Peer Review Comments and Responses

for

An FSIS-Contracted Comparative Risk Assessment for *Listeria monocytogenes* in Ready-to-Eat Meat and Poultry Deli Meats

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by

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Introduction

The FSIS Comparative Risk Assessment for *Listeria monocytogenes* in Ready-to-eat Meat and Poultry Products was independently peer reviewed under contract to the Research Triangle Institute in accordance with Office of Management and Budget Peer Review Guidelines.[1] Below are (i) brief biographical sketches of the reviewers, (ii) the charge to reviewers, and (iii) reply to reviewer comments.

Reviewers

An independent peer review of this risk assessment was conducted under contract to RTI International. The reviewers were:

Joe Frank: Dr. Frank holds a joint Professor appointment in the Departments of Food Science and Technology and Microbiology at the University of Georgia. His research focuses on the control of *Listeria monocytogenes* in the food processing environment. Dr. Frank has authored or co-authored 41 peer-reviewed articles related to *Listeria monocytogenes*, 19 book chapters, and edited one book. In addition, he has served as a scientific co-editor for the *Journal of Food Protection* since 2002. Dr. Frank was recognized by the International Association for Food Protection in 2005 as a Fellow and with the President's Recognition Award. He received his degrees (B.S. in Bacteriology, M.S. in Food Science, and Ph.D. in Food Microbiology) from the University of Wisconsin at Madison.

Akier Assanta Maf: Dr. Maf is an Associate Professor in the Department of Food Science at Laval University (Canada) and conducts research for the Food Research and Development Center at Agriculture and Agri-Food Canada. He is also a Professor with the Agri-Food Institute in the Democratic Republic of Congo. In 2007, he was awarded by The International Council for Science under the United Nations for his work in food safety in developing countries. He has authored or co-authored more than 24 peer-reviewed publications and has presented his research at more than 50 international conferences. Dr. Maf holds a DVM from University of Lubumbsahi (Democratic Republic of Congo), an M.S. in Pathology and Microbiology, and a Ph.D. in Food Microbiology.

Donald W. Schaffner: Dr. Schaffner is an Extension Specialist in Food Science and Professor at Rutgers, The State University of New Jersey. His research interests include quantitative microbial risk assessment and predictive food microbiology. Dr. Schaffner

[1] Office of Management and Budget's "Final Information Quality Bulletin for Peer Review" (December 2004): http://www.whitehouse.gov/omb/memoranda/fy2005/m05-03.pdf. This bulletin establishes government-wide guidance aimed at enhancing the practice of peer review of government science documents.

has authored more than 100 peer-reviewed publications, book chapters and abstracts. Dr. Schaffner has served on expert committees for US National Academy of Sciences, the World Health Organization and Food and Agriculture Organization of the United Nations, and has chaired two expert workshops on microbial risk for WHO/FAO. He was most recently a member of Institute of Food Technologists Expert Panel that developed a quantitative risk ranking framework for the Food and Drug Administration. Dr. Schaffner is currently serving a 5 year term as Editor for the Journal of Applied and Environmental Microbiology. In May 2005, he was appointed to serve on the National Advisory Committee on Microbial Criteria for Foods (NACMCF). He is active in several scientific associations including the International Association for Food Protection, the Institute of Food Technologists, the Society for Risk Analysis, and the American Society for Microbiology. He holds a B.S. in Food Science from Cornell University and a M.S. and Ph.D. in Food Science and Technology from the University of Georgia.

Mary Alice Smith: Dr. Smith is an Associate Professor in the Department of Environmental Health Science at the University of Georgia. She is also a collaborative scientist in the Division of Research Resources at the Yerkes National Primate Research Center. Her research focuses on chemicals and pathogens affecting pregnancy and development, including developing dose response data in support of risk assessment for *Listeria monocytogenes*, effects of pathogens including *Enterobacter sakazakii* on pregnancy outcome and development, and investigating mechanisms by which exposure to perfluorinated compounds results in birth defects. Dr. Smith has authored or co-authored more than 35 peer-reviewed publications, and she currently serves on the Editorial Board for the journal *Reproductive Toxicology*. Previously, Dr. Smith was an invited member of the task force to draft a publication on "Microbial Risk Analysis in Food Safety" for the Council for Agricultural Science & Technology, and was an invited member of an international expert panel for drafting a white paper assessing the risk from exposure to *Listeria monocytogenes*. She holds a B.S. in Biology Education, an M.A. in Teaching Secondary School Science, an M.S. in Developmental Biology, and a Ph.D. in Toxicology/Pharmacology.

Haibo Zhou: Dr. Zhou is an Associate Professor at the Dept. of Biostatistics, University of North Carolina at Chapel Hill. He is the Director for Biostatistics for the Center for Environmental Medicine, Asthma, and Lung Biology at UNC. He collaborates with investigators at National Institute of Environmental Health (NIEHS) and the U.S. EPA Human Study Division. His statistical expertise is in outcome-dependent sampling, survival analysis, missing data and auxiliary data problems. Dr. Zhou is interested in environmental statistics, reproductive epidemiology, human fertility, children's health development, risk assessment, and respiratory diseases due to environmental exposures such as smoking and air. He has published extensively in both statistical journals and the subject matter journals. He is currently an associate editor for Biometrics, a leading professional journal in statistics. Dr. Zhou holds a Ph.D. and M.S. in statistics from the University of Washington.

Charge to Reviewers

Peer reviewers were asked to focus on the following points when reviewing the risk assessment:

1. The overall clarity and structure of the report. Is it well written and organized in a logical fashion? Do the figures and tables present data and results in a manner that is easy to understand?

2. The quality of the data generated by the National Alliance for Food Safety and Security. Are these data more useful than those used previously? Are there limitations to the NAFFS data? If so, how can these limitations be addressed/dealt with in the risk assessment? Are additional data needed?

3. Are the data and analyses sufficiently convincing that *Listeria* contamination is taking place at retail? Are the data and analyses sufficient to require USDA to begin to collect environmental and food contact surface samples at retail establishments? Are the data and analyses sufficient to develop a regulatory strategy for dealing with contamination originating at retail?

4. Is it necessary to attempt to model cross-contamination of *Listeria monocytogenes* in establishments and at retail? If so, please comment on why you feel this is necessary; the types of data necessary for such modeling; whether these data are available; and the additional uncertainty you anticipate would be introduced to the overall model.

5. Please make suggestions as to the types of data necessary for modeling the pathways of cross contamination between RTE meat and poultry products and their environment at retail; whether these data are available; and the uncertainty you anticipate would be introduced to a model making use of them.

6. For reviewers with expertise in risk assessment and Excel spreadsheets, please review the Excel model to identify any errors. It is based on a modified version of the FDA Risk Ranking model (2003). The FDA model has been peer reviewed, so a detailed analysis of it is not necessary. Comments on the modifications needed for this risk assessment are needed however.

