: No Response needed.

However, there are serious concerns about the validity of the estimates produced by the modified EPA Method. In particular, this method makes a number of approximations to the NCI Method, but it does not fully explore the implications of each of these approximations, nor does it fully justify the approximations that are made. Furthermore, details were lacking regarding some of the statistical methods including: validation of the modified EPA Method, construction of BRR weights, inclusion of covariates in models, and construction of subgroup estimates. From the report, it is not apparent that the time savings from making a number of approximations in the modified EPA Method is worth the potential loss in bias and efficiency of the estimates produced. The dataset that was constructed of fish consumption for NHANES participants appeared to be developed making reasonable assumptions and I have no concerns about the dataset used. I am concerned that the statistical methods utilized to estimate the distribution of usual fish intake is not well justified, and could lead to biased estimates.

EPA Response: In the process of reviewing and responding to the comments, we simplified and improved the model while retaining the basic approach and methodology. Thus the model described in the final report is somewhat simpler than the model described in the draft report. Additional revisions to the text provide additional details requested above on the methods and additional comparisons between the NCI and EPA Method.

In the report, we did not fully justify the EPA Method by providing specific numbers on the time savings we achieved using it over the NCI Method. While we consider the NCI Method as the preferred method and believe the results to have minimal bias, with large sample sizes and many predictors the computation time required to run the NCI Method and calculate confidence intervals was unacceptable given the schedule and budget for the work. Additionally, our preferred model has

more predictors than the NCI Method is set-up to handle. The EPA Method was developed to provide acceptably unbiased estimates with a reasonable computation time. We are using non-publically available data from NHANES that can only be accessed on-site at NCHS. This precludes our use of alternative computing scenarios that might reduce the computation time.

An illustration of the time savings: we ran a simplified model with 4 main effects (age, race/ethnicity, income, and frequency of fish consumption). The NCI Method took 9.5 hours for one run of one fish type. To obtain an estimate of the precision of the estimates we need to run the model 65 times, one for each replicate weight. This gives us an estimated time of over 25 days of continuous computer time for each fish type. There are 18 fish types. Thus, to obtain estimates for all fish types would take 450 days. The EPA Method took 1.5 minutes to run the same model, thus approximately 1.5 hours for each fish type.

We added detailed information to the report about the trade-offs that were made and why the EPA Method is best for this purpose. We also added more comparisons of results obtained using the two methods.

Response to Charge Questions

Charge Question 1
Is the document logical, clear and concise? Explain. If not, how could the document be improved?

Reviewer 1

I found the document logically ordered and the writing clear and concise but confusing in a couple of places. The document defines its objective in the Background section and identifies the major data source in Chapter 2. Chapter 3 introduces the NCI Method, which is again described in Sections 4.4.1 and 4.4.2. Not certain why one even needs Chapter 3 since the material in Chapter 3 might be better as a background section in Chapter 4 (or a new Statistical Methods Chapter).

Chapter 4 combines a number of "methods" that could very easily comprise their own chapters. The methods discussion around habitat apportionment (Section 4.1) and trophic level assignment (section 4.2) could be combined in one chapter describing how fish-related characteristics are used in estimating (stratified) consumption rates. The specific comments to Question 2 suggest some ways that these Sections (or new Chapter) might be better organized. In particular, organizing the apportionment discussion around the "rules" and data sources used in apportionment would improve understanding. Section 4.3 on "Extracting reported amounts of fish consumed" could be a part of Chapter 2 since it really describes how the FNDDS files were processed to find food codes containing finfish and shellfish, hence it tells us in more detail what NHANES data were actually used. Section 4.4 (Statistical Methods) deserves its own chapter (called Statistical Methods) since it contains the key discussions of the NCI Method for estimation of fish consumption and described the modifications of this approach that constitutes the "EPA Method." This discussion could benefit from a short discussion relating sample size to estimate uncertainty to help answer the question of "How many observations are needed to estimate consumption to a specified level of precision?" Chapter 5 (Results) can benefit from more discussion of model goodness of fit.

EPA Response: All of the above comments were taken into consideration during revision of the document. We moved the data processing methodologies to Chapter 3 and made Chapter 4 the statistical methods. We also reorganized Chapter 4 to include the brief introduction to the NCI Method that was previously Chapter 3 and the comparisons between the NCI and EPA Methods, moving Section 5.3 into Chapter 4. Section 5.3.6 includes a discussion of precision. Thus, in the final

report, Chapter 3 discusses the data processing methods, Chapter 4 discusses the statistical methods, and Chapter 5 discusses the results and uncertainty.

Overall, there is a need to standardize labels. In the report I find references to the "NCI Method," the "NCI model," the "EPA model," the "EPA approach," the "EPA Method," the "Modified NCI Method" (page 22) and in the Figures, the "Westat Modified NCI Method." It initially was difficult to know how many "methods" were really under consideration. Was it two or three? Only after one reads Chapter 4 do you realize there are only two "methods," with two "models" for each method, one for probability of fish consumption and one for amount of fish consumed. I will refer to the NCI and the EPA "methods" in my remarks. Occasionally, I will refer to the model for estimating the probability of fish consumption and the model for amount of fish consumed for specific methods. There are also two "methods" for simulating UFC based on the fitted NCI or EPA Method estimated parameters and associated models.

EPA Response: The NCI Method and the EPA Method are composed of two main steps – 1) Fit the NCI/EPA probability and amount models to the reported consumption data; and 2) Calculate the usual intake from the model parameters. Thus there are places where it is important to make the distinction between the method and models. We agree that the EPA Method needed to be consistently labeled as such (remove referrals to "modified method" and "EPA approach," etc.). We edited the document to consistently label the EPA Method.

Additional suggestions for report improvement can be found in my replies to the remaining questions.

EPA Response: No response needed.

Reviewer 2

In general, yes; however, the dietary data processing needs to be described more clearly.

EPA Response: As noted above, we clarified the details of the dietary data processing.

Reviewer 3

Yes. However, it could go into more detail for the non-statistician on the choices of distributional methods. Overall these seem reasonable, and the comment that there is very little difference between log-logistic and lognormal distributions is helpful. It might also be helpful to explain, if it is true, that the logistic distributions were selected for modeling because of greater mathematical tractability than lognormals.

EPA Response: We added a discussion of the choice of distributional assumptions and additional descriptions for the non-statistician. However, the report does not mention the log-logistic distribution. The logistic distribution is commonly used to model the relationship between a continuous predictor and a categorical outcome. The amount of fish in a meal with fish is modeled using a power transformation, assuming the transformed amounts have a normal distribution. This is a relatively general assumption. Although a lognormal distribution is consistent with a Box Cox transformation, the transformations used when modeling the consumption amount were somewhat different from a lognormal distribution. The lognormal assumption was only used for calculating confidence intervals.

Reviewer 4

In general, the document is clear, logical, and concise. The document is logically organized in the order of presentation, and outlines all necessary sections of the study population, methods, and results. The results are clearly presented. There are some details lacking in the statistical analysis section (see questions 4 and 5).

EPA Response: Additional details have been added to the statistical analysis section.

Charge Question 2
Were scientific and statistical assumptions explained and are they appropriate? Explain.

Reviewer 1

I did not find any specific sections discussing scientific or statistical assumptions in the report. Scientific and statistical assumptions seem to be discussed as needed throughout the document. I think it is appropriate that it be done this way.

EPA Response: No response needed.

Further, discussion of assumptions is needed in a number of places as outlined below.

Page 1: We are told that the current default fish consumption rate (FCR) used by OW are the 90th and 99th percentile estimates from the freshwater and estuarine fish consumption distributions computed from the CSFII. When you get to the bottom of Page 2 you find that we will actually be provided with "the UFCR estimates and 95 % CI of the mean and the 25th, 50th, 75th, 90th, 95th, 97th, and 99th percentiles." There is no discussion (or justification) for why these particular percentiles (probably to illustrate the right tail of the consumption distribution which is where risk assessment interest is greatest). Why not also provide 5%-tiles up to 95% and illustrate the whole distribution?

EPA Response: The reviewer is correct – we focused the percentiles on the upper end of the distribution as that is where risk is greatest.

Page 1: It is stated that "As fish consumption may have changed over the past decade…" What is the evidence for this as a reasonable assumption on which to justify the effort of creating new estimates? [One or a couple of references to current studies, popular reports, NOAA landings values, etc. would satisfy this need.]

EPA Response: The important factors that led to updating are that the data on which the current rates are based in from 1994-1996 and 1998. As there are more recent data available, EPA wanted to update the rates in order to keep them current. There are also improved algorithms, represented by the NCI Method. The report was revised to remove the apparent emphasis on the possibly changing fish consumption in the US.

Page 1: Reference is made to the NCI Method. Have other methods been proposed but rejected?

EPA Response: The NCI Method is a validated, well respected method and thought to be the most appropriate method to estimate rates of episodically consumed foods. The Iowa State method does not allow for the use of covariates in the estimation which would leave out important predictors of fish consumption in the US.

Page 1: It is stated that "The calculation using the NCI Method are very time consuming." It is assumed that either: 1) EPA does not have the time to make these calculations or 2) EPA cannot find the computational power to makes these calculations in a reasonable amount of time. I don't find this discussed anywhere. Acceptance of this assumption is key to justifying the development and use of the EPA Method.

