Response to Peer Review Comments

Risk Assessment of the Impact of Lethality Standards on Salmonellosis from Ready-to-Eat Meat and Poultry Products

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Prepared For:

Office of Public Health Science
Food Safety and Inspection Service
United States Department of Agriculture

By:

Decisionalysis Risk Consultants, Inc.
Ottawa, Ontario, Canada K1H 6S3

as a Sub-Contractor to SAIC

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The following table presents the main comments from the peer review and the response/action taken. To review the Risk Assessment of the Impact of Lethality Standards on Salmonellosis report and model, expertise in the following primary areas was required: microbiology, food safety, food processing and modeling. Five reviewers were chosen for this task.

The Risk Assessment Division of FSIS recruited the reviewers through SAIC. The identity of the reviewers was withheld from the principal author of the peer review comment and response document at the time of writing. The reviewers are Charles Kaspar, Don Schaffner, Gary Acuff, James Dickson, and Tom Ross.

Note that the following only lists non-editorial comments. All editorial comments (for example, typing errors) have been considered and dealt with appropriately. Note that the page references refer to the Peer Review Draft version of the document and the correspondingly titled Analytica model. Some of the cited estimates may have change in the final version of the document, in response to these comments.

Comment: In my opinion, the "scaling up" of bacterial concentration to CFU/Mkg is very confusing, unnecessary and inappropriate. Maybe this is a common practice with this type of manuscript, but I find it distracting and have difficulty relating the estimates to reality.

Also:

Page 96, lines 25-27. Maybe it is common to "scale up" the bacterial concentration to CFU/Mkg for estimating pathogen burden, but I find this conversion awkward and I get a sense that numbers have been abnormally inflated to a level that is difficult to relate to reality

Response: *Text has been added to the report (page 4) to justify this. In addition for transparency key tables are presented in units of both CFU/Mkg and CFU/g. The conversion is simply a matter of adding or subtracting 9.*

Comment: In my opinion, the Cooked Poultry Deli Meat estimated related illnesses seem extremely high and out of sync with the other presented estimates

Also:

Page 33, First table. Cooked Poultry Deli Meat estimated at 4357 cases? In comparison to other products evaluated, this seems out of sync with reality. This also brings the response to Question 7 (page 45) into doubt

Response: *The estimate of risk is heavily influenced by the consumption mass. The consumption mass is a straight multiplier on the risk per Mkg, therefore products with relatively larger risk estimates per MKg and a large consumption mass will be associated with relatively larger estimates of risk at the product level. To illustrate this, consider Cooked chicken and Cooked chicken patties. Both products have an estimated log risk per Mkg of -0.65. However, Cooked chicken has an estimated consumption mass of 1,346 (Mkg),*

compared to a consumption mass of 117 Mkg for Cooked chicken patties. These consumption masses result in product risks of 2.47 and 1.41 (log cases per annum) or 298 and 25 for Cooked chicken and Cooked chicken patties respectively.

Note also that the reviewer did not provide any data upon which to judge that this was in any way 'out of sync'. The number 4357 is calculated under a scenario where poultry was treated at 5-logs, which is not the current expected reality (7 logs) and should not be expected to represent the current reality.

Product	*Risk Per Mkg*	*Consumption mass (Mkg)*	*Log Product Risk*
Roast Beef, Corned Beef	*-5.43*	*85*	*-3.50*
Fully Cooked Beef Patties	*0.04*	*0*	*-1.10*
Cooked Pork (Cooked Ham, Pork BBQ)	*-5.96*	*100*	*-3.97*
Cooked Turkey (non-Deli)	*-1.63*	*386*	*0.96*
Cooked Chicken (Nuggets, Tenders, non-Deli)	*- 0.65*	*1346*	*2.47*
Cooked Poultry Deli Meat	*-0.54*	*455*	*2.12*
Cooked Chicken Patties	*-0.65*	*117*	*1.41*
Beef / Pork Frankfurters	*-1.82*	*400*	*0.78*
Bologna, Liverwurst, Polish Sausage, other Cooked Sausages	*-1.52*	*132*	*0.60*
Poultry Frankfurters	*-1.10*	*305*	*1.38*
Summer Sausage, Thuringer, Cooked Pepperoni	*0.65*	*55*	*2.39*
Salami, Uncooked Pepperoni, Chorizo, Soudjuk	*0.83*	*55*	*2.57*
Meat Sticks	*1.31*	*18*	*2.57*
Beef Jerky	*1.38*	*10*	*2.39*
Uncooked Country Ham	*-2.37*	*32*	*-0.87*
Prosciutto, cappicola, pancetta, basturma	*-1.23*	*3*	*-0.70*

Comment: Page 12, lines 14-18. Is this text referring to calculations carried out in this document or a reference to someone else's work? It would be helpful to include a reference for this example of most probable number (mpn) enumeration or clarification should be provided to indicate that this occurred within the present study.