7. Please provide recommendations for supplementary/future research that you feel would strengthen the assessment.

Reply to Reviewer Comments

Reviewer #1
The report is not generally well written. Most table and figure captions do not supply sufficient information to be understood independent of the text. I have provided "Major comments" and "Minor comments" that include suggestions for improving the writing. Major comments are those that must be addressed adequately for the report to be acceptable.

Reviewer #2
Overall, the report is well written and presented in a logical way. The figures and tables are easy to understand. However, there are some important data details missing from the reports. It also reflects on the appropriateness of the statistical approaches the results are based on. See comments on points below.

Reviewer #3
This document reports on the number of cases from *Listeria monocytogenes* in ready-to-eat meat and poultry products. Overall, the report is clear, structured and well written and organized. However, there are some changes that should be done to get the document in the step of publication (See additional comments).

Reviewer #4
The report appears to have been written is a hurried fashion, and it contains numerous typos, and excessive jargon and colloquialisms. Detailed comments can be found below. The organization of the report does appear logical. Clarity of the tables and figures could be improved. (See additional comments)

Reviewer #5
The document is organized as a typical risk assessment document that provides information on hazard identification, hazard characterization, exposure assessment, and risk characterization. The figures and tables often need more information for clarity. Risk assessments are quantitative but not necessarily accurate because of assumptions that must be made where data and direct information are missing. When specific numbers are calculated for illness and death, explanations need to be made concerning uncertainty and that these estimates are for excess illnesses and deaths above a certain background (See additional comments)

RESPONSE: Table and figure captions have been expanded. Specifics are addressed below.

Reviewer #1
The data are of sufficient quality to serve the purpose of the report. Limitations of the data are adequately addressed.

Reviewer #2

The quality of the data generated by the NAFFS is clearly better than the previous available data set in that it has a much larger sample size, covers more broadly of the national data, and is more representative of the underlying population. The limitation of the data set is that the observed data is clustered, i.e., multiple visits are conducted to the same store. That said, the clustering sampling/testing may be the only practically feasible way to collect the data and it certainly can be readily addressed by the proper statistical analysis methods.

The Data Collection Methods section is too sketchy in describing the sampling design and data structure. Important information is left out. In particular, there is no mention on how many stores are visited in each sites and how many repeated visits/tests are conducted for each store. Because of potential cross-contamination from a same store, the test results from a same location will be correlated. Such correlation needs to be addressed in the data analysis.

Clarification: p. 14, 3rd to last paragraph, if "1000 samples were analyzed for each subcategory and from each site" is true, that will lead to more than 3000 samples from each site? This is contradicting to Figure 2 which shows the maximum sample in a site is 2295.

Reviewer #3

Regarding the quality of the results, the difference between these data and those used previously is not evident. Both presented data show the same traditional parts of a risk assessment report: hazard identification, hazard characterization, exposure assessment and risk characterization. NAFFS data focused mostly on the exposure assessment from which a complete experimental design has been built and conducted by a large and competent scientist group. This approach is useful and should probably be recommended for the other parts of the risk assessment.

Reviewer #4

The NAFFS data certainly do bring new and useful information to the table. I'm quite puzzled and discouraged by the fact that the NAFFS contains a majority of blank fields where information was requested on antimicrobials. Clearly changes in the industry with respect to antimicrobial use may impact *L. monocytogenes* risk.

As noted below, the effect of faster consumption on risk posed by retail sliced product could in fact be tested by running simulations with different consumption rates: 25% faster, 50% faster etc.

The question is not "are additional data needed/" because we will always need more data, the question is what decision do we need to make now, and would more data effect these decisions.

It is not clear from the report exactly what risk management questions the risk assessors were being asked to address, which makes the need for additional data impossible to determine. The risk management questions should be clearly identified.

Reviewer #5
Why were data gathered from only 4 states, particularly California because it already had been sampled? Why was the data from Maryland not included in this risk assessment? If there was concern that the previous data from 2 states was different, then why would four states be adequate for the present study?

RESPONSE: The data for stores visited and the number of visits per store were not provided as part of the blinded data. An estimate (based on time and date of sampling) was made for some locations, and this discussion has been added to the report. A more detailed analysis of the clustering effect (multiple samples at some stores) has been added. A more detailed comparison of the results of this work and those of Gombas *et al.* (2003) has been added. Data were not combined with earlier Gombas *et al.* data because different sample collection techniques were used. An evaluation of faster consumption of retailed sliced product is interesting, but was considered beyond the scope of work at this time. The wording concerning the sampling plan has been modified.

Reviewer #1
The data are sufficiently convincing to justify sample collection and a regulatory strategy at retail. This is in spite of significant questions concerning the appropriateness of the data analysis that are addressed in the “Major comments” section.

Reviewer #2
While the conclusions are likely to be valid, statistical approaches used to derive these conclusions are not appropriate and some additional details and analysis are needed in the report.

The biggest issue is how to deal with the repeated testing results from the same store. The report correctly pointed out the possible cross-contamination, but does not appear to have addressed the issue of correlated data due to such cross contamination. Treating the 6000+ samples as independent might artificially inflate the significance of the results. As Figure 9 demonstrates, the stores that have positive *Listeria* test results are contributing multiple positives in general. Clearly, a data set where one store with 10 positive results does not provide as much information as a data set where 10 stores each with one positive test result. It is not clear if these are taken into consideration in the analysis. A possible approach for consideration is outlined as follows:

1. From a 2X2 table calculation, classified with (Pre-packaged, Deli sliced) by (positive, negative), the expected frequency for the smallest cell, the pre-packaged and positive

(observed at 6, not including the chub portion of data), is about 28. This suggests the large sample theory should be OK in this case. Hence,

2. One could therefore try a GEE type analysis to adjust for the cluster effect in the data, based on the following logistic regression model:

$$\text{Logit}(p_{ij}) = a + b_1 * \text{Deli}_{ij}, \quad i=1, \ldots, S, \text{ and } j=1, \ldots, m_i.$$

Where $p_{ij}=\Pr(Y_{ij}=1|\text{Deli}_{ij})$, Y denote if the test result is positive, Deli is indicator variable for if the sample is Deli-sliced, S is the total # of independent stores and m_i is the total # of test samples from store i. The effect of timing of the day (p.21) and season (p.21) can also be evaluated in the above model.

For simplicity, the Chub data can be left out from the above analysis. Information on Chub by sites and positive test results by Chub would also be helpful if provided in the report.

Finally, timing of day is listed as an important finding. For the reasons stated above and the lack of detailed information on this variable in the report, I am not totally convinced about this conclusion. The effect of timing of day still remains to be determined in the analysis with adjustment of correlation. For example, if all positives from one particular store are all obtained in the afternoon, the analysis that ignores the correlation will likely attribute this as the effect of timing rather than the effect of the same store contamination.

It will also be helpful to specify the type of test and the exact null hypothesis being tested in the report. e.g., in Figure 7, is this a global test? Why using all data and not just the retail portion of data? Is the data sampled distributed evenly across deli-sliced and prepackaged in term of timing and season?