EPA Response: We added detailed information to the report about the trade-offs that were made and why the EPA Method is best for this purpose. Briefly, the NCI Method macros would not run with all of the desired covariates (including interaction terms), and, when running a simplified model with 4 main effects, the NCI Method took 9.5 hours and the EPA Method took 1 minute. One issue with using alternative computing scenarios that may decrease the computational time is that the geographical data which are important predictors for fish consumption are not publically available and thus have to be used only at NCHS Research Data Center with permission.

Page 2: Estimates are desired for 18 different categories of fish. It is assumed that each category is important to some entity. Nowhere is there discussion as to why these categories specifically are chosen.

EPA Response: These fish types were chosen as they represent various categories of interest to states and tribes. For example, a coastal state may be interested in knowing the UFCR of total fish and of marine and freshwater + estuarine, separately. An inland state may only be interested in freshwater fish UFCR. Additionally, as fish bioaccumulate toxins at different rates depending on their trophic level, UFCR were also calculated for fish by trophic level. We added a discussion of why the fish types were chosen.

Page 3: Chapter 2 discusses the NHANES as a quality source of finfish and shellfish consumption for the general US population. Are we to assume that this is the only source of such data? A

discussion of other potential sources for fish consumption data and why the NHANES was used is needed.

EPA Response: NHANES is the only source of nationally representative data on fish consumption in the United States.

Page 5: The FNDDS is discussed in general (here, but in more detail in Section 4.3), but the "science" behind this database merits at least a paragraph. This database is used in the critical step of translating what is eaten (a menu item) to how much fish is consumed.

EPA Response: We expanded the discussion of FNDDS in Section 3.3.

Page 7: The scientific and statistical assumptions of the NCI Method are covered in Question 4.

EPA Response: No response needed.

Page 8: While "The assignments of species were completed by a fisheries biologist" it is not clear what assumptions and/or rules were employed in this assignment. If I were to employ a different fisheries biologist, would that individual come up with the same habitat apportionment? By providing insight into the assumptions and rules used by the fisheries biologist, we are better able to ensure repeatability (a scientific method characteristic) to this process. The "decisions" listed in the four bullets are actually some of the "rules" used by the fisheries biologist in the assignment. Are these all of the rules? It is clear that NOAA landings data factor into these "rules" (Section 4.1.2). In addition, the final rule is "that unspecified fish consumed was assigned the overall average habitat apportionment of all species reported consumed." Is this reasonable?

EPA Response: We expanded the discussion of the habitat apportionment to clarify these questions. Appendix A provides the percentage we used for each species that comprises a group/food code and the apportionment for each species, so users of the document can clearly see exactly how fish were apportioned. NOAA landings data were used to determine the proportion of species landed for "groups" (such as clams) that have species that live in different habitats. We made the assumption that unspecified fish have the same distribution as those that were specified as we do not know why these species were unspecified – it could be because the participant did not know what they ate because they didn't buy it or cook it or just did not remember. We don't have a reason to believe that the distribution of species among the unspecified is different than among the specified.

Page 11: The statement, "No species in a group was assigned 0 percent based on a 0 count in the files, because it may be reported in another NHANES cycle," requires additional clarification. What was the rule used to assign the value greater than zero?

EPA Response: As stated in the report, we used un-coded 24-hour recall files from NHANES from 2007-08 (which are not publically available, and the only cycle made available to us) and counted the number of times a species was reported. Some species did not appear in these un-coded data; however, since these un-coded data are only one set of 4, we cannot assume that they do not appear in other NHANES years. We can assume they are less common than those that were reported in the 2007-2008 data. Thus, these species were assigned between one and five percent of their group, depending on how many species are included in the group and how many times other species in their group were reported consumed. Where possible, we also used NOAA landings data to determine a logical percent. Again, Appendix A provides the percentage we used for each species that comprises a group/food code and the apportionment for each species, so users of the document can clearly see exactly how fish were apportioned

Page 14: The fourth bullet on this page refers to "best professional judgment" and an example in catfish is described. Is catfish the only NHANES grouping that is impacted by this "rule"? Table 3 might be modified to indicate which fish allocation is impacted by "best professional judgment." The scientific issue here is repeatability.

EPA Response: If the vast majority of the species in a group are within one trophic level, then that trophic level is assigned. If species span two levels it is split 50-50. For example, the NHANES grouping for catfish includes four species that are assigned to trophic level 3 and three species assigned to trophic level 4. Thus, it is assumed that half (50 percent) of consumption in the catfish NHANES grouping is from TL3 and half from TL4. Other fish this rule of "best professional judgment" applies to are croaker, flatfish, and shrimp. We expanded the discussion of the trophic level apportionment to clarify these questions. Note that all of the bulleted rules (including the one discussed here) are the same as those used in "Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (2000) Technical Support Document Volume 2: Development of National Bioaccumulation Factors," December 2003, EPA-822-R-03-030.

Pages 17-20: Assumptions for statistical methods presented in Question 5.

Page 20: (Section 4.4.3) It is not clear from the first sentence in this section whether the bulleted statements represent constraints on the NCI Method estimates when used for simulating fish consumption or whether these statements are constraints under which the NCI Method estimates are derived. I think these bullets are actually establishing the specific "reality" we are attempting to simulate using the information from the fitted NCI model.

EPA Response: The bullets are explaining the differences in the equations used to fit the 24-hr fish consumption data and the equation used to fit the simulated data. Because usual fish consumption is different from reported fish consumption these equations differ. We revised the discussion of the simulation of usual fish consumption to clarify these questions.

Paragraphs 4 and 5 on page 54 (Section 5.4.2) initiate a discussion on model assumptions but doesn't really take it very far. In paragraph 4, you say "The validity of these assumptions can be discussed and, to some extent evaluated using data." but don't elaborate. Maybe a little elaboration is justified. At the bottom of page 54, you write "In our opinion, the NCI Method makes reasonable assumptions and, given the assumptions, has adequate sample size to provide estimates with little bias relative to the confidence interval width." I personally tend to agree with the report on this, but I suggest giving the reader a little more, especially about the reasonableness of the method assumptions.

EPA Response: We revised and expanded the uncertainty section and provided more detailed discussion to clarify these questions.

The issue of how fish never-consumers are handled is never addressed:

> One issue that is not addressed in the report impacts how the results of this study are used in a population risk assessments when the population consists of a fraction of individuals who, for personal reasons, never eat fish. Estimates of US residents who self-report as vegetarian or vegan range (not fish consumers) from a low of about 2.5% to a high of about 13.7% of the population (see *http://en.wikipedia.org/wiki/Vegetarianism_in_the_United_States#USA* for details).
>
> The NCI and EPA Methods seem to assume that every individual who provides data via the NHANES 24-hour or 30-day surveys has a positive probability of consuming fish over the covered time period. In statistical jargon, they assume an underlying continuous distribution of consumption. With this assumption, for any individual if we were able to effectively

record consumption for a long enough period of time, every individual would be observed eating fish at least once in that time period. The reality is that the underlying fish consumption distribution is a mixture distribution with a positive probability of fish non-consumption (of say p=.025 to .137) and one minus this probability of consumption.

The problem lies in that the NHANES survey does not have a question that identifies individuals who would "never eat fish," hence it does not allow us to easily split out "fish consumers" from "fish non-consumers". The individuals who report no fish consumption are a mixture of "never consumers" and "low likelihood consumers." The NCI Method estimate of the probability of fish consumption in a 24-hour period essentially uses one probability for the mixture. This issue is not a problem at the estimation phase but does come up when the estimated model is used to simulate an individual's long-term probability of fish consumption. The equations on page 21 suggest that the long-term probability of fish consumption (Q_{Uj}) will always be greater than zero (distribution is assumed Logistic, a continuous distribution, and hence the probability of a single value (0) is zero.) But this model uses the estimated 24-hour consumption probability (P, page 19) that includes the mixture. So, the problem is that the simulation is really about fish consumers, but one of the parameters used in the simulation (P, which affects the estimate of the other "pi_s") represents both consumers and non-consumers. The ultimate result is that the percentiles for the fish consumption distribution are all likely to be over estimates which conveniently adds a conservative lean to population risk assessments.

EPA Response: The comment is correct that the model does not include an adjustment for never consumers and the predicted long-term probability of fish consumption will be greater than zero for all individuals, although perhaps very small. Unfortunately we do not have the data needed to identify non-consumers. Having non-consumers in the data will lower the overall probability of fish consumption (P) but increase the variance of the probability of fish consumption among individuals. The resulting effect on the upper percentiles of the distribution is not clear. The text was modified to discuss the effect of non-consumers on the estimates.

Reviewer 2

Yes, the assumptions underlying the NCI Method were well explained. However, the assumptions made about the standardized recipes in the FNDDS were not mentioned. A statement of the assumption that the reports of 24-hour dietary intake were accurate, precise, and unbiased is also missing.

EPA Response: We added a discussion of the assumptions associated with the standardized recipes and stated that the methodology to estimate the rates assumes that the 24-hour dietary intakes are unbiased reports.

Reviewer 3

The statistical assumptions were described but the reasoning underlying them could have been more fully explained (see previous comment).

EPA Response: We expanded the discussion of the statistical assumptions.

