Peer Review Comments and Responses on the

2003 FSIS *Listeria* Risk Assessment

FSIS had the *Listeria* risk assessment reviewed by experts in risk assessment modeling, predictive microbiology, and public health. Experts were drawn from both within USDA (but outside of FSIS) and from other governmental agencies, academia and the private sector. Specifically, reviews were received from three agencies within USDA: Office of Risk Assessment and Cost-Benefit Analysis, Agricultural Research Service, and the Animal and Plant Health Inspection Service; from Health Canada; from three academic institutions (i.e., Cornell University, Tuskegee University, North Carolina State University); and from Decisionalysis, Inc., a private risk consulting firm.

Reviewers were asked to: 1) evaluate whether the modeling approach used in the FSIS *Listeria* risk assessment answered the specific FSIS risk management questions; and 2) to evaluate the data and underlying assumptions used in the FSIS *Listeria* risk assessment. The specific risk management questions were:

1) How effective are various food contact surface testing and sanitation (corrective action) regimes (e.g., vary the frequency of testing by plant size – large, small, and very small plants) on mitigating *L. monocytogenes* contamination in finished RTE product, and reducing the subsequent risk of illness or death?;
2) How effective are other interventions (e.g., pre- and post-packaging interventions or the use of growth inhibitors) in mitigating *L. monocytogenes* contamination in finished RTE product, and reducing the subsequent risk of illness or death?; and
3) What guidance can be provided on testing and sanitization of food contact surfaces for *Listeria* species (e.g., the confidence of detecting a positive lot of RTE product given a positive food contact surface test result)?

(* Note: none of the questions relate to non-food contact surfaces.)

In general, all of the reviews acknowledged that the FSIS *Listeria* risk assessment was a "substantial" accomplishment in the timeframe allotted for its development. Secondly, most found the risk assessment modeling approach appropriate to inform risk management decision-making. Finally, there were comments about underlying assumptions that conflicted with one another (e.g., some thought that the calibration of the model was appropriate and a standard approach, while others thought it was not appropriate).

Many of the reviewers had editorial comments or corrections, which will be incorporated into the revised report. Comment summaries, grouped by topic, and Agency responses follow.

I. Reviewer Responses on Whether the Modeling Approach Used in the FSIS *Listeria* Risk Assessment Answered the Specific FSIS Risk Management Questions

Almost all reviewers found the risk assessment modeling approach appropriate for answering the specific risk management questions. One review noted that the risk assessment satisfied several important criteria for good risk analysis, including: providing a probabilistic range of estimated public health benefits; disaggregation of the estimated public health benefits by well-specified consumer subpopulations (age classes); consideration of a broad range of regulatory alternatives, including the minimum food contact surface testing provisions of the proposed RTE rule (66 FR 12569, February 27, 2001); clear presentation of the data, assumptions, and methods used in the analyses and their limitations; evaluation of model stability; and analysis of the sensitivity of the results to different assumptions regarding important implementation and biological variables.

One reviewer suggested that because of a lack of sufficient data, the risk assessment (and presumably any risk assessment) would not be able to inform risk management decisions. This is a misunderstanding of the purpose of risk assessment as a public health tool, which is to use available data and information in a model to predict outcomes (i.e., effectiveness of an intervention in reducing illnesses) to inform decision-making. Without risk assessment, the public health benefit of selecting one policy intervention over another would be unknown. On the other hand, waiting to have all the data would prevent public health measures from being implemented in a timely manner. The risk assessment methodology is a tool designed to inform decision makers when all of the data or information are not known. Risk assessment allows there to be informed decision-making.

A couple of the reviewers were unable to determine if the FSIS *Listeria* risk assessment modeling approach was appropriate to answer the risk management questions. These indeterminate reviews were based on concerns expressed about the appropriateness of assumptions, data, or both. These concerns are addressed in the next section.

II. Reviewer Responses on Appropriateness of the Data and Underlying Assumptions Used in the FSIS *Listeria* Risk Assessment Comments on the In-Plant Dynamic Model A. Contamination Event

a. Time Between Contamination Events (Frequency of Contamination)

Comment: Almost all reviewers commented that the assumption that the time between contamination events is random. The use of a lognormal distribution was challenged. Use of an exponential distribution was suggested as being more theoretically supported. Yet, one reviewer demonstrated that the difference between the lognormal and exponential distribution fits to the data appeared to be small. A few reviewers were concerned that only data available was from a single plant linked to a *L. monocytogenes* outbreak.