Reviewer #3

Data analysis is very strong and clearly demonstrates that contamination by *Listeria* takes place mostly at retail level. It seems that more actions should be taken for better understanding of the problem (sources of contamination, behavior of *Listeria* in the environment, impact and efficient of the actual regulatory food safety enhancement system particularly regarding *Listeria monocytogenes*). However, the statistical methodology has not been well described, particularly how the significant differences between groups were determined.

Reviewer #4

I think the data do suggest that *Listeria monocytogenes* contamination at retail is a very significant part of the problem. The analysis does support the need to collect environmental and food contact surface samples at retail establishments. It may be

beyond the scope of this report, but I'd like some clarification as to the jurisdictional issues here. I thought retail food safety was the province of the states.

I don't think the data and analyses are currently sufficient to develop a regulatory strategy for dealing with contamination originating at retail, and again, I'm a little confused about the jurisdictional issues.

Reviewer #5
Yes, the major advantage for risk assessment is the ability to compare different scenarios. However, it was the data on prevalence that was most convincing. There are many assumptions in the calculations of concentrations that may over or underestimate. For example, why does the distribution for retail sliced (Fig 11) show a long left-sided tail compared to plant sliced? Because the detection limit was the same for each and the N was similar, I would expect the tail to be about the same on the left, but much different on the right.

RESPONSE: Further details on the statistical tests used have been added. An evaluation of the repeated measures from the same store has been added based on the logistic regression approach suggested by Reviewer 2.

Reviewer #1
Modeling cross-contamination at retail should be considered, but first, data on sources of contamination and microbial ecology needs to be obtained. This data should be collected using a combined molecular epidemiology and conventional microbiological approach. The most practical approach would be to select 4 or 5 representative delis and do comprehensive sampling and testing of incoming product and the deli environment along with subtype characterization of L. m isolates. Sampling over a period of one year may be needed. A decision about the necessity of modeling cannot be made until this type of information is obtained.

Reviewer #2
I think it is. The data is suggesting such phenomenon.

Reviewer #3
Cross-contamination of RTE meat and poultry products by food handlers and consumers is a major risk factor for listeriosis. The central idea of the proposed regulation on the control of *Listeria monocytogenes* is setting the pathogen reduction as targets in RTE, mainly for the retail establishment in order to meet these targets. In this context the targets for *L. monocytogenes* could be established. However, there is still a lack of knowledge for the best available means of preventing the *L. monocytogenes* infections at the environment production level, which may hamper the setting of realistic targets and drawing up the control programs. Thus, hygienic food handling practices in the food services should be promoted.

Reviewer #4
Taking the questions in reverse order: I suspect that adding cross-contamination modeling would add additional variability AND uncertainly to the model predictions.

While a complete set of cross contamination models for all retail foods and all retail surfaces is not available, there are some data from several research groups (Ryser at U Michigan, Schaffner at Rutgers University, and the Dutch RIVM group) that allow approximate rate calculations.

A more important need than the cross-contamination rates data would be both a modeling platform that allows discrete event simulation and data on the sort of discrete events taking place at retail. For example, it is not enough to know cross-contamination rates, one must also know the order in which events occur, and the variability in that order: one day ham might be sliced before cheese, on another day after.

My advice is that instead of beginning another modeling exercise for cross-contamination at retail, a better course of action would be to begin to collect environmental and food contact surface samples at retail establishments, as noted in question 3 above. Modelers should be involved in discussions as to what data will be collected, so that when the data are collected, their utility for modeling will be maximized.

Reviewer #5
This depends on the purpose of doing so. I do not see that it is necessary for this risk assessment.

RESPONSE: FSIS will continue to evaluate the need for cross-contamination modeling at retail, but generally agree that more detailed contamination and ecological data are needed.

Reviewer #1
See answer to number 4.

Reviewer #2
No comments.

Reviewer #3
Viewing that the document demonstrated a high level of *Listeria monocytogenes* in RTE meat and poultry at retail, a change in regulatory policy on *L. monocytogenes* (cross contamination between RTE meat and poultry products and their environment) should be brought up within the framework of a risk analysis scheme (by identifying the sources and factors contributing to *L. monocytogenes* in the retail environment) which could be possible through the basis of a complete revision of the risk assessment.

Reviewer #4
Rates between meats and slicers have been well characterized by Ryser's group.

Data are needed on the types of events that happen in retail. This will require either video taping retail workers or using an observer trained in notational analysis to track a series of events. Several research groups have done this for consumer kitchens, but I don't think it's been done for retail yet. Ben Chapman at Guelph is doing it now for restaurant kitchens.

Data on meats and other surfaces those meats may contact are needed (meat to worker gloves, work gloves to many retails surfaces); survival of *L. monocytogenes* on retail surfaces when transferred from meat to hands to surface.

Clearly adding this information to models would increase variability and uncertainty, but it would also make the models more realistic.

Reviewer #5
Samples would be needed at different times of day, for different products and perhaps of the equipment itself.

RESPONSE: FSIS will continue to review retail level data as it becomes available.

Reviewer #1
NA

Reviewer #2
No comments.

Reviewer #3
Regarding the excel model, the information appeared proper and no noticeable errors were identified. Also, with respect to the results, no relevant comments on the modification for this risk assessment could be outlined.

Reviewer #4
The model does not appear to contain any errors, however the long run time for the model (hours) makes evaluation challenging. This is further compounded by the choice of excel with VB as the modeling environment. I realize this was a choice made by FDA, not the current modeling team, who only had to live with the FDA choice.

Reviewer #5
There is not enough information regarding the spreadsheets to review the model. For example, there is no description of what each spreadsheet contains. Each file contains

multiple spreadsheets within it, but there is no explanation of what each spreadsheet contains or the purpose of each spreadsheet. The formulas for calculations need to be listed and described either in the text or an appendix. The exposure assessment models are large and cumbersome. It takes over 8 hours to run one of the spreadsheets. The quality assurance needs improvement. For example, when I tried to stop a run of the exposure assessment model, the iterations would stop, and then continue at the next step (If it was at #29 with 44,876 iterations, it would automatically go to #30 when restarted). The instructions with the files only describe how to start the run, but do not give any details of how the program uses the data.

There is an error in the dose response model. When I tried to run the program (by clicking on the Run button), I got an error message for each file (elderly, intermediate, and neonatal). The error message was: compile error, can't find project or library. If I needed to input data before the run, this was not clear in the instructions.

In the extra materials "Simple instructions for running FDA-FSIS risk ranking models," the instructions for running the model are not adequate. First, there is no file named Delimeat6 FSIS Scenario 1.xls file, but if the Delimeat6 files specific for each scenario are used, then there is no "Results" worksheet—do they mean "Output"? These instructions are very confusing.

RESPONSE: To reviewer 5: Unfortunately, there is no manual available for the FDA model. A full development of the approach is given in

> FDA/FSIS. 2003. Quantitative assessment of relative risk to public health from foodborne *Listeria monocytogenes* among selected categories of ready-to-eat foods. Washington, DC. Available at http://www.foodsafety.gov/~dms/lmr2-toc.html.