Response: *It has been clarified in the text that the data in the baseline study are reported as MPN.*

Comment: Page 13, line 8 (also page 96, lines 25-27). Why did the authors express pathogen load in terms of CFU/Mkg? Aren't lethality performance standards expressed in required/expected log reductions per g?

Response: *Text has been added (page 4) to justify this. In addition, for transparency, key tables are presented in units of both CFU/Mkg and CFU/g. Further, lethality performance standards are expressed as log reductions. The units of mass (e.g., per gram) are not relevant to expressing lethality performance, but may be expressed to indicate the completeness of the application (i.e., to every gram).*

Comment: Page 56, lines 23-26 "If the process applies a 4-log reduction, this implies that each organism has a 0.01% (or p=0.0001) chance of survival."

A process that applies a 4 log reduction is a process which reduces the population *per gram of food* by 10^4 cfu. Given the authors two levels of initial contamination ("2 organisms per unit" or "1,000 organisms per unit") the surviving population, would be zero in both cases, assuming a 4-log reduction, even assuming that a "unit" was one gram.

I believe that this is a fundamental misunderstanding by the authors, in regard to what the performance standards actually mean. The authors need to provide a through explanation for this, because it takes considerable effort by the reader to determine exactly how they arrive at this conclusion

Response: *The reviewer here is in fact mistaken. More text has been added to the document (page 4) to explain the interpretation of log-reductions in the context of the risk assessment model. In brief, the logarithmic scale is defined as a scale of measurement in which an increase of one unit represents a tenfold increase in the quantity measured. Similarly, a decrease in one unit represents a tenfold decrease in the quantity. Therefore, a process which results in a 1 log reduction results in a tenfold reduction in the population level (or 10%). This can be interpreted as each organism having a probability of 0.1 of surviving the process. A 4 log reduction results in a 0.01% reduction in the population level.*

Assume a contamination level in a product of 1cfu per 100 grams. On average there are therefore 1/100 cfu per gram, which is equivalent to -2 log cfu per gram. Although it is not physically possible to have 1/100cfu per gram as bacteria are discrete units, this is the contamination ***rate*** *per gram of product such that for 200 grams there are 2 cfu, 300 grams – 3 cfu etc. If it is assumed the* ***rate*** *is 0 cfu/g then there cannot be 1cfu per 100g, or 2cfu per 200g etc.*

Applying a 2-log reduction results in a reduction in this contamination rate to -4-logs per cfu. This means than there is now a contamination rate of 1 cfu per 10,000g of product. This can be interpreted as 1 gram of product has a probability of 0.0001 of being contaminated with 1 cfu. Therefore, because of the discrete nature of bacterium, 1 gram out of every 10,000 grams produced will be contaminated with 1 cfu, therefore demonstrating that a 2-log reduction does not eliminate risk. At small levels of production this level of risk may be considered negligible. However, at high levels of production, for example 1Mkg this translates to a contamination level of 2 logs.

Comment "Beef MPN Measure Overide" and "Beef MPN Measure Overide Value") that should enable the effect of assumptions concerning the value of the maximum MPN value to be estimated (for MPN = 1000 and MPN = 10,000), but it was not apparent how this option is available to model users. It is not present in the pork or poultry MPN calculation modules.

Response *These nodes were added as a mechanism to test the assumption that a value of 240MPN/g applies for samples reported higher than 110 MPN/g. It is not intended to be available to model users. Furthermore, the problem related to the assumed value of 240 MPN/g only applies to ground beef in the baseline study as it was the only product in which all tubes in the MPN procedure were positive (for one sample).*

Comment: A list of assumptions and a summary of their potential importance would aid decision makers relying on the model.

Response: *It is agreed that this would be a desirable addition to the current documentation, however this is also a time consuming task. Every effort will be made to make this addition within*

the timescale of the project. A new section on uncertainty analysis may assist with this assessment of importance.

Comment: The inclusion of the 'no growth' and 'low growth' estimates in the outputs (and calculations leading to them) is redundant because the no growth scenario always corresponds to a fixed frequency of contamination with one cell per serving (resultant risk 0.00252) which is always ten times higher than the low survival scenario (1/10th the frequency of contamination resulting in a risk estimate 1/10th as great, i.e. 0.000252).

Response: *These results are included for transparency. The no growth scenario presents a baseline case. The structure is in place to allow future updates to the model for example changes to the assumptions regarding low growth.*

Comment: The response to question 1 is somewhat frustrating because, having gone to great lengths to establish a model to perform the required calculations to begin to answer the question, no answer was given despite that an answer is implicit in the risk estimates presented. Similarly, despite numerous appropriate illustrations of how one might answer question 4 the questions seems to remain unanswered.

Response: *The question is essentially answered by indicating the increase and decrease in cases of salmonellosis implied by changing lethality standards. Public health significance is captured by the change in the numbers of cases.*

A section termed "insights gained from the model" will be added to the final draft of the document which includes graphs and tables of the findings of the model.