Reviewer 4

The document demonstrates a thorough understanding of the NCI Method and the assumptions that it makes. There are no concerns about the implementation of this method; however, it was only used to compare to the EPA Method, not to make the estimates in the report. The authors used what they are calling the modified EPA Method to produce the tables in this report, and the implications of the assumptions of this method are not as clearly described as the assumptions of the NCI Method. In Section 5.4.2, the assumptions made and discussed are that of the NCI Method; however, the modified NCI Method is what is used in this report, and the assumptions that it makes should be addressed in this section, rather than that of the NCI Method. It is not clear from this report that the authors understand what the implications of the assumptions of this modified EPA Method are. For example, the authors compare their method to the NCI Method, and show that in some cases it provides higher estimates than the NCI Method. However, it is not clear from the report why this is so, and what assumptions of their method lead to this potential bias.

EPA Response: The assumptions behind the NCI and the EPA Method are very similar. However, we agree that the differences are not clearly presented in this section. The uncertainty section was revised to make a distinction between the NCI Method and the EPA Method, when applicable.

Charge Question 3
Has appropriate literature been cited? Explain. Are there publicly available, peer-reviewed papers that should be included? Explain.

Reviewer 1

A number of places need citations.

Page 1: References to justify the statement that fish consumption rates have been changing. Reference to increasing NOAA landings values might suffice here, although looking at NMFS total landings data suggests decreased tonnage from 1993 to 2012 (4.6 MT in 1993 to 4.2MT in 2012).

EPA Response: The report states that fish consumption may be changing and thus the rates should be updated to represent current consumption. It does not state that fish consumption is changing. The main reasons for updating the report are more recent data and new analytical methodologies. The text was modified to remove the focus away from possible changing fish consumption.

Page 8: The second bullet incorporates a quote but there is no indication where this quote comes from. (I assume this is part of the Clean Water Act, but not certain.) This statement also requires further clarification since the current sentence structure is complex making it difficult to understand.

EPA Response: This section was edited for clarification. It is EPA's long-standing interpretation of section 303(c) (2) (A) of the Clean Water Act.

Page 13: The two references used for tropic level assignments are EPA technical reports from 2002 and 2003. Have these documents been examined recently to ensure they continue to describe "best science?"

EPA Response: We did not find more recent information on trophic levels for the required fish species/groups.

Page 22: Section 4.4.4 - This section should be significantly increased. A reference for method of computing confidence limits on the log scale and back transforming is provided below. The method for using full sample weights and replicate weights with NHANES data can be complicated for the uninitiated. I don't think the NHANES web site provides sufficient information for the reader of

this report to understand how weights should (are) used in the analysis. The design effects discussion in the NCHS 2005 reference given is inadequate for this. A reference or two here, and/or a short discussion in an appendix, would ensure that future readers are not confused on what was done here. The four steps for computing the CIS really need to be described in greater detail. Again, the issue here is ensuring that readers are able to replicate the report results (scientific validity).

Gilbert, Richard O., Statistical Methods for Environmental Pollution Monitoring, 1987, Van Norstrand Reinhold, NY, NY, Chapter 13 Characterizing Lognormal Populations, pp 164-176.

EPA Response: The final report provides additional details on the calculation of standard errors and confidence intervals as requested in the comment and we added an appropriate reference, the Gilbert reference provided by the reviewer.

Page 22: A reference/web link for the MIXTRAN macro is needed.

EPA Response: We added a link to where the NCI Method macros can be found.

Reviewer 2

For the most part, yes. The Freedman paper is irrelevant to this analysis and should be omitted. It may be helpful to list Kipnis et al., 2009, "Modeling data with excess zeros and measurement error: application to evaluating relationships between episodically consumed foods and health outcomes," *Biometrics* 65, 1003–1010, because it demonstrates the usefulness of food frequency data as covariates (although for a different purpose).

EPA Response: We removed the reference to the Freedman article and we added a reference to Kipnis, et al., 2009.

Reviewer 3

These might be cited for background and for the distributions of exposure to seafood-borne contaminants:

Hattis, D. and Burmaster, D. E. "Assessment of Variability and Uncertainty Distributions for Practical Risk Analyses" Risk Analysis, Vol. 14, pp. 713-730, 1994.

Hattis, D., "Using Indicator Information for Managing Risks," Chapter 14 in: Environmental Indicators and Shellfish Safety, C. R. Hackney and M. D. Pierson, eds., Chapman & Hall, New York, pp. 364-380, 1993.

Ahmed, F. E., Hattis, D., Wolke, R. E., and Steinman, D., "Human Health Risks Due to Consumption of Chemically Contaminated Fishery Products," Environ. Health Perspect., Vol. 101 (Suppl. 3), pp. 297-302, 1993

Probably there are other more recent references that would be appropriate for similar reasons.

EPA Response: We have added relevant references.

Reviewer 4

It appears that appropriate literature has been cited in this report, with the exception of the modified EPA Method that is presented. No literature is cited to support the modified EPA Method that is used for the estimates given in the table. It appears to be an ad hoc method that has not been peer reviewed.

EPA Response: Ideally, we would have used the NCI Method as it is validated and peer-reviewed. However, it was not feasible for our needs. We modified it for the purpose of the analyses discussed in the report. We expanded the discussion of why it was necessary to modify the NCI Method and the comparison between the NCI and EPA Methods.

Charge Question 4

Is the methodology as presented and defined in the report scientifically appropriate for meeting the objectives of the project? Additionally and specifically:

a. Please comment on methods for calculating fish consumption rates.
b. Please comment on the means for combining fish frequency data.
c. Please comment on the method used to apportion species.

Reviewer 1

I will assume that this question is asking about the methodology of processing the NHANES data to obtain short-term fish consumption likelihood and amount. Questions 5 and 6 ask for specific comments on the NCI and EPA EPA Methods for estimating long-term probability of fish consumption and amount consumed distributions.

The approach requires two broad steps. First is obtaining food consumption and from these self-reported types and amounts, estimating the amount of fish consumed. These data also allow estimation of the short-term probability (likelihood) of fish consumption. Next is to model the likelihood and amount of fish consumed, as obtained from NHANES, in such a way that the parameters of interest for risk assessment, the long-term fish consumption probability or likelihood, and the distribution of fish consumption (intake) given reported consumption are estimable. These two components are then used to estimate usual fish consumption (intake) as a long-term mean. This approach is both practical and has historically been used by others.

EPA Response: No Response needed.

a. Please comment on methods for calculating fish consumption rates.

The method used to estimate the amount of fish consumed using NHANES data and detailed recipe analysis is state of the science.

There is no discussion in the report about the uncertainties associated with the fish proportions associated with each food code presented in Appendix B. In addition, the uncertainties associated with percent moisture loss for each processing method in Table 4 are not discussed or provided. In the future, if someone was interested in understanding how variation in fish proportions in foods or moisture loss in processing methods impacts the usual fish consumption estimate (e.g. sensitivity

analysis), it would be beneficial to have published standard errors of these key proportions. I do not know if standard errors are available from the original sources of these data.

EPA Response: We agree that a sensitivity analysis of how moisture loss values impact the rates and of the use of the standard recipes would be highly beneficial. This was not part of the work at this time, but could be a subject of future work. We added a discussion concerning the uncertainties in the recipe data and moisture loss estimates.

b. Please comment on the means for combining fish frequency data.

The data needed for the NCI and EPA modified models is A_{ij}, the amount of fish consumed, in grams, reported in a 24-hour dietary recall. This amount can represent all fish and/or shellfish, or can represent some subset of fish groupings, tropic class, or habitat class (defined in Chapter 4, Sections 4.1-4.2). In this report, the food codes (recipes) were decomposed to provide the fish proportion of the food and multipliers to which are used to calculate total fish and fish/shellfish subsets. This is all straightforward.

EPA Response: No response needed.

The text does not describe how the multipliers in Appendix B are actually used. I had to work through the following example to understand these. An example like this should be placed in the report somewhere to help the reader interpret the column heading and the values therein.

> Let's examine the first line of Table B-1, "Shrimp dip, cream cheese base." Assuming one gram of this recipe, we would have .262 grams of fish or shellfish. To adjust for moisture loss (25%), the .262 grams would be assumed to be 75% of what was originally there. Hence, the pre-processed amount of fish would be .262/.75=.349 grams. This value (.349) is identical to the "Multiplier for total fish" so this column identified the amount of pre-processed fish in the recipe. I assume the .062 value for "Multiplier for marine fish" then indicates the amount of marine fish in the pre-processed recipe that produced one gram of final food. Since shrimp is the only fish in the recipe, we use the marine proportion for shrimp in Table 1 to assign 17.6 of the total fish to marine (.349 x .176=.062). And so on…

EPA Response: We clarified the section in the report describing how reported amounts consumed were adjusted to raw weight and we produced a simpler Appendix B showing the final number of grams of raw weight, edible portion fish per 1 g of the final prepared recipe in each fish-containing food code reported in the NHANES data 2003-2010. This simpler version makes it clear what final

values were used. Note that the values in Appendix B changed due to the corrected calculation for converting to raw weight. We added an example as suggested by the reviewer. We also added text to Appendix B providing a detailed description of how the FNDDS recipes files were processed and applied to the NHANES data.

c. Please comment on the method used to apportion species.

Overall, I have little to say about the apportionment of species other than the comment in Question 4b above on use of multipliers, and Question 2 comments for pages 8 and 11 about replication of "professional judgment."

EPA Response: No response needed.

Reviewer 2

a. Please comment on methods for calculating fish consumption rates.

The modifications made to the NCI Method seem satisfactory, but I defer to the statisticians.