This model has previously undergone peer review. The models are not designed to be stopped and restarted. The likely error for the dose-response model was improper installation of the DoseFrequency.msi program.

Reviewer #1

See Major Comment #1 (in additional comments).

Reviewer #2

Statistically speaking, the answer to this question will depend on the new analysis results after adjusting for the correlated nature in the data set.

Reviewer #3

For the future, I think that it is more appropriate to have *Listeria monocytogenes* picture in the environment at retail establishments and on food contact surfaces viewing that it is well known that microorganisms could attach on the surfaces and serve as a source of potential contamination for any product coming in contact. High levels of *L.*

monocytogenes cells in the ready-to-eat meat and poultry products in a retail facility as a possible mitigation of the organism in the products should be, as well, considered.

Reviewer #4
Taking the ideas laid out above, if I was in charge, this is the order in which I would proceed. Tasks #1 and #2 can proceed in tandem.

1. Collect environmental and food contact surface samples at retail establishments
2. Collect data on specific retail events using video or notational analysis
3. Build draft models using 1, 2, and published data as a preliminary exercise.
4. Consider full cross-contamination model after review of the results from #3

Reviewer #5
To really improve risk assessment for listeriosis, I believe we must examine the assumptions made for dose response modeling. More research is needed in dose response, particularly for the different subpopulations. For example, it is likely that the intermediate group (assuming mostly healthy adults) would have a different dose response curve than elderly or neonatal.

To the exposure assessment, there were a lot of samples collected, but the text is confusing on how much information was known about each sample. If there were duplicate samples taken from the same source, it is not clear and these would not be independent samples. From this report I cannot determine whether additional samples are needed or not.

RESPONSE: Additional analyses have been included to evaluate the duplicate samples from each store.

Additional Comments

Reviewer #1
Major comments and significant editorial revisions
(These must be adequately addressed for the report to be acceptable.)

Page 8.
1. "The analysis indicates the need for three types of data…." I disagree with this conclusion. The first and second type of data should be part of the same study and so are closely related; subtyping data is needed to interpret ecology data. The subtyping and ecological data should be from the same data set to allow for the best interpretation. I suggest revision to "…indicates the need for two types of data. Epidemiological/ ecological data to indicate how *L. monocytogenes* contamination occurs and its origin in the retail environment, and data on how consumers treat ready-to-eat product sliced at retail versus product sliced at the manufacturing facility." Leaving the report as written

could result in three different studies being funded, when only two different studies should be funded.

Also, I disagree with examples of types of data needed. Subtypes for this type of study are better distinguished based on gene sequencing, not antimicrobial susceptibility or PFGE patterns. Gene sequencing provides better discrimination and is less expensive to obtain.

RESPONSE: The sentence has been changed to mention only gene sequencing and serotype results.

Page 9.
2. “a serious public health problem”. Many public health professionals would disagree with this and classify listeriosis as a minor public health problem, even though the disease itself can be serious. On page 11, listeriosis is called a “rare” disease. Coronary heart disease, various types of cancer, and AIDS are examples of truly serious public health problems because of their higher mortality. Please revise accordingly.

RESPONSE: Changed to “a serious food-borne public health problem.”

3. “…reached a plateau.” A plateau implies leveling off a high level. In fact, one can argue that listeriosis is leveling off at a low level; more of a plain then a plateau. Of course it could go lower (perhaps to sea level), but where it is now does not constitute a plateau at this time.

RESPONSE: Changed to: has since leveled off.”

4. “The risk assessment described here is one of several ….” This sentence is unnecessarily complex and confusing. Suggest revision to “The purpose of this risk assessment is to evaluate the relative risk of contracting listeriosis from deli meats sliced and packaged in FSIS regulated processing establishments compared to deli meats sliced and packaged at retail.”

RESPONSE: Changed to suggested text.

Page 11.
5. “with a mortality rate of 30-40%...” I do not know where these mortality rates come from or how old they are, but they need to be checked and updated. The CDC MMWR, data on listeriosis from 1998-2002 shows 256 confirmed cases with 38 deaths. This is about 15% mortality. The mortality rates should be consistent with the age specific illness/mortality ratios given on page 33. (This whole paragraph may need a rewrite, most sources list mortality at 20-30%)

RESPONSE: Changed mortality rate to 20-30%. Added a reference to Mead (1999).

6. “ingested dosage, but also whether the food consumed is …” I understand the intent of this statement, but poor grammar makes it inaccurate. In fact, the influence of high or low risk food on likelihood of contracting listeriosis depends primarily on ingested dosage. Therefore, the “but” conjunction makes this an inaccurate and confusing statement. Revise to indicate that the high and low risk foods are classified as such because they are associated with a likelihood of ingesting different dosages.

RESPONSE: Reworded first half of paragraph.

Page 14.
7. “The following product types were sampled:…” “an antimicrobially formulated product” does not fit with the list. (“antimicrobially” is not actually a word) Was this one product that was sampled? If you sampled a cured poultry product with antimicrobial, what product type would it be classified as? Why is “antimicrobial formulated product” not in figure 4? The description of product types and what was sampled is important and must be clearly described. Were all product types tested with and without antimicrobial? Sentence is not clear.

RESPONSE: Deleted “antimicrobially formulated product” as product type. Added, “Use of any antimicrobial or growth inhibiting agents was to be noted at the time of sample collection. A goal of at least one thousand samples with and without an antimicrobial agent was planned.”

Page 16.
8. “The total number of unique chubs is uncertain….” I understand that each chub was sampled multiple times. According the described procedure, selected chubs yielded five core samples for testing. If you know how many chubs underwent the multiple core sampling, the total unique chub samples can be calculated. Explain why the total number is uncertain. What information is missing that prevents you from doing this calculation? If there were 405 samples, does that mean 81 chubs? May have been sampled many times or were sampled 5 times? Paper says both, very confusing.

RESPONSE: Note that the standard sample size for sliced product was 125 grams, larger than the 25 grams normally used. This larger mass was designed to provide a lower detection limit (0.008 MPN/g rather than the 0.04 CFU/g.
For chubs, multiple core samples were combined to form one larger sample for testing. Apparently, only two sites collected chubs: Minnesota and Tennessee. California and Georgia did not. It appeared likely from the data provided that multiple “large” samples were sometimes prepared from the same chub. Thus the number of unique chubs is uncertain.

Page 18.

9. Classification of product type. Is the category "bologna", actually "bologna of unknown species composition"? Are all the "mixed" samples bologna? The categorization should be explained more clearly and in more detail. The reader should have a clearer understanding of what types of products were actually collected and how they were categorized.