Response: The decision to use the lognormal distribution in the risk assessment was based on convenience and our determination that the lognormal distribution fit the data better than the exponential distribution. The difference between the lognormal and exponential distributions is, as noted by the reviewer, not substantial. The available data to estimate the time between contamination events came from an in-depth verification investigation of an establishment producing ready-to-eat meat and poultry product associated with an outbreak of *L. monocytogenes.* As noted by other reviewers, this was the only data available for this model parameter.

Comment: One reviewer commented that there was a typo in the calculation of the mean time between contamination events. Specifically, 13 days instead of the correct value of 17 days between events for one of the observations in Table 2 of the *Listeria* risk assessment report.

Response: The calculation was redone using the correct value of 17 and this resulted in a slight change in the mean time in contamination event (i.e., 23.5 ± 39.2 days rather than the previous 23.1 ± 38.4 days).

b. Duration of Contamination Event

Comment: Some reviewers were concerned that available data for estimation of the duration of a contamination event was limited (i.e., Tompkin (2002)).

Response: The Tompkin (2002) data was peer reviewed, represented industry data, and is currently the best available data. Therefore, FSIS concludes that its reliance on these data was appropriate, but food safety research in this area would be valuable for future iterations of this risk assessment to guide decision-making.

Comment: A few of the reviews questioned the selection of a lognormal distribution and requested justification for this selection.

Response: As noted by one reviewer, the available data were fit to several plausible statistical distributions, taking into account censored data. Initially other theoretical distributions were considered, but in light of technical comments within the Agency to select a distribution based on fit, a lognormal distribution was selected. The choice between the top two ranked distributions (loglogistic and lognormal) was not important, however, because the difference in the fit is <1%. The lognormal distribution was selected for ease of implementation and interpretation.

c. Level of *Listeria* species transferred from the Plant Environment to Food Contact Surface

Comment: Two reviews commented on the estimation of the level of *Listeria* species transferred from the environment to food contact surfaces. One review thought that the calibration of the model to obtain this parameter was arbitrary. Another reviewer commented that, given the current lack of data on *L. monocytogenes* levels in ready-to-eat product, the calibration approach was the "best of the limited options available to FSIS."

Response: FSIS concurs that the calibration of the model to obtain this input was preferable to other options (e.g., expert elicitation to estimate the level of *L. monocytogenes* transferred to food contact surface). Model calibration consists of changing values of model input parameters in an attempt to match the model's output with independently derived values within some acceptable criteria. Calibration has been used for decades as a standard step in the modeling process, particularly when specific parameter values are unknown and relevant data do not exist. Calibration is well-founded in the scientific literature. While it would be desirable to have data regarding, for example, the concentration of *Listeria* spp. on food contact surfaces, such data do not exist. In this case, it was entirely appropriate to use calibration methods to estimate the distribution of the concentration of *Listeria* spp. on food contact surfaces by matching the model's output with the FDA/FSIS risk ranking model's estimated input for *L. monocytogenes* contamination at retail.

Note that model calibration is distinct from model validation. Model validation is a process for assessing how accurately the model predicts actual phenomena in nature. Validation involves the comparison of model predictions with empirical data not used in developing the model. Given the limited data available to develop this risk assessment model, validation was not accomplished. Nevertheless, because annual mortality from *Listeria monocytogenes* in ready-to-eat foods is expected to be reasonably constant from year to year (absent some purposeful intervention to prevent such mortality), this model's predictions about annual mortality are expected to be reasonably consistent with estimates from future public health surveillance data. Such consistency provides a limited validation of this model.

Comment: Several reviewers were concerned about the assumption of homogeneity of contamination for the food contact surface and for the product.

Response: Homogeneity of contamination is a reasonable default assumption often used within the field of microbial and environmental risk assessment. The degree of spatial cluster is unknown and selection of the extent of cluster would be arbitrary. Furthermore, an assumption of clustering should be coordinated with assumptions of sampling design strategies. For example, if we know the agent is limited to a specific fraction of the food contact surface area, sampling strategies might be designed to ensure at least sampling of that area. It should be recognized that a clustered distribution assumption would require recalibration of the concentration distribution and result in higher concentrations in the contaminated area. This heightens the likelihood of detection if any portion of this contaminated region is sampled. A sampling plan with many composited samples each over a very small sampled area, would compensate for the clustering.