EPA Response: No response needed.

b. Please comment on the means for combining fish frequency data.

If this refers to Section 2.2.2, then the methodology is appropriate.

EPA Response: No response needed.

c. Please comment on the method used to apportion species.

Reasonable.

EPA Response: No response needed.

Reviewer 3

Yes, except that for understanding dosage distributions. I think it would be helpful to calculate fish consumption per unit body weight per day in addition to raw fish consumption per day.

EPA Response: As mentioned in a comment above, this is an item for future work.

a. Please comment on methods for calculating fish consumption rates.

These seem reasonable and generally appropriate.

EPA Response: No response needed.

b. Please comment on the means for combining fish frequency data.

As far as I could tell, the authors also seem to have made reasonable choices here.

EPA Response: No response needed.

c. Please comment on the method used to apportion species.

Seems OK.

EPA Response: No response needed.

Reviewer 4

The methodology for creating the dataset of fish consumption by individuals in NHANES from the FNDDS files for the 24-hour recall appears to be appropriate.

EPA Response: No Response needed.

The statistical methods used to estimate the distribution of the fish consumption dataset are not well-validated, and may produce biased estimates.

EPA Response: As mentioned above, we consider the NCI Method as the preferred method and believe the results to have minimal bias. The final report has additional information on the bias and precision of the EPA Method which has minimal bias and acceptable RMSE for the intended purpose. The discussion in the final report was modified to provide additional information on the computation time, bias, and precision. The comparisons in Section 4.6 in the final report (moved from Section 5.3 in the draft report) provide information on the bias and precision of the EPA Method.

a. Please comment on methods for calculating fish consumption rates.

The methods for estimating the distribution of fish consumption are based on the modified EPA Method. It appears that this method was created for this project to estimate the distribution of fish consumption in order to provide estimates of consumption more quickly than using the more time consuming NCI Method. In order to do this, the authors made a number of simplifications to the method with respect to the transformation selected, the modeling of probability of consumption, the modeling of the consumption day amount, the simulation of the usual fish consumption, how subgroup estimates were derived, and the calculation of the confidence intervals. Although there are well-accepted methods for modeling repeated measures binomial data (including generalized linear mixed effects models, which the NCI Method uses, and GEE), the report presents what appears to be an ad hoc approach that is not cited in the statistical literature, nor is well validated in this report. Although this method saves computing time, it appears that it may lead in some cases to biased estimates of fish consumption rates for the US population.

EPA Response: In response to various comments, the EPA Method was simplified and improved. The final report has additional information on the bias and precision of the EPA Method. The EPA model presented in the final report has minimal bias and acceptable RMSE for the intended purpose. The discussion in the final report was modified to provide additional information on the computation time, bias, and precision.

b. Please comment on the means for combining fish frequency data.

The methodology for extracting the reported amounts of fish consumed from the 24-hour recall using the FNDDS files appeared to be appropriate. With respect to the statistical methodology, it is not clear if (and how) the 30-day fish consumption frequency data from the questionnaire were used as a covariate in statistical models; this is an appropriate way to use this information, but it is not clear if it was used in this manner.

EPA Response: Yes, the frequency of consumption was used as a covariate in the statistical models. The report was revised for clarity.

c. Please comment on the method used to apportion species.

The method used to apportion species appears to be appropriate based on the food codes and the supporting data presented in the report.

EPA Response: No response needed.

Charge Question 5

Please comment on appropriateness of the models used for estimating fish consumption rates, focusing on both the "NCI Method" and the "modified EPA Method."

a. Is the EPA Method clearly described and supported? Explain.
b. Are uncertainties in the EPA model identified and characterized? Explain.

Reviewer 1

I would like to make a few remarks about the NCI Method here since the specific sub questions focus on the EPA Method. These comments relate to Section 4.4.2.

The first paragraph states that "The NCI Method can be implemented using two SAS macros…" Does this mean that the reader can use this tool but for this report a different approach was used? Or does this mean that for this report the NCI Method "was implemented" in SAS using two macros that can be obtained from the NCI? (But it doesn't tell me now to get them… do I write the Director?)

EPA Response: We edited the language referred to above and added a link to where the NCI Method macros can be obtained.

In the second paragraph,

- The limits on k are not defined. What are the covariates? Are they all continuous, all categorical or mixed? The text was modified to provide additional details on the covariates.
- It would be clearer if you specified that j=1 for most individuals and only a few individuals have j={1,2}. Almost all respondents have two 24-hour recalls. This information is used in the model for probability of fish consumption. Only a portion of individuals have 24-hour recalls reporting fish consumption and a smaller portion had two 24-hour recalls with fish consumption.
- Given that "The usual daily consumption is the weighted average of the weekday and weekend estimates" and given Friday is part of the weekend, the weights for this weighted average would be 4/7 x (Weekday average) + 3/7 x (Weekend average). Is this correct? Unclear. The text has been modified to provide some more discussion of this issue.

- What are the default starting values that NLMIXED uses to initiate its search (provided in a table for define how computed)? Are the MIXTRAN and DISTRIB macros to be provided in the report so that an informed user could examine this code to determine this? (issue of repeatability). The MIXTRAN macro runs simpler univariate and non-linear mixed models to obtain the starting parameter values for the full NLMIXED model. For the runs with the NCI model, we used the starting values calculated by MIXTRAN. For the EPA method, the default NLMIXED starting values were used when estimating the variance components. No starting values were needed for the logistic and linear regression steps..

- C_{ij} is never defined (assumed to be "indicator of consumption").

- The λ is not defined (the Cox transformation parameter).

- The π_i are not defined as the person level effects for likelihood of consuming fish.

- The α_{ij} are not defined as the person level effects for amount of fish consumed at the jth 24-hour recall.

- The π_{Xk} are not identified as the coefficients that relate covariates to likelihood of fish consumption.

- The α_{Xk} are not identified as the coefficients that relate covariates to amount of fish consumption.

- Note it might be nice to indicate that in this model, C_{ij}, α_{ij} and π_i are all random effects, the rest of the parameters are fixed effects.

  The description of the models and the equations were revised to provide more description of the parameters, as suggested in the comments above.

Note that P_{ij} is the probability of consuming fish in a 24-hour period.
According to this model, $0 < P_{ij} < 1$.

P_{ij} can never be 0 or 1 for any individual which assumes there are no fish non-consumers in the fitted data. Since it is highly likely that this is not true, the model is not quite realistic for its given data.

EPA Response: The model does not include an adjustment for never-consumers and the predicted long-term probability of fish consumption will be greater than zero for all individuals, although perhaps very small. Unfortunately we do not have the data needed to identify non-consumers. Having non-consumers in the data will lower the overall probability of fish consumption (P) but increase the variance of the probability of fish consumption among individuals. The resulting effect

on the upper percentiles of the distribution is not clear. This text was added to the uncertainty section of the report.

a. Is the EPA Method clearly described and supported? Explain.

The description of the EPA Method begins at the bottom of page 18. It would be better if the EPA Method had its own section separate from the description of the NCI Method.

EPA Response: We reorganized the report and separated the two discussions.

First, I think it is very important to state in a way that the reader notices it, that from one method fit to one set of fish consumption data, all of the sub-population estimates are derived. That is, all of Table C-1 comes from one fit of the EPA Method run applied to the total finfish and shellfish consumption data. The estimates of the model parameters obtained from the fit of the method to the data provide everything needed to compute all of these consumption distribution estimates. This tends to get lost in the report. This is important statistically because all of the data (for fish subset being run) are used to estimate the model parameters and, hence, all of the data are factored into subsequent confidence intervals. You aren't running fits to smaller and smaller datasets for subpopulations which would produce even wider confidence intervals.

EPA Response: We clarified this in the final report.

The justification for simplifying the NCI Method for parameter estimation is weak and I feel should be discussed in more detail. Some statistics on run times for the NCI Method, run on a current model PC and used to estimate one fish consumption scenario, would likely be justification enough. Is the NCI Method susceptible to running distributed on a computer grid (such as the World Community Grid - http://www.worldcommunitygrid.org/) where thousands of computers could be used to produce the needed results? If so, that weakens the need for a EPA Method.

EPA Response: As mentioned above, we added detailed information to the report about the trade-offs that were made and why the EPA Method is best for this purpose. Briefly, the NCI Method macros would not run with all of the covariates necessary (including interaction terms). And, when running a simplified model with 4 main effects, the NCI Method took 9.5 hours and the EPA Method took 1 minute. One issue with using alternative computing scenarios that may decrease the computational time is that the geographical data which are important predictors for fish

consumption are not publically available and thus have to be used only at NCHS Research Data Center with permission.

The last paragraph on page 18 is actually a synopsis of the EPA Method, used before you get into the formal details of the method. Rather than talk about what the SAS macro does, talk about the modification to the NCI Method and then simply indicate that the approach has been implemented into a SAS macro called ??? (name never given) and available from ??? (location not provided).

EPA Response: We clarified the changes that were made to the NCI Method macro. We included the EPA Method macro in an appendix.

You indicate the use of a "normal scores plot" (a q-norm plot I assume) as an aid to determining the initial lambda* estimate (Box and Cox power transformation parameter). Exactly how is this done? Can you provide a reference to this approach? A good discussion and references to estimating the Box and Cox transformation parameter can be found in:

> Piegorsch, Walter W. and A. John Bailer, 1997, Statistics for Environmental Biology and Toxicology, Chapman & Hall, London, GB, Pages 130-131

EPA Response: The text was modified to provide additional information on this step.