RESPONSE: Changed the paragraph to read:

Some differences existed among the different sites for labeling types of products. After correcting for obvious misspellings and accounting for multiple orderings, the types of products listed in the data were

> beef, beef/chicken/pork, beef/chicken/turkey, beef/pork, beef/pork/turkey, bologna, chicken, chicken/pork, chicken/turkey/pork, ham, mixed,
> pork, pork/turkey, poultry, poultry (chicken), poultry (chicken/pork), poultry (chicken/pork/beef), poultry (turkey), poultry (turkey/pork), and roast beef

Many of these had very few samples. For purposes of this analysis, these categories were combined into 5: beef, bologna, pork, poultry, or mixed. Product labeled as "bologna" was classified into different product types. If labeled by the sampler as "beef bologna", it was categorized as beef. If labeled with mixed components, it was categorized as mixed. If labeled simply as bologna, it was categorized as bologna. Product listed as poultry but containing mixed components was categorized as mixed. For example, the samples labeled "poultry (chicken/pork)" were categorized as mixed

Page 22.
10. "Of the 57 positives…." Revise to "Of the 57 samples positive for *L. monocytogenes*…." Otherwise, the reader might think they were positive for antimicrobial.

RESPONSE: Revised as suggested.

Page 24.
11. "Approximate cumulative density functions…." , and figure 10 caption. I do not understand why these functions are "approximate". Are these not actual functions calculated from actual data? If not, why not? Please revise to explain. Approximate due to lack of data and detection limits? Are both only approximate? Needs explanation.

RESPONSE: Removed "approximate" and reworded other cumulative density plot labels as appropriate.

12. Bottom of page. Instead of "may indicate" revise to "is an indication that". This makes for a stronger statement. "May indicate" implies that you really do not know if it indicates it or not. (Use of the term "indicate" does not require proof, only evidence.)

RESPONSE: Revised as suggested.

13. Bottom of page. "There were not significant differences **in prevalence of *L. monocytogenes*** among the four …." Is this what you meant to say? There are many ways for sites to be significantly different.

RESPONSE: Revised as suggested.

Page 25.
14. "Premovement indicates the time prior to the implementation of the Interim Final Rule" The explanation of "premovement" is not sufficiently clear or precise. (What is the "time prior" to implementation? 1 day? 5 years? 30 years? What is the movement?) The term "premovement" is perplexing, because the reader must decipher what the "movement" is, what if anything is moving, for how long it is moving, and when the movement occurred. None of this is clear. If the "movement" is the implementation of the Interim Final Rule, why not call it "Before Interim Final Rule Implementation". Yes, this requires a few more words, but it is clear. If you must use an obscure term such as "premovement" in the table captions, at least add footnotes that precisely define it. When was the economic study completed to determine time prior to IFR.

RESPONSE: The term "premovement" is jargon and it has been removed from the document. The economic study was conducted after the implementation of the Interim Final Rule to estimate any benefits that occurred as plants shifted among the possible alternatives.

15. "Note that the current use of growth inhibitor is quite different." Different from what? Revise to make a precise comparison. Greater use of GI? Need to specify.

RESPONSE: Revised as suggested. Now reads "Note that the current use of growth inhibitor is quite different from industry practice prior to the implementation of the Interim Final Rule, "

16. Table 1 and 2 (and others). All data presented in tables and figures should be given units. What are these numbers?

RESPONSE: Units now provided for all tables and graphs. Table 1 are counts, Table 2 is a fraction of production.

Page 26.
17. "These fractions were found to be 0.206…." Please add an explanation of the value or subsequent use of these fractions. Used for EGR calculation only?

RESPONSE: Modified to read: By summing all alternative AG1 and AG2A fractions, the total fraction of product with growth inhibitor was calculated to be 0.206. Similarly, by summing alternatives 2B and3, the fraction of product without growth inhibitor was

calculated to be 0.794. These product fractions were used in the exposure assessment of the risk assessment to calculate the exponential growth rate (EGR) as described below.

18. "Most of these reference data **are** from the late …."
The logic here is unclear. Why would the EGR change with the movement (or after the premovement)? *L. m* was probably unaware a movement occurred and therefore would have the same growth properties pre- and post-movement. Please add an explanation.
Also, EGR is not defined when first used. EGR calculated based on fraction of plants using GI and no using GI. Is that what is implied by change with the movement?

RESPONSE: Added to beginning of paragraph: Prior to the Interim Final Rule, fewer plants were in alternatives AG1 and AG2A and therefore less product was formulated with an antimicrobial agent when compared to current conditions. The growth rate of *Listeria* should be lower currently because the nature of the product is different – a greater fraction of product contains antimicrobial agents.

19. "Note that the 14 days is a …." What are the FDA Food Code limits? Please include this information.

RESPONSE: The FDA Food Code limits do not specifically discuss product storage time. The line was deleted.

Page 27.
20. Model results.

The report must provide a clear and convincing justification for fitting data to a log normal distribution. Selection of the distribution type is one of the most important decisions in risk assessment, and therefore must be well justified. This is the basis for many subsequent calculations, but the reader has insufficient confidence that the distribution assumption is correct. Was the data fit to other types of distributions and the distribution that best fit the data used? This is what should have been done. Low count data usually does not fit a log normal distribution. Stating that the "relatively few positive results required that the distribution be considered only approximate" is not good reason for selecting a specific distribution, and actually provides an argument that a distribution other than log normal would probably better fit the data.

There are enough positive results for the retail sliced products to select the best distribution that fits the data. If the data does not fit any distribution type very well, than one should go with the distribution that theoretically would better fit the data (perhaps a Poisson or Weibull). The key point, is that it appears that the data is being fit to an arbitrary distribution rather than selecting a distribution that fits the data.

RESPONSE: Multiple distributions were tested, and greater detail on these results has been added. The cumulative density plots now include both the fitted distributions as well as the observed data so that readers may better judge the quality of the fit. (Note that the

fit was to *Listeria* concentrations – a continuous variable.) The detection limit was also reduced from 0.04 MPN/g to 0.008 MPN/g based on discussion with NAFSS, and this had a major impact on the distribution fit..

21. Figure 11. How well do the simulated distributions represent the real data? Perhaps the number of positives for Plant Sliced is too low to represent this, but how about the Retail Sliced data. You have many positives for retail sliced data and should be able to represent the real data distribution along with the simulated distribution.

RESPONSE: Graphs now include both observed data and fitted distributions.

Page 28.
22. The table caption is not sufficiently informative. Use footnotes to define symbols (i.e. sensor type).

RESPONSE: Censor types now defined in table footnote.

Page 29.
23. Should also show the actual distribution for the retail sliced data.

RESPONSE: Graphs now include both observed data and fitted distributions.

Page 30.
24. Figure 12 is not self-explanatory. Please revise the caption.

RESPONSE: Figure has been revised.

25. Table 5. Are these "estimated" concentration quantiles? What is this cumulative frequency of? Please explain so that the table can be understood independent of the text.

RESPONSE: Table title has been revised.

Page 31.
26. "For example, 32.2% of servings were assumed to be…" The 32.2% figure is better described as a calculation based on the model. Revise to "For example, 32.2% of servings were calculated to be …."

RESPONSE: Revised as suggested.

