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 <u>Listeria</u> 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 <u>not</u> known. Risk assessment allows there to
be informed decision-making.

A couple of the reviewers were unable to determine if the
FSIS <u>Listeria</u> 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 <u>Listeria</u> Risk
     Assessment**

<u>**Comments on the In-Plant Dynamic Model**</u>

A.   Contamination Event

  **a. Time Between Contamination Events (Frequency of
     Contamination)**

<u>Comment</u>: 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.

Histogram of TC.bounded
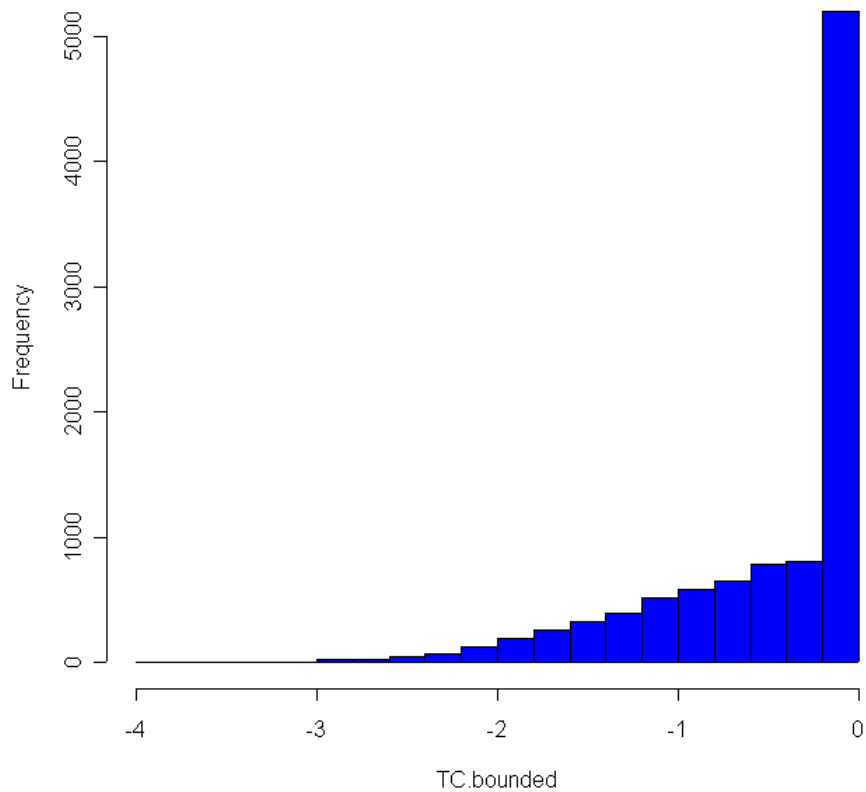
An alternative approach was considered – to simply draw

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.

Cumulative Density Function Plot

Fn(x) — Log Transfer Coef
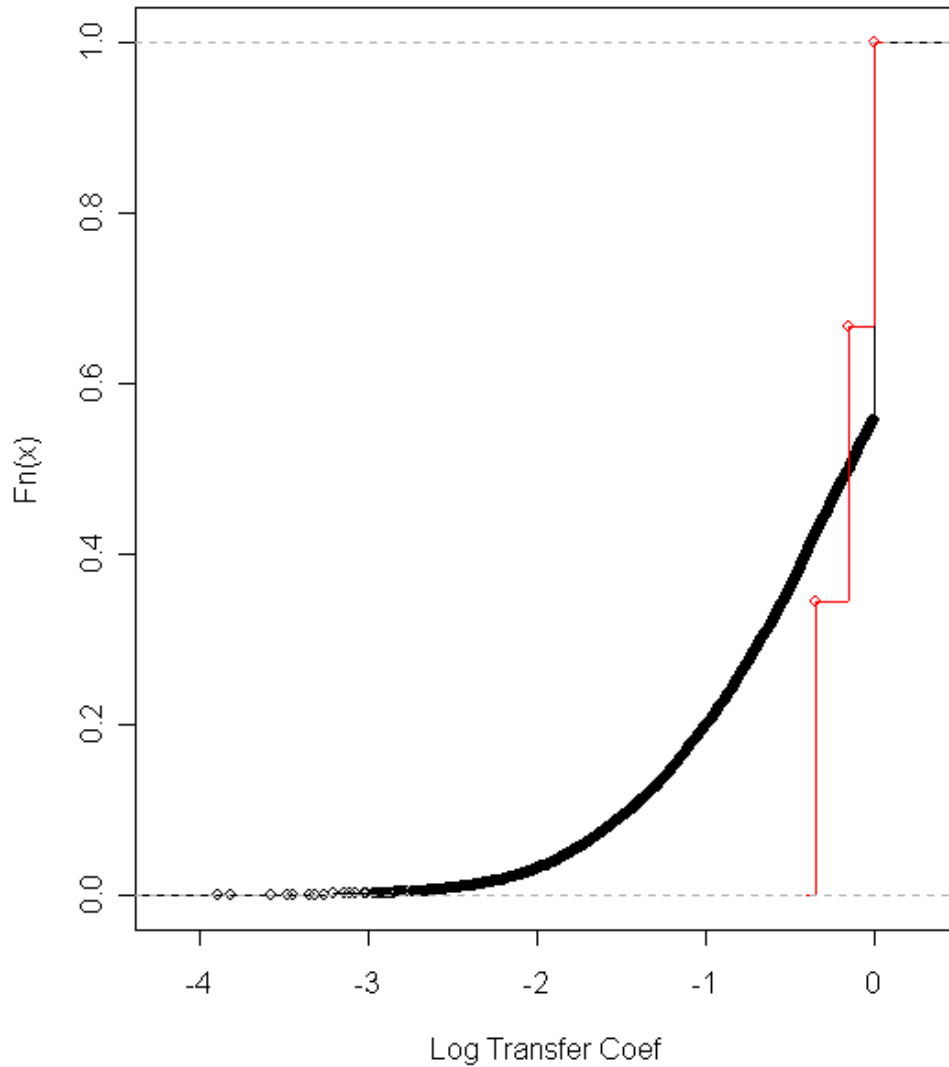
C. Ratio of Listeria species to L. monocytogenes

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.