It might be clearer if you list the EPA modified procedure as a series of steps. (I did this to help me understand the method but suggest it might also help other readers.)

> Step 1; compute the four summary statistics for each individual.
>
> Step 2; fit the logistic regression model.
>
> Step 3; iteratively fit the constrained logit model to minimize a weighted Chi square statistic and estimate individual level effects for the probability of fish consumption.
>
> Step 4; estimate the correlation between person-level random effects by using the residuals from the probability model as a predictor in the amount sub-model. Fit the amount sub-model using only records from the first 24-hour recall.
>
> Step 5; estimate the within-person variance component.
>
> Step 6; estimate the person-level random effect variance.

EPA Response: We added a list of steps to the beginning of the discussion as an introduction. In response to comments, the EPA method was reviewed and improved. As a result, the steps are modified from those listed in the comment.

The four equations found on the fifth line of page 19 should be stacked to be consistent with other equations. If you list these statistics vertically, you can add their "labels" to the right and remove the next two lines. Since j can at most be equal to 1 or 2, you are only averaging, summing or counting for a few individuals.

The statement "The person-level random effect is included by assuming the predicted logit when excluding the random effect is proportional to the predicted logit when including the random effect." is not clear at all. It made more sense AFTER I look at equation 4 on page 19.

Ok, here is where I get confused. In equation 4 you have log (P/(1-P)) as the response in the logistic regression. But for this to work shouldn't the P be P_i? But then in equation 5 you use P_i in the response and regress it against the logit of the P_i? Is the critical element here that equation 4 is fit incorporating survey weights, whereas equation 5 does not use the weights? Please clarify.

EPA Response: Using the equation numbers in the comment, equation 4 is a logistic regression model fit using the SAS SURVEYLOGISTIC procedure. Equation 5 is used to estimate beta and the variance of the random effect. Both calculations use the weights. In response to comments, the EPA method was reviewed and improved. In the process the equations in the report were revised, including correcting the error noted above (replacing P by P_i).

Equation 5 basically says that the observed and (survey weighted) predicted P_i are proportional to each other and the residual is the individual level effects. This is not a particularly intuitive relationship and seems to be the key to why the EPA Method would work. I think it is really important to motivate this step. Why would you expect this to work? How do you know that this results in normally distributed π_i?

EPA Response: We edited the equations to discuss and clarify the issues above and justify the model assumptions.

We do not know that π_i is normally distributed. Both the modified EPA and NCI Methods assume the between person random effect is normally distributed in the logit scale.

You write that "Calculation of standard errors requires: 1) calculation of replicate weights consistent with the NHANES survey design and strata and PSU variables; 2) running the macros using the full-sample weight and each replicate weight; and 3) combining the results to estimate the standard errors." I assume this is true for both the NCI and EPA Method. I assume that these calculations occur each time SAS Proc SurveyReg is used. The reader needs to know or understand Proc SurveyReg to understand the importance of this quote. Another place a reference is needed.

EPA Response: A reference to variance estimation was added to the report. The comment is correct that the three steps are needed for both the NCI and EPA Methods. The discussion of variance estimation was expanded to provide additional details about the variance estimation.

b. Are uncertainties in the EPA model identified and characterized? Explain.

There is no place in the report where NCI or EPA Method parameter estimates and their corresponding standard errors are displayed (uncertainty relates to parameter precision). Estimates and approximate standard errors must have been calculated for all model parameters – these would be required output from the statistical estimation routines. Not sure most readers would be interested in seeing these estimates in the body of the report, but since these estimates are important for the simulation of UFC these values should be available, either in an appendix or in an online file (repeatability issue again).

Nowhere is goodness of fit for either model discussed (prediction uncertainty). Do these models fit equally well for particular data? Since the methods predict two outcomes, probability of fish consumption (logistic regression) and amount of fish consumption (regular regression), you would need two tables. An adequate (generally accepted) goodness of fit statistic like the R^2 for regular regression is not available for logistic regression. Reporting the final scaled deviance would allow comparison for the logistic regressions. Along with the number of parameters in the model, these statistics form the basis for many proposed goodness of fit statistics for generalized linear models and hence might be the minimum required fit information that would need reporting. There are similar issues with the Cox and Box transformed linear regression since the R^2 statistic is actually a function of the lambda* estimate. Still, reporting R^2 values would allow some comparison.

Section 4.4.6 compares the predicted UFCR from the two fitted methods. This is not the same as the model fit which examines predictions to actual for a specific model and data set. Both the NCI and EPA Methods might predict the observed data adequately and still differ in predicted UFCR values.

EPA Response: Consumption data (both usual intake and reported intake) were simulated consistent with the model assumed by the NCI Method. Ideally, when analyzing the simulated data, parameter estimates from the NCI and EPA Methods will agree with the parameters used to simulate the data and the estimated percentiles of usual fish consumption will agree with the corresponding percentiles in the simulated data. Differences can indicate programming errors or possible bias associated with to the estimation method. Different scenarios were used to evaluate the EPA Method, with good agreement between the parameter estimates and percentiles compared to the values used to simulate the data.

We created plots to illustrate the results of the comparisons. The plots in the final report show the percentile and parameter estimates derived from the NCI and EPA models compared to the values from the simulated data. The plots and analysis suggest that the EPA Method provides a good approximation to the NCI Method and the true values when lambda is greater than zero and, for negative lambda, the EPA Method appears to provide better estimates than the NCI Method when compared to the true values. It should be noted that: 1) for positive lambda, whether the NCI or EPA estimates are closer to the true value is different for different simulated data sets using the same simulation parameters; 2) for negative lambda, the NCI and EPA Methods provide more similar results when the magnitudes of the variance components are smaller, and 3) the NCI Method could be modified to allow for negative lambda values. These details and plots have been included in the final report.

For linear regression, the model fit can be judged by the R-square. However, calculation of the R-square is complicated by the weights and the presence of variance components. The SAS SURVEYREG procedure used in the EPA method provides an estimate of R-square, adjusted for the weights, when predicting the amount of fish consumed. This R-square is a measure of the weighted variance of the data that is explained by the independent predictors. The unexplained variance is associated with a combination of the within person and between person variance components. For logistic regression, a generally accepted goodness of fit statistic is not available. However, an approximate goodness of fit measure can be calculated if the logistic regression model fit by the SURVEYLOGISTIC procedure is instead fit as a linear regression using the SURVEYREG procedure. Using this approach, the following table shows the r-square for the logistic and linear models when predicting six types of fish consumption using five predictors: frequency of fish consumption, age, income, race, and gender (in Table 6, models with Pred. vars = FAIRM). The first column is the approximate R-square for the logistic model predicting probability

of fish consumption and the second column is the R-square for predicting the Box-Cox transformed amount of fish consumed, when it is consumed.

	R-square	
Fish Type	Probability	Amount
Finfish	0.055	0.071
All	0.078	0.069
Freshwater (FW)	0.030	0.081
Shellfish	0.032	0.068
FW+Estuarine	0.065	0.051
Marine	0.071	0.041

The R-square values range from roughly 3% to 8%. The average R-square in the table is about 6%. Somewhat higher values would be expected when using all predictors in the final models, including region, coastal/non-coastal, and some interactions. Nevertheless, most of the variance is associated with the variance components.

Reviewer 2

a. Is the EPA Method clearly described and supported? Explain.

Defer to the statisticians.

EPA Response: No response needed.

b. Are uncertainties in the EPA model identified and characterized? Explain.

I believe so, but defer to the statisticians.

EPA Response: No response needed.

Reviewer 3

a. Is the EPA Method clearly described and supported? Explain.

Yes. The comparisons indicating comparable results for the modified EPA Method and the NCI Method build confidence. However, aside from leaving out some specific variables, I was not clear on the exact differences between the methods.

EPA Response: We added a bulleted list of the differences between the NCI Method and the EPA Method to Chapter 4.

b. Are uncertainties in the EPA model identified and characterized? Explain.

They seem to be reasonably well identified, although a clearer summary would be helpful. The assumption of normality in the transformed parameters seems a reasonable approximation but the difference between the actual data and the distribution imposed by the normality assumption could be more explicitly shown to the reader to further build confidence in the method and results.

EPA Response: We expanded the discussion of the EPA Method and uncertainties.

Reviewer 4

a. Is the EPA Method clearly described and supported? Explain.

As cited in the response to 4a, the EPA Method is not well supported by the report. There are no citations to the statistical literature to support its use. There are no simulation studies to show that it will provide unbiased estimates, efficient estimates of usual intake (under the assumptions that the 24 hour recall is unbiased). It is described in the report, although some key details, such as how the BRR weights were created and used, are omitted, and the methods are not well justified.

EPA Response: In response to comments, the EPA method described in the draft report was reviewed, revised and improved. In response to this comment, the report now compares the EPA and NCI methods using simulated data. The description of the model was revised to clarify the assumptions and calculations, including the construction of the BRR weights and the calculation of variances. The EPA method was developed for the calculation of usual fish consumption in this

report, not as a general purpose method to replace the NCI method. As a result, the EPA method has no citations in the statistical literature.

b. Are uncertainties in the EPA model identified and characterized? Explain.