27. "Given the movement among different alternatives…." This is unclear and obscure. What or who is moving among the alternatives? Revise to something like: "Given the **increased implementation of *Listeria* control procedures at the processing plant and growth inhibitor use in product**, these values are likely to overstate **estimated** deaths …"

RESPONSE: Revised as suggested.

Page 32.
28. Table 8, 9, and 10. These tables are giving **estimated** number of deaths. No people actually died during the running of the models (I hope). All references to deaths in this section should refer to "estimated" deaths or "calculated" deaths.

RESPONSE: Revised as suggested.

Page 34.
29. "include serotype results, antimicrobial …." Serotype results, antimicrobial susceptibility data and PFGE patterns are all poor examples of discriminatory data that should be collected. The information required can be obtained more economically, quickly and reliably through gene sequencing as developed and used by Meinersmann, Katheriou, and Wiedmann. (Gene sequencing gives lineage information which relates to serotype.)

RESPONSE: Revised as suggested.

30. "Results of the risk assessment suggest …." This is a poorly formulated conclusion that is not well founded as written. (Perhaps the intent was correct, just the expression of it flawed.)

The risk assessment report does not provide a basis for suggesting that FSIS reallocate resources to reduce listeriosis, or that such a reallocation would better protect the public health as the final statement implies. Such a reallocation should be made on the basis of comparing various risks to public health (i.e. E. coli O157: H7, Salmonella, Campylobacter). This report does not provide evidence to suggest that reallocation of resources from one risk type to another would improve public health. The report does provide a basis for suggesting that resources employed to prevent foodborne listeriosis would be better employed at the retail level than at the processing plant level. Therefore a shift of resources from processing plant to retail control is warranted.

RESPONSE: Revised as suggested.

Minor editorial comments
Page 7.

1. "Based on these findings …." Delete "performing"
2. "While these results were compelling…." Delete and substitute "The data collected in this study had important limitations."
3. "To gain a fuller understanding", Move "Therefore" to the front of the sentence
4. "assessment done," substitute "completed" for "done"

RESPONSE: All revised as suggested.

Page 9.
5. "The assessment was designed to identify and compare…." Poor grammar as the assessment does not identify the effectiveness of industry practices and controls.
Revise to "The assessment was designed to identify industry practices and controls, and compare their effectiveness in reducing contamination of deli meats with *Listeria monocytogenes*, …."
6. "formulation were predicted…." Delete "much".

RESPONSE: All revised as suggested.

Page 10.
7. Subsequently, in 2003, …." Delete "performing"
8. "Results suggested **that** deli meats sliced and packaged at retail posed the greater risk."
9. "Of the 1,674 annual cases…" This appears to be a number from a specific year, as we do not have 1,674 cases every year. If so, it should read, Of the 1,674 cases reported in (give year).
10. "While these results **are** compelling." I assume the compelling nature of the results has not changed.
11. "suggesting variations in the number…" substitute "differences" for "variations."
12. "Before proceeding, a comment…" Substitute "By convention, food safety risk assessment reports are …."

RESPONSE: All revised as suggested. In addition, some of the specific sentences referenced above are not included in the revision.

Page 11.
13. "Here, however, we…." Delete "slightly".

RESPONSE: Revised as suggested.

Page 12.
14. "This chapter….." . Revise to "This section…." I do not think the section actually describes what is claimed in the first sentence. Revise to correct.

RESPONSE: Revised as suggested.

Page 13.
15. "Because of limited data…. Delete "a study was done to examine". At the end of the sentence add "was determined".
16. "Beginning in 2004…." Delete "conducted a study of", add "determined"

RESPONSE: Revised as suggested.

Page 14.
17. Data collection methods. Revise the following paragraph to:
"Samples were collected by the researchers through the purchase of deli meat. Deli meats were purchased discreetly so that the selected retail establishment would not modify their sanitation procedures. The meat samples were tested for presence and levels of *L. monocytogenes* in NAFSS laboratories using FSIS methodology. (give the reference)
18. "Four designated sites…" Poor grammar. Revise to "The sampling group was comprised of four designated sites in the …"

RESPONSE: Revised as suggested. The methods have been described in detail.

Page 15.
19. "Specific instructions…." No capital for "Researchers".
20. "Collectors were standardized…." Revise to "Sample collection was standardized to maintain consistency."
21. "laboratory method for L. mon…." revise to "was **implemented by the** laboratories…"
22. Footnote. Revise to: "This information was collected, encoded, and tabulated for use in data analysis. Analysts received only coded information for each sample. The FoodNet site, county of purchase…." (I do not think you actually blinded the information, as information has inherently poor sight.)

RESPONSE: Revised as suggested.

Page 16.
23. Revise title to "Number of ready-to-eat samples analyzed at each site."

RESPONSE: Revised as suggested.

Page 18.
24. "The product type for bologna can vary." Product type is a constant not a variable and therefore can not vary. Revise to "Bologna was classified into different product types."

RESPONSE: Revisions made. Entire paragraph now gives more detail on product type.

Page 20.
25. "The nationally …." Delete "much". (Use of "much" implies a subjective judgment.)

RESPONSE: Revised as suggested.

Page 22.
26. "There is some evidence of clustering…" Revise to: "There is an indication that positive samples are clustered by sample location…." "No identifier (or code) for the processing establishment….." (Assuming this is what you intended to say.)
27. "Minnesota did not generally …" Delete "problematic" and add "not possible"

RESPONSE: Revised as suggested.

Page 24.
28. "Samples testing positive…." Revise to: Samples testing positive were further tested for levels *L. monocytogenes*.
Delete "listed as" and add "of"
Delete "Concentrations in excess of >110/g were not enumerated." (This is redundant and a statement of the obvious.
29. "Establishments. The link between positive result and **sample collection time** as well as the …'

RESPONSE: Revised as suggested.

Page 25.
30 "housed in" suggest "formulated" instead of "housed" (although there may be a better word).
31. "made by running" delete and substitute "calculated using"

RESPONSE: Changed "house in" to "maintained." Other changes made as suggested.

Page 26.
32. "temperature is specified…" Delete "not" and insert "nor"

RESPONSE: Revised as suggested.

Page 27
33. "retail is consumed more quickly **than** …"

RESPONSE: Revised as suggested.

<u>Reviewer #2</u>
1. p.10, L -8, "robust" does not fully reflect "extensive", "complete", and "larger sample size".

RESPONSE: Changed "robust" to "comprehensive

2. p13, L -9, add "previously" before "limited data".

RESPONSE: Revised as suggested.

3. p. 19 Figure 5, add the exact number on top of the bar, e.g. 18/2295 for Tennessee. Same suggestion goes for other Figures.

RESPONSE: Revised as suggested.

4. p.21, what is the distribution of the morning vs. afternoon?

RESPONSE: Table added

5. p.22, Figure 8, what about test for the deli-sliced data only?

RESPONSE: Test results added.

6. p. 24, Figure 10, add a smoothed line for each type, and replace one of the type with hollowed symbol.

RESPONSE: Left as is. The smooth line version of the graph was added later after a discussion of the distribution fitting.