B. Transfer of *Listeria* species from the Food Contact Surface to RTE Product

Comment: One reviewer commented that while the derivation of the values used from the data is clear, the distribution and parameters used, and subsequent truncation at 100% transfer produces a distribution with two peaks (i.e., one is a low transfer coefficient and the other is a peak at one, indicating complete transfer of *Listeria* species from the food contact surface to the ready-to-eat product). The reviewer suggested that this assumption be tested with a sensitivity analysis.

Response: The actual approach used does not result in a two-peaked distribution. It is certainly true that because of the truncation in the generation of the transfer coefficients, the resulting distribution is not normal. The figure below presents a histogram of 10000 simulations for the transfer coefficient using the approach in the risk assessment. There is no evidence of a bimodal distribution. An alternative approach was considered – to simply draw with replacement from the 3 transfer coefficient values provided by Midelet and Carpentier. The empirical cumulative density functions for both approaches are shown in the figure below. In both cases, 10000 values for the transfer coefficient were generated. The black curve (below) represents the algorithm selected for the risk assessment. The impact of the truncation can be seen in the jump at a log transfer coefficient of 0. Approximately 45% of the log values are set to 0. Twenty percent of the values are less than –1. The alternative approach is shown in red. Only 3 values are available, so the resulting curve resembles a step function. Using this approach, 33% of the data have a log transfer coefficient of 0, 33% have a value of –0.14, and 33% have a value of –0.34. Obviously, the method chosen results in more variable transfer coefficients, with the possibility of much lower values than available from the alternative approach. This seemed an appropriate approach given the limited data.

C. Ratio of *Listeria* species to *L. monocytogenes*

Comment: One reviewer commented that the assumption that ratio of the level of *Listeria* species to *L. monocytogenes* would be may not be a reasonable assumption.

Response: Given the lack of specific data, the assumption that the ratio of *L. monocytogenes* to *Listeria* species prevalence applies to the ratio of the concentrations is a reasonable use of available data. Moreover, in another review of this risk assessment, it was found that the assumed truncated normal (52%, 26%) distribution compared to a non-parametric empirical cumulative distribution of the data provides a reasonable fit.

D. Growth of *L. monocytogenes* from Plant to Retail

Comment: Reviewers requested further explanation for incongruity between the prevalence of *L. monocytogenes* in ready-to-eat product at retail versus the prevalence in ready-to-eat product in plants.

Response: As discussed in the risk assessment, there appear to be contradictions between the reported prevalence of *L. monocytogenes* in ready-to-eat product produced at the plant compared to recent data on the prevalence found at retail. It was not possible to reconcile these differences among available data. Extensive analysis of this discrepancy was completed in Appendix B of the risk assessment report.

E. General Comments

Transparency of the FSIS *Listeria* Risk Assessment

Comment: Reviewers commented that since the FDA/FSIS risk-ranking model will not be released until this summer, the FSIS *Listeria* risk assessment (which uses the exposure pathway for deli meats and dose-response relationship from a revision of this model) is not transparent.

Response: The exposure assessment pathway for deli meats and dose-response relationship is from the draft FDA/FSIS risk-ranking model that has been updated based on public comments. Changes to the exposure pathway for deli meats are included in Appendix A of the risk assessment report. Moreover, data used to make these updates to the exposure assessment pathway for deli meats from the 2001 FDA/FSIS risk-ranking model (posted on the web at: http://www.foodsafety.gov/~dms/lmrisk.html) are available in Docket 03-005N.

Use Additional Data

Comment: Several reviewers suggested that research be conducted to fill data gaps in the FSIS *Listeria* risk assessment model.

Response: The FSIS *Listeria* risk assessment was based on available data in the peer-reviewed literature or provided to the Agency. In some instances, presentations were made to the Agency, but none or limited data were made available to the Agency. Data used in the risk assessment must be made available in the docket so that the risk assessment is transparent and reproducible. Anecdotal evidence and statements made about experience need to be supported by data to provide a sound scientific-basis for risk assessments. The Agency welcomes the submission of data to the docket for consideration.