The statistical models used are described for estimating probability, amount, and the simulations. The statistical methods regarding the calculation of confidence intervals and BRR weights are not well described in the report. The number of simulations used to estimate the distribution (N=5 vs N=100 for NCI Method) is not well justified. To fully identify and characterize this model would require a more extensive analysis with statistical simulations and comparison to the NCI Method and other methods for estimating the distribution of usual intake for different scenarios of episodically consumed foods. Although estimating the SE for the percentiles is quite time consuming, taking 64 BRR runs per models, the percentile estimates (without SEs) are estimated from 1 run. The authors could have obtained these estimates for all the models and compared them to the point estimates from the EPA Method.

EPA Response: As described above, the report was modified to describe the calculation of the replicate BRR weights and variances based on the replicate weights.

The number of simulations affects the precision of the estimates. Due to having over 29,000 NHANES respondents over eight years, estimates are relatively precise with either 5 or 100 simulated values per NHANES respondent. We ran some models with either 5, 10, 20, 50, and 100 simulated values to evaluate the effect of the number of simulations on the precision, as judged by the RMSE (see Section 4.6 in the final report). The results indicated that there was little or no improvement using more than 50 simulations. After review of our procedures, the number of simulations was changed to 100 and a justification was provided for that choice.

We agree with the respondent that we have not fully characterized the statistical characteristics of the modified EPA Method for different scenarios. This method was developed not for general use in place of the NCI macro but as a method for obtaining estimates with acceptable precision when estimating usual fish consumption from the NHANES data. The comparisons in Section 4.6 for the final report provide information on the precision and bias for this application. The comment suggests that the NCI Method could have been used for getting the estimates without the standard errors. However, the time for even that objective was not practical. The report was modified to clarify the computational problems that were encountered and to clarify that the bias and precision in the results is acceptable for the current use given the constraints.

Charge Question 6
Is the EPA Method adequate for accomplishing the objective? Explain.

Reviewer 1

Adequacy here relates to the extent to which the EPA Method suitably duplicates the NCI Method results. Clearly the figures in the report indicate that on a distributional basis both methods seems to produce similar fish consumption distributions so to this extent the EPA Method is adequate.

EPA Response: No response needed.

I still worry about the issue of fish never-consumers and how they are handled by both methods. Of course, from a risk assessment point of view, fish never-consumers are never exposed to the contaminants that might be found in fish and hence might be considered not part of risk picture. Still, when examining population risks, ignoring fish never-consumers in these methods results in risk being over-estimated (the risk distributions are shifted to the right).

EPA Response: No response needed.

Reviewer 2

It seems reasonable.

EPA Response: No response needed.

Reviewer 3

Yes, it seems to be quite adequate based on the comparisons provided.

EPA Response: No response needed.

Reviewer 4

If the objective is to obtain an unbiased estimate of the distribution of the various types of fish consumption in the report, under the assumption that the 24-hour recall provides an unbiased estimate of fish consumption, then the EPA Method does not appear to be adequate for accomplishing this objective. It is not fully validated, and the results in Section 5.3 indicate that it may be biased.

EPA Response: We agree that the modified EPA Method is not validated for general use and that approximations were made so that the results could be obtained in a reasonable time, but, with some bias. In response to comments, the EPA method was review and revised. The revised method has less biased than the model used for the draft report. EPA considers the tradeoff between computation time and bias, as documented in Section 4.6 of the final report acceptable for this purpose.

Charge Question 7

Specifically in regards to the analysis:

a. Were sufficient information and explanations given that describes how the data were used and what criteria were used to determine the suitability of the data? Explain.
b. Were these criteria adequate? Was the methodology appropriate? Explain. If not, how could the methodology could be improved?

Reviewer 1

I assume in my reply below that this question is specifically about Section 5.3 (and indirectly the material in Section 4.4.3) where the NCI Method is compared to the EPA Method (which is referred to only in this section as the Modified NCI Method). To me, this section represents an analysis of the EPA Method.

a. Were sufficient information and explanations given that describes how the data were used and what criteria were used to determine the suitability of the data? Explain.

In Section 4.4.3, we are provided with the methodology for simulating UFC with the NCI and EPA Methods. After reading this section, I had a number of unanswered questions.

The "modifications" listed in the three bullets at the bottom of page 20 really describe the objective of the simulation exercise – a desire to compare UFC for a "standard week" ignoring recall-to-recall and within person variability. I get this, but I am not sure WHY you might want to limit the comparison this way. Justification or motivation needed here?

EPA Response: These modifications to the model are required to estimate the usual fish consumption from the model parameters and the model fit to the data. EPA is interested in long-term average intake (usual intake), thus a standard week.

Why 100 simulated values for each person? Optimal? Adequate? Just a number used for demonstration purposes (likely)? You fail to mention that you will be simulating fish consumption for every individual for which we have fish consumption data from NHAMES. You could just have likely created a synthetic cohort of fish consumers as the basis for the simulation.

EPA Response: The text will be modified to clarify that we are simulating values for each individual. The input data set provides the population distribution of the independent predictors in the model predicting probability of fish consumption and amount of fish consumption (we could have created a synthetic cohort if we had also modeled the characteristics of the population). The simulation of the random effects provides information on the effect of the variation in the probability of consumption or amount of consumption on the usual fish intake. The simulations replace complicated integration to get the desired estimates. More simulations provide greater precision in the final estimates. The authors of the NCI Method appear to consider 100 to be adequate. Due to the large number of respondents in the NHANES data, we felt that 5 simulations were adequate in the implementation of the modified model. After review of our procedures, the number of simulations was changed to 100 and a justification was provided for that choice.

Oh! There is that 3/7 weight which just shows up here without explanation. See bullet 3 question 5.

EPA Response: We clarified the text as to the explanation for this term

You need to make clear that the model parameter estimated values used for the NCI Method simulation are different from the model parameter estimated values used for the EPA Method (another reason to report these estimates in a table somewhere). Similarly, the lambda values used in the back transformation, B_{Ui}, values may be different for the NCI and EPA Methods.

EPA Response: We modified the text to clarify that the parameter estimates from the NCI and EPA Methods are slightly different due to differences in the equations, particularly approximations used in the EPA Method to get the program to run more quickly. We added a table and plots to Section 4.6 of the final report that includes parameter estimates from comparable NCI Method and EPA Method analyses.

The statement "This equation includes an adjustment with the within person variance in the fish consumption amount (σ_3^2). This adjustment makes the untransformed fish consumption essentially unbiased compared to the original mean across the 24-hour recalls." needs a reference at a minimum and maybe even some motivation for why this is even needed.

EPA Response: The text was modified to reference the Tooze articles on the NCI Method.

How often is a simulated $T_{Ui} < -1/\lambda$? Does this happen more often for the EPA Method?

EPA Response: The probability that $T_{Ui} < -1/\lambda$ depends on the standard deviation of the transformed fish consumption amounts and on λ. We saved counts of this occurrence and found that it never occurred in the analysis.

OK, so 100 Q_{Ui} and T_{Ui} are available for each individual. How do I interpret these values? Theoretically, an individual has only one true "long-term probability of fish consumption." The average of the 100 Q_{Ui}s is an estimate of this true value. Does this mean that the variance of these Q_{Ui}s is an estimate of the uncertainty in our estimate for individual i? Same for the T_{Ui}. The first time I read the equation at the top of page 22 I thought that you were multiplying the mean Q_{ui} with the mean T_{ui} to get the UFC for individual i, but actually you are computing 100 U_{Ui}s and then computing the mean (call it U_i) of these values to get the UFC for individual i. Is this correct? Oh, wait, you use the NHANES survey weights in here, so clearly you are computing individual averages by method.

EPA Response: Each simulation generates one value for the probability of fish consumption and one value for the amount of fish consumption, when consumed, and the product of these two is the usual fish consumption. For an individual, the distribution of simulated usual fish consumption represents the distribution of values that individuals with the same population characteristics (predictor variables) might have. The survey weight represents the number of those individuals in the population. We are trying to estimate the usual fish consumption for the population, not for each individual.

So, you DO NOT compare the U_{i_NCI} to the U_{i_EPA} but instead compare overall mean UFC_{NCI} to UFC_{EPA} and compare distributional tiles with a quantile-quantile plot. I understand that and to a certain extent it makes sense from a risk assessment point of view. What is important is that the methods simulate similar UFC distributions, overall and for strata. Still, for a model goodness of fit assessment, I would also be interested to see statistics/graphics that compared the U_{i_NCI} to the U_{i_EPA}. Doing this comparison will require some careful thought. In particular, a randomly simulated individual effect (for either probability of consumption or amount of consumption) might be generated once and used in the appropriate place for the different NCI and EPA Methods to avoid the U_{i_NCI} to the U_{i_EPA} difference reflecting differences in random effect values.

EPA Response: It does not make sense to compare the NCI and EPA simulated values for a person. We could compare the mean simulated value for the person. However, this is basically the same as the predicted mean from the model.

The reviewer's comments listed above in reply to question 7 a. were used to edit the discussion of the EPA Method and compare the two procedures in Section 5.3.

b. Were these criteria adequate? Was the methodology appropriate? Explain. If not, how could the methodology could be improved?

I think the methodology used to compare the two methods is appropriate and makes sense for a tool focused to risk assessment. The methodology might be inadequate to aid understanding of whether the EPA Method and NCI Method produce similar estimated UFC for individuals with similar demographics.