7. p.26, L.3, "There" should be "The".

RESPONSE: Revised as suggested. Also added "from Table 2."

8. p.30, Figure 12, the lines and symbols are totally indistinguishable here. Very confusing.

RESPONSE: Figure revised somewhat to include observed data. Color is used to distinguish the lines. Over the scale needed, there is overlap at the upper fractions.

9. Some details for the models used in Risk Characterization section will be helpful.

RESPONSE: As discussed early in the introduction, the Risk Analysis relies heavily on the FDA_FSIS risk model. The reader is referred to documentation for that model.

Reviewer #3

1.1- Page V, Table 5. The key words in the title must be in uppercase such as form as *L. monocytogenes* Concentration Quantities for Retail and Plant Sliced Products.

RESPONSE: The table and figure titles have been expanded so they may better stand alone. Title case is probably not appropriate with this change.

1.2- Page 7, paragraph 4: To gain ……at retail, therefore it was necessary to gather more nationally representative data. The sentence could to be: To gain ……at retail, it was, therefore, necessary, to gather more nationally representative data.

RESPONSE: Revised as suggested.

1.3- Page 8, point 3: Replace have by had in the following sentence: "Prevalence was found …..etc, have no impact on … *L. monocytogenes*".

RESPONSE: Revised as suggested.

1.4- Page 14, paragraph 2: delete are in the following sentence: Four designated …… catchment ~~are~~ comprised the sampling group.

RESPONSE: Revised as suggested.

1.5- Page 15, paragraph 1: Added for the between tested and presence in the following sentence: chub tends to ….pound. A random number ….intact chub. The core sample …. were then tested … presence and level of *L. monocytogenes*.

RESPONSE: Revised as suggested.

1.6- Figures 3, Page. 17, must be removed and the relevant data should be outlined in the text by a sentence.

RESPONSE: Figure not removed, but sentence outlining the data was added.

1.7- Page 19, Statistical Comparison. Add "for *L. monocytogenes"* after 6 in the following sentence: Fifty-seven samples …..rate of 0.76%. Two of these ….. samples, 6 ….in prepackaged …..retail-sliced samples.

RESPONSE: Revised paragraph

1.8- Figure 6, Page 20, should be deleted viewing that all data are in the text. The rest of Tables, Figures, data and results are presented in a way that is easy to make out.

RESPONSE: Figure not removed. While the same data are presented in the text, a visual display is more readily interpreted by some readers. The exact counts of positives and samples were added to the figure.

1.9- Page 26, paragraph 2; Replace not by nor in the following sentence: FSIS *L. monocytogenes* Compliance …… of the product. No temperature is specificied ……. Life, not is ….its self specified.

RESPONSE: Revised as suggested.

1.10- Page 27, paragraph 1; add a between was and left in the following sentence: *The L. monocytogenes* …….adjusted. As there are no …. For this parameter, it was ..left unchanged …..FDA/FSIS model.
Note: It is important to check all the italic forms for *L. monocytogenes* in the text of the document.

RESPONSE: Did not see a need to add "a" anywhere in the sentence. Instead added "the" between "of…FDA/FSIS model." Italics were checked throughout the document and any corrections made.

Reviewer #4
Itemized comments:

Page vi: Bookmark not defined.

RESPONSE: The Table of Contents has been revised and corrected.

Page 8: "chub' needs to be defined, "concentrations > 0.92 cfu/g" is awkward, I suggest rewriting with words. Should all > and < symbols be changed?

RESPONSE: Chub definition added. Math symbols left.

Page 8, last paragraph. It's not clear how FSIS would reallocate its resources, since it does not inspect retail facilities.

RESPONSE: This language has been removed from the risk assessment report in an effort to ensure the report remains focused on the technical risk assessment.

Page 10: "sliced at packaged at processing" typo.

RESPONSE: Corrected

Page 11: There is no "infectious dose" for *L. monocytogenes*, or any other pathogen. There is only a dose response function, that predicts probability of illness. Eliminate the phrase!

RESPONSE: Revised as suggested

Page 14: "Researchers" should not be capitalized, error is repeated throughout the document. Reference missing from end of first complete paragraph. "Blinded" is jargon. Explain for the lay reader. "antimicrobially formulated" is awkward.

RESPONSE: "Blinded" and "antimicrobially" reworded. "(ref)" removed.

Page 15: "tested presence and level" grammar error, What does "collectors were standardized' mean? Trained? If so how?

RESPONSE: Sentences rewritten

Page 18, fig 4: define "n/a"

RESPONSE: Revised as suggested

Page 21: Why were 3rd quarter samples more contaminated? If unknown, then state this.

RESPONSE: Revised as suggested

Page 22: Why were 6,387 fields blank? Why were 50 fields blank? It seems like an important opportunity was missed here. Was any analysis performed using the antimicrobial data? Did it have any effect?

RESPONSE: We do not know why some fields were supplied as blanks. No formal statistical test or data analyses were performed on the antimicrobial data. The antimicrobial data provided here was not used in the risk assessment. Instead, industry data on the fraction of product using antimicrobials was used for the risk assessment.

Page 23: Can any tests be done to determine if this "store effect" is actually statistically significant? The terminology site "visit" is confusing in the figure legend. Is this actually a site number? i.e. site 1 = Joe's market, site 2 = Fred's market, etc.

RESPONSE: The terminology has been modified, and more formal statistical tests at the store level have been added. Recall however that the data provided did not include store identifiers, even encoded/blinded. Store identifiers for this analysis were judgment based on the data and time of sampling. Ties were not included for Minnesota samples, so no store identifiers were possible.

Page 24: I'm not sure the word "time" is correct. It seems that it was only the period of the day (morning or afternoon) that was recorded, not an actual time.
RESPONSE: Added more formal explanation and analysis for time of day testing.

Page 25: "housed" is jargon or a colloquialism. It is not clear how paragraph 2 is actually relevant to the other text on the page. Paragraph 4, clarify which interim final rule. "pre-movement" is an odd phrase. I know what it means from the explanation and context, however I think the readers would be served by finding a better term, i.e. "pre-interim final rule" or "pre-(date of interim final rule)". The "current data" in tables 6-7 does not appear to be exactly analogous to that in tables 1-2. "Volume fractions" is jargon.

"HAACP" is misspelled. It'd not clear how the 14 day assumption is reasonable, given that ~20% of the product is consumed after 14 days!

RESPONSE: "Housed" and "pre-movement" terms were changed. Paragraph 2 edited to provide better context. Misspelling corrected. The dates of Tables 1&2 are different from Tables 6&7. Tables 1&2 were used to calculate exponential growth rates for product with and without growth inhibitor. Tables 6&7 gave the current production of each category of product. The older data was used for calculating growth rates because it better matched the time frame of reported growth rates. This explanation has been added to the text.

Page 27: second paragraph. The effect of faster consumption on risk posed by retail sliced product could in fact be tested by running simulations with different consumption rates: 25% faster, 50% faster etc.