EPA Response: We expanded the section comparing results from NCI Method and the EPA Method – showing more comparisons of models and included more discussion.

Reviewer 2

a. Were sufficient information and explanations given that describes how the data were used and what criteria were used to determine the suitability of the data? Explain.

Not really. As stated above, the handling of the dietary intake data is unclear.

EPA Response: As noted above, we clarified the details of the dietary data processing.

b. Were these criteria adequate? Was the methodology appropriate? Explain. If not, how could the methodology could be improved?

The procedures/methods for handling the dietary data are unclear.

EPA Response: As noted above, we clarified the details of the dietary data processing.

Reviewer 3

a. Were sufficient information and explanations given that describes how the data were used and what criteria were used to determine the suitability of the data? Explain.

The national representativeness of the NHANES data is fully described, as is the sampling protocol and the use of the population weights. All of this seems appropriate.

EPA Response: No response needed.

b. Were these criteria adequate? Was the methodology appropriate? Explain. If not, how could the methodology could be improved?

Yes. Only, I think in introducing the body weight factor to allow better representation of the distributions of consumption controlled for this major variable.

EPA Response: No response needed.

Reviewer 4

a. Were sufficient information and explanations given that describes how the data were used and what criteria were used to determine the suitability of the data? Explain.

Further information could be given about the predictors used in each model. In Section 4.4.5, the report cites that "all significant predictors" were used, but no criterion for significance is given, and it is not clear which predictors were used in which models. Although Section 2.2.2 outlines that the 30-d fish consumption frequency data could be used in statistical models, it is not clear if these data were used in any models, as they are not included in the list of variables in Section 4.4.5. It is not clear if people were excluded if they were missing covariate data. Furthermore, the methodology for creating subgroup estimates by age, gender, geographic region, etc. is not described in the report. It is important to know if covariates were used to define subgroups, or if the models were stratified by subgroup.

EPA Response: We edited the report to clarify what models were fit: 1) what populations or sub-populations were used and 2) what predictors were used for those models.

b. Were these criteria adequate? Was the methodology appropriate? Explain. If not, how could the methodology could be improved?

I think it is appropriate to include all plausible 24-hour recall data from NHANES for this analysis, as long as there are no apparent data entry or recipe errors. The report did not detail whether any type of data cleaning was done.

EPA Response: We did not cleaning of the NHANES or FNDDS data. To the extent that data entry or recipe errors could be identified within the scope of the project, not data entry errors or obvious outliers were found. There were possible inconsistencies between the food code description and the ingredient description in a few FNDDS recipes, depending on how the recipes were interpreted, in which case the ingredient description was used.

Charge Question 8

Are the results presented in the report understandable and appropriate for meeting the objectives of the project? Explain. If not, how could the presentation of the results be improved?

Reviewer 1

My responses to all of the other questions contain suggestions for improving the presentation. There are places where the material is not clear and the writing should be improved. There are a couple of places where material that should appear together, such as the background for the NCI Method and the discussion of the method itself, are in separate chapters where they might be better presented as one.

EPA Response: No response needed.

Reviewer 2

Need to state in the text and tables that the results are uncooked amounts and for edible portion only if that is the case.

EPA Response: We made this change.

Reviewer 3

The results as far as they go are presented reasonably. As indicated above, I would like to see further analysis of parameters relevant for risk assessment and singling out of particularly important results for risk assessment implications.

EPA Response: We added a discussion section to discuss and summarize the results.

Reviewer 4

The results presented in the report appear to be understandable and appropriate to the task. I believe that the authors of the report presented what they were asked to do; however, I have concerns with the validity of the estimates produced.

EPA Response: The reviewer's concerns about the validity of the estimates are addressed in previous responses, above.

Charge Question 9
Are scientific uncertainties explained and are they appropriate? Explain.

Reviewer 1

I assume that this question is directed at Section 5.4 and my reply is focused on this section.

Section 5.4.1: How might the results have been changed if a different fisheries biologist been used? Was the variability of NOAA landings from year-to-year incorporated in this analysis?

EPA Response: The discussion of the uncertainty associated with the habitat apportionment was increased.

Section 5.4.2: The first sentence seems to imply that the largest portion of the uncertainty in CI for the estimated distributional p-tiles (from the NCI Method) comes from uncertainty in estimation of the within- and between- person variance components. Is this correct? Was this determined via a sensitivity analysis? Or was this determined by looking at the standard errors for the variance component estimates? It might be useful to expand on this since this has implications for future data needs (the need for more multi-day 24-hour recall records – something many EPA scientific review panels have asked for).

EPA Response: Whether the largest component of variance is associated with the estimation of the variance components is unclear and will depend on the data. The magnitude of the variance components is important when estimating the upper percentiles, but less important for estimating the mean. Consistent with the comment, a minimum of 50 individuals with two recalls with two fish reported fish consumption is recommended for use of the NCI Method. The report was modified to discuss this point.

When you say "The model," I suggest you use a more complete descriptor - "The NCI Method."

EPA Response: We clarified the terminology throughout the report.

Section 5.4.3 (page 55): This paragraph is difficult to read because the phrase "the weighting" may not be clear to the reader. All the information is here, just improve the writing to be clearer of what the message is. An illustrative example of the issues at stake might help here.

EPA Response: We edited and clarified the language.

Section 5.4.4: The statement "However, they generally collect data in northern counties in the summer and southern counties in the winter." represents in my mind the biggest shortcoming of using these data for this analysis and the greatest potential for bias. I think this issue should also be discussed closer to the beginning of the report.

EPA Response: This information was added in to the discussion of the NHANES data.

Section 5.4.5: OK except the label "Modified NCI Method" should be standardized to the "EPA Method."

EPA Response: We clarified the terminology throughout the report.

Reviewer 2

For the most part, yes, except as described above.

EPA Response: No response needed.

Reviewer 3

Generally, yes. However, the key issue of within-person correlations of fish consumption appears to be based on just two days for each individual. This means that the degree of correlation of fish consumption on different days must be measured with some error. The degree of uncertainty in estimates of the within-person correlation probably should be discussed as it may tend to produce uncertainties in the allocation of variance between person-to-person differences and within-person differences. In addition to this, the report explains that there are reports of habitual fish consumption over a prior month. It would be good to see some explicit analysis of these data, or at least a clearer explanation of how these data contributed to the overall analysis.

EPA Response: The text was modified to include a discussion of the important of having enough respondents with two fish consumption reports to estimate the variance components and

correlation. The correlation is based on N>50 individuals with two recalls with reported fish consumption. There are uncertainties associated with all the parameters, including the estimates of the variance components and correlation. In preliminary work, the correlations were generally close to zero. As a result the uncertainty in the correlation may not have much effect on the variance components.

The NHANES data includes reported frequency of consuming various fish species in the previous 30 days. We assume this is what is meant by "habitual fish consumption". The reported frequency of fish consumption was included as a predictor of usual fish consumption. We modified the report to include more details on the models and covariates.

Reviewer 4

Estimating usual fish consumption of specific species is a difficult task, and requires a number of assumptions in terms of data summary and analysis. The way in which the data were summarized appeared to be consistent with other studies and there was some discussion regarding the assumptions with respect to regions, seasonality, and habitat. From my knowledge of this area, these appeared to be appropriate. With respect to the statistical methodology, it appears that there are additional uncertainties that were not addressed to the degree that they could be (see my response to previous questions for details). It would be helpful to discuss the statistical methodology used in the previous report, to explain the discrepancies between the previous estimate of the 90th percentile of consumption compared to the new estimate.

EPA Response: A discussion was added about the estimation procedure used in the previous calculation.

Charge Question 10

The data used in the analysis have been subdivided based on demographic and geographical characteristics of the respondents. Are the subsets of data sufficiently robust to characterize fish consumption within the subgroups for the purposes stated in the report? Please provide your response for each of the major subgroup categories included in the main body of the report.

Reviewer 1

The stratification or subdivisions seem reasonable and justified. The categories seem to cover most of the fish consumption categories that would be needed for risk assessments.

EPA Response: No response needed.

Just a thought, not an action item: If I were to suggest one additional demographic factor it might be education level coded at two levels; "high school diploma/GED and below" and "some college and above." Education is highly correlated with income so most of the education effect is captured by the finer coded income factor. The non-Hispanic White category has the highest sample size and I wonder if it might be possible to break out a category of "Asian and Pacific Islander" and/or "Native American/Alaskan Native." These two later categories are likely to be higher consumers of fish but also, given the design of NHANES, are unlikely to be very well represented in the sample and not represented at all in many geographic regions.

EPA Response: The more finely categorized income variable is highly significant in the probability submodel and is included as a predictor for all fish types. It was not found to be significant in the amount submodel at the 5 percent level for any fish type. We believe that the income variable is highly correlated with education.

It is not possible to break-out any other racial/ethnic groups using NHANES data.

Reviewer 2

As stated in the report, it is preferable to estimate fish consumption for the subgroups using a statistical model, rather than the same fish consumption rates for everyone.

EPA Response: No response needed.

Reviewer 3

I think so.

EPA Response: No response needed.

Reviewer 4

Table C-56 details the number reporting fish consumption on both 24-hour recalls by fish type. In general, one would want at least 50 participants per cell in order to estimate the variance components for between and within person variation. As mentioned previously, it is not clear exactly how the subgroup estimates were derived. If they were derived from covariates in one large model, it may be appropriate to assume the same ratio of between with within variance holds for the smaller subgroup. However, if the models are stratified by subgroup (which I do not think they were, but it is not completely clear), then the sample size of some of these subgroups would not be of sufficient size to produce stable estimates of variance components.