RESPONSE: While these assessments could be performed, they would largely be a mathematical exercise without any data to inform the analysis. This work may be undertaken at a later date.

Page 28: Define "censor type" and censor abbreviations in Table 3.

RESPONSE: Revised as suggested

Page 31: What is the "July 2007 10,240-1"database? "must be input" is jargon. Why even mention the scaling factors and the un-calibrated mode if this was not used? ":Given the movement" is also jargon.

RESPONSE: Form 10,240-1 has been described in the revised report. The text on uncalibrated mode has been removed.

Page 33: same comments apply to summary as to identical text on page 8.

RESPONSE: This language has been removed from the risk assessment report in an effort to ensure the report remains focused on the technical risk assessment.

Reviewer #5

The overall logic of the risk assessment is adequate. Basically, the risk assessment uses the structure of the risk assessment conducted by USDA/FDA/CDC for L. monocytogenes risk assessment (2003). Certain assumptions were accepted for use in the present risk assessment. For example, the shape of the dose response curve was based on a mouse model using an exponential fit. If this assumption is not the most appropriate for *L. monocytogenes*, then the risk assessment will have to be modified at a future date. The description of the data used in this risk assessment is not always complete. Specific examples will be given below. In addition, there are many editorial and grammatical

mistakes in the text that sometimes makes it difficult to interpret. The document needs a thorough editorial revision.

Risk assessments should be transparent to people with expertise in this area. This risk assessment is not. The exposure assessment and dose response models are not well described. Even if this assessment is depending on the former FDA risk assessment for the models, formulas and assumptions should be clearly stated. The dose response models did not run. The error message is described below.

RESPONSE: The FDA/FSIS risk assessment is well documented, has undergone peer review, and is cited throughout the current work. FSIS feels that repeating the FDA/FSIS is worthwhile, except where assumptions or limitations impact the current risk assessment.

On P8, Conclusions, it is not clear why further discrimination of *L. monocytogenes* isolates is needed. What would this contribute to the risk assessment?

RESPONSE: Paragraph reworded for better clarity

P8, 2nd bullet, sentence beginning with "Of the 49 samples sliced at retail…" needs editing. The meaning is not clear.

RESPONSE: Sentence revised.

P9, Background, 1st line: CDC was also listed on the 2003 risk assessment and should probably be cited.

RESPONSE: Personnel from several agencies participated in the 2003 risk assessment, and are acknowledged in that document. However, only FDA and USDA are listed as authors.

P10, L20 – "at packaged at processing establishments..?
RESPONSE: Sentence corrected.

P11, Listeriosis: Information in this paragraph should be referenced. Also, the statement "…intrauterine or cervical infections in pregnant women," is misleading. It is the fetus or neonate that has the severe outcome, not the pregnant woman. The pregnant woman is exposed and the bacteria cross the placenta and invade the fetus. Paragraph may need to be rewritten.

RESPONSE: This information has been removed from the document.

P12, Epidemiology: There is a superscript 7 at the end of the 1st sentence. Is this a reference? If so, why are there only 3 references for the document (P35)?

RESPONSE: Reference added and converted to standard format.

P13, *L.* monocytogenes Dose Response: There were many assumptions and uncertainty factors used in the FDA/FSIS risk assessment (2003) that need to be addressed in this document. Were these uncertainty factors used in the dose response model for this assessment? If so, they should be listed even if the original risk assessment dose response curve was used. For example, were uncertainty factors used for differences in strain, virulence, and extrapolation from mouse to human. If so, these need to be listed and briefly described.

RESPONSE: The dose response model used in this risk assessment and the FDA/FSIS risk assessment were identical. Differences in strain and virulence are not explicitly included. As this is described in the cited document, FSIS does not feel it needs to be repeated here.

P14, Data collection methods: Researchers should not be capitalized. 1st paragraph has (ref) that needs to be added. 2nd paragraph, 2nd line: delete "are". 2nd paragraph, last sentence: How is the accuracy of the CDC data known? It is probably the only estimate of listeriosis in the US based on continuing surveillance.

RESPONSE: Revised as suggested. Deleted CDC line.

P14, Data collection methods, Sampling: The description of the sampling is not very clear. How was the number of samples collected from supermarkets and independent retailers weighted? Also, what is meant by "…deli exposure is estimated to be 50-75% of the total exposure…." This is very confusing, don't they know exactly how many were purchased at deli counters? Isn't this the purpose of this study?

RESPONSE: Paragraph reworded for clarity.

P14, Data collection methods, paragraph 5: What is meant by "At least 1000 samples …from each site"? That sounds as if 1000 samples were taken from each site (ie grocer, four states?) for each category.
RESPONSE: Paragraph reworded for clarity.

P14, Data collection methods, 6th paragraph: 2nd sentence needs editing. Meaning is not clear.

RESPONSE: Paragraph reworded for clarity.

P16,L3: If the total number of unique chubs are unknown, then how can an analysis be done for the chubs. Assuming that each chub should be a N=1 and multiple samples of one chub should be combined. This seems to compromise the validity of this data.

Figures: Legends need to be added to each figure giving a better explanation of what is shown. Also there are no error bars shown on any figures. If all data shown are discreet numbers (rather than averages) then putting the number of samples above each bar would be helpful. For example, Fig 5, show the number of samples from each state.

RESPONSE: Because of the encoding/blinding used, the exact number of independent chubs could not be determined. So the chub data was not used for any statistical analysis. All bar graphs now include counts above the bars.

Figure 9 is very confusing. The numbers given in the paragraph do not match the numbers of the graph. For example, where are the 41 sites. How this graph shows that a few retail stores were more likely to have contaminated product across sampling days is not clear.

RESPONSE: Figure has been revised somewhat with additional explanation.

P26, 3rd paragraph, Line 12: 75-58%-- is this a typo?

RESPONSE: Yes, typo. Corrected to 75-85%.

Table 4 needs more explanation. What are the parameters given?

RESPONSE: Mean and standard deviation, as given in the column headings.

Figure 12: Cannot distinguish which line is retail or plant sliced.

RESPONSE: Current version of the document is designed for color viewing.

Table 8, 9 and in text: suggest adding "Estimated" before "…number of deaths…" to emphasize that these numbers are based on many assumptions, many of which would overestimate the number of deaths. For example, assuming that a negative result had 0.04 CFU/g when some may have had zero and that these were set to a total of 390 deaths.

RESPONSE: "Estimated" added throughout.

P33, 2nd paragraph: Is the illness/mortality ratio correct? If so, does this mean that the intermediate group had a very similar ratio as neonatal, and the elderly were much lower?

RESPONSE: Ratios are correct. Keep in mind that the FDA/FSIS model calculates deaths first, then imputes illnesses. The dose-response models (i.e. susceptibility) for mortality are different among the 3 age groups.

P34. last sentence: This is a risk management decision and may not be appropriate for the risk assessment.

RESPONSE: The document has been rewritten to focus on the technical risk assessment and to remove discussion of risk management/policy implications.