EPA Response: The subgroup estimates were derived from covariates in one large model (for each fish type). As noted above, we edited the report to clarify what models were fit: 1) what populations or sub-populations were used and 2) what predictors were used for those models.

Response to Specific Observations

Reviewer 1

Page	Paragraph	Comment or Question
16	2	Adjustment factors “are also used” instead of “were also used” in the two reports. The reports exist today even though they were created in the past. Active writing style recommends the use of present tense where possible. The tense was corrected in the sentence.
16	3	Sort alphabetically by Processing Method or numerically by Percent moisture. Current table uses neither. Recommend sort by % moisture. The table was sorted by percent weight change.
18	5	In the discussion around lambda estimation, you talk about estimation being “consistent with the model,” but I think you mean “consistent with the data” and the assumption of normality (which is part of the model or method). Correct. The text has been changed to say “consistent with the data”.
19	4 lines from bottom	Shouldn’t this be 24-hour recall rather than 12-hour recall? Correct. In response to other comments, the EPA Method was revised and improved and the description was changed, including this phrase.

Reviewer 2

The following line numbers refer to the attached version of the report. It also includes editorial suggestions (track changes) for making the document clearer; suggestions made for tables apply to other tables in addition to where they appear.

The tracked changes supplied by the reviewer were used in the editing of the report.

Line 237 [page 3]—Add "Survey participants are not asked to provide detailed recipes for mixed dishes. For those, standard, default recipes are used." This has implications since participants are not queried about the types of fish used in stews, sandwiches, etc. This is a limitation that should be acknowledged.

This sentence and a section on the uncertainty associated with use of standard recipes were added.

Lines 303-307 [page 5]—This paragraph should be edited as follows: "The USDA Food and Nutrient Database for Dietary Studies (FNDDS) is the underlying database used to code dietary intakes for NHANES. It is a database of foods, their nutrient values, and gram weight equivalents for various amounts of foods. For each new version of FNDDS, foods, gram weights, and nutrient values are reviewed and updated to reflect the U.S. food supply by incorporating new foods based on what is reported in the survey and updating existing entries." The weights found in the FNDDS are not necessarily for "typical" portion sizes.

These edits were made to the final report. This section was moved to 3.3.

Lines 316-319 [page 5]—It should be explained in detail earlier in the document that the FNDDS contains standard recipes. How those recipes were used in this analysis should also be described.

In response to a previous comment above, we added a sentence saying that NHANES participants do not provide detailed recipes (Section 2.1). We increased the detail on how the recipes were used in Section 3.3, and included an example.

Lines 433-436 [page 8]—These "groupings" are the unique food codes, right? Why not call them that? The term "food codes" is used elsewhere. Suggest instead, "When the raw 24-hr recall data are processed by NHANES, fish species reported are assigned food codes. The list below presents the

food codes for fish that are specified in the FNDDS and the additional species that are included in each."

The food codes apply to grouped fish species and cooking methods. We clarified the text to make it clear to readers. "When the raw 24-hour recall data are processed by NHANES, fish species reported consumed are grouped, and foods (e.g., Pompano, baked or broiled) are assigned food codes. The list below presents the species of fish that are specified in the USDA Food and Nutrient Database for Dietary Studies (FNDDS) and the additional species that are included in each group."

Line 503 [page 10]—Smelt must have been reported before 2003; otherwise, the code would not exist. This should say instead, "[not reported in 2003-2010]."

Yes, we meant that it wasn't reported in the data we are using. The text was modified as suggested.

Lines 520-521 [page 11]—This is unclear. Would it be correct to say, "For these groups, we used raw (uncoded) 24-hour recall files from NHANES from 2007-08 (which are not publically available, and the only cycle made available to us) and counted the number of times a species was reported"? If so, the text should be revised accordingly; if not, the procedure should be described more clearly.

Yes, that is what was done. The text was clarified as suggested by the reviewer.

Lines 614-625 [page 16]—This section is particularly unclear. It is unclear if the amounts of fish tabulated are cooked or uncooked. This should be specified. If they are uncooked, how were the cooked amounts from the NHANES data converted to uncooked amounts? These "adjustments" should be explained in detail. Furthermore, are these uncooked amounts of edible portion only, or are they uncooked amounts of whole fish? Do they include skin? Do they include bones?

The fish consumption rates were meant to be raw weight, edible portion. However, due to a programming error, processing and cooking adjustments were only made to food codes with recipes that used processed/cooked fish. We revised the programming code to adjust the prepared amounts reported in NHANES to raw weight for all food codes. We edited the text and added more details on the methodology and provided a detailed description in Appendix B.

Lines 614-615 [page 16]—Some fish are prepared and cooked by the consumer. Please explain the differences between "pre-processing," commercial processing, and cooking by the consumer and how these were handled in the data processing.

There are two fields in the FNDDS files that provide information on the cooking/processing method. One field (main_food_description) provides information on how the food was cooked or prepared for consumption and the other (sr_description) provides information on commercial processing if an ingredient is pre-cooked/processed before used in the recipe (such as canned tuna in a tuna salad sandwich). The adjustment factors were originally only applied using sr_description (a programming error). This was corrected for the final report.

Lines 621-622 [page 16]—Adjustment factors were applied to the proportions of what? Shouldn't they be applied to the gram amounts?

The adjustment factors were applied to the fish type proportions for each food code and summed by food code (some food codes contain more than one species) and then the resulting values were multiplied by the gram amount reported by the participants. The report was edited to clarify these steps.

Lines 621-625 [page 16]—These factors are the percentages of moisture that is lost through processing. What is missing are the factors that were used to convert the cooked/processed fish, reported in NHANES, back to the uncooked/unprocessed form.

These factors were added.

Tables—What does "Inc Ref" mean? Because these are population estimates, the last two rows in the income section of the tables should be combined into something like "Income unknown."

"Inc Ref" means income refused. The tables were edited to make this clear.

Reviewer 3

Page	Paragraph	Comment or Question
17	2	I had to look up what a logit distribution was. A clearer mathematical description of what this is in general and why it was selected would be helpful. **From Wikipedia, logit(P) = log(P/(1-P) = -log(1/p – 1)** The text was modified to provide additional justification for using the logit transformation. The logit transformation is commonly used as the link between the continuous predictors and the probability of a discrete outcome, as in logistic regression.
17	3	Similarly, the Box-Cox distribution should be explained and the why of the choice of this transformation described. Also, nowhere is there a presentation of which lambdas (power numbers) were indicated by the data. This could be done in an appendix. The text was modified to provide more description of the Box Cox power transformation as well as providing summary information on the lambda's used in the models.
20	1st bullet	"The predicted values reflect a standard week (3 weekend days and 4 weekday days) rather than the distribution of weekday and weekend recalls in the data." It seems odd to describe a "standard week" in this way, rather than one with 2 weekend days and 5 weekday days. The why of this choice needs to be explained, and perhaps there should be a brief description of how much difference this makes in the results. A footnote was added to help explain the definition of weekday versus weekend. The NCI Method includes Friday as part of the weekend. A study of CSFII data showed that intake on Friday was more similar to Saturday and Sunday than to the rest of the week days (Monday – Thursday). Haines, P. S., Hama, M. Y., Guilkey, D. K. and Popkin, B. M. (2003), Weekend Eating in the United States Is Linked with Greater Energy, Fat, and Alcohol Intake. Obesity Research, 11: 945–949. doi: 10.1038/oby.2003.130
23	2	The description of the age groups in this paragraph makes no mention of the 1-<3 age group included in Table 5. It seems to me this age group should be added to the description or the reader will wonder why children under age 3 are not covered. The reviewer is correct. 1 to <3 years was added to the list of childrens age groups.
C-1		The tables in this appendix should give the units (g/day). The units g/day were added to the tables.

Reviewer 4

Page	Paragraph	Comment or Question
1	5	The NCI Method simultaneously models probability and amount. The text has been revised to use the word "simultaneously".
20	4	More detail should be given on the "NHANES survey weights" used. Are they the dietary weights that are adjusted for non-response? BRR weights? Additional description of the survey weights has been added to the text.
21	4	Was a 9 point approximation considered? We assume this refers to the equation for calculating an unbiased estimate of the usual amount consumed. We used the formula used in the MIXTRAN macro. Results using simulated data suggested that this was adequate. We did not consider a 9 point approximation.
22	2	More detail on the BRR weights and these calculations should be provided. The discussion of the BRR weights and their use was expanded.
22	3	The highest correlation of what? This procedure is unclear. In response to the comment, the procedures were revised and more detail was provided on how the transformation in the EPA Method was selected.
54	1	The first sentence in Section 5.4.2 is unclear. When one produces estimates of the distribution of usual intake without partitioning between and within person variability, the estimated variance of the distribution is over-estimated, leading to over estimates of person in the tails of the distribution. I think this sentence is referring to the SE for the estimates of the percentiles, but it may be misinterpreted as the variance of the distribution of intake (as it does not specify the variance of what, it just says "the variance"). The uncertainty section has been revised to clarify and address this confusion.
C-1++		The tables in Appendix C do not have units given – units should be added. Units (g/day) were added to the tables in Appendix C (Appendix E in final report)