Comment: The limited data presented by Juneja (cited by the authors) offers a little insight into the likely outcomes for *L. monocytogenes* and *E. coli* of alterations to processing conditions based on expected *Salmonella* inactivation (as discussed below in relation to the Comparative Lethality sub-model). Also, this reviewer notes that the question asks about lethality on these two organisms but the response to Question 2 address the difficulty of estimating public health consequences.

Response: *The text has been clarified. The intent was to convey issues regarding the wide variability in the manner in which lethality might be applied across the range of products considered. This variability makes it intractable to predict the effect upon other organisms, as the way in which organisms will respond will be specific to the exact mechanism by which the lethality standard is implemented.*

Comment: P.7. L5/6. This example appears to contradict the earlier statement (P2, L2/3) that the method of inactivation is largely irrelevant to the risk assessment questions posed.

Response: *The text has been clarified here to read: "For these reasons, it is unnecessary to provide detailed characterization of the mechanisms and techniques that are applied to achieve the lethality, other than those related to process involved in general product distinctions (for example drying, curing, heating), assumptions regarding the level of compliance with the standard and, in the case of non-compliance, the extent of deviation from the candidate standard*."

Comment: It is unclear how the calculation of poultry contamination (i.e. *Salmonella per* kg) was determined. This may simply be due inadequate/ambiguous communication but, whereas the translation from *Salmonella* contamination *per* cm2 to contamination *per* kg is transparent, the translation from *Salmonella* concentration *per* ml of whole bird rinses to Salmonella *per* kg of flesh is not. Does the factor 400 in the first table on P. 100

represent the surface area (in cm2) of a bird carcass, or is it the volume (in ml) of the rinse?

Response: *On page 100, the number 400 refers to the number of milliliters of rinse fluid used in a whole carcass rinse to determine the carcass contamination level for broilers and turkeys. This has been clarified by adding units to the table.*

Comment: Section 16: The approach used to estimate consumption levels appears reasonable, though explanation of the "Uncertainty factor" is not very clear. It reads as though this factor is simply "gut feel". Interestingly, the overall consumption level *per* person-year is very similar (within 10%) to estimates recently derived from a similar study concerning food-borne disease risk from ready-to-eat processed meats in a developed, Western, nation.

Response: *The uncertainty factors are currently not used in the risk model calculations to generate the results. The column has been removed from the table in the revised document. The test has been clarified in this section and the uncertainty may be investigated further in a new section to be added to the document called "Uncertainty analysis"*

Comment: SUB-MODEL: Storage and Dose-Response
The modelling in this section is generally sound, but lacks transparency, e.g. the basis of the minimum growth temperature and uncertainty bounds used should be documented as should the source of exponential growth rate at 25°C (n.b the rate used is consistent with published estimates), and selection of parameters (and uncertainty intervals) for the dose-response model used (i.e. WHO/FAO Salmonella in poultry risk assessment).

Response: *Text has been clarified.*
The uncertainty intervals in the model are not used to estimate the levels of risk in the main part of the Analytica model – only the mid values of the probability of illness are used as input to the overall estimates of risk. However the uncertainty will be investigated further in the new section of the document called "Uncertainty analysis"

Comment: SUB-MODEL: STORAGE AND DOSE-RESPONSE
contains an error in the growth rate modelling approach. ..it appears that the minimum temperature for growth (~7°c) has been used instead of the *tmin* value (~4°c). it is recommended that the consequences of the growth rate modelling error identified above be assessed and, if necessary, that the growth model used within the risk assessment be amended to make it consistent with minimum growth temperatures and *tmin* values for salmonellae and the risks reassessed.

Response: *This error is acknowledged. It has been rectified in the model and results in the model have been updated to include this change.*

Comment: Recommendation: The assumption (P58, L15 *ff*.) that "*the rare nature of locally high levels of contamination that would result in multiple surviving organisms …. counteracts the incremental risk associated with these portions is such …..is not significant…*" should be more critically evaluated and more transparently justified.

Response: *To evaluate this assumption the probability of illness after growth and storage that results from 1, 2, 3, 4, 5 and 6 cfu per serving was estimated using the risk model. The results are shown in the following table. The vast majority of servings will have only 1 cfu per serving. Therefore, given the incremental increase in the probability of illness observed with increases in the cfu per serving reduce at larger values of the starting cfu, the development of the model based upon the assumption that servings are contaminated with 1 cfu will not results in a significant under-estimation of the total risk.*

Start cfu per serving	*Probability of illness after growth and storage*			
	low survival	*no growth*	*growth*	*low growth*
1	*0.0003*	*0.0025*	*0.1596*	*0.0889*
2	*0.0005*	*0.0050*	*0.1705*	*0.1012*
3	*0.0007*	*0.0074*	*0.1775*	*0.1095*
4	*0.0010*	*0.0098*	*0.1829*	*0.1161*
5	*0.0012*	*0.0121*	*0.1875*	*0.1216*
6	*0.0014*	*0.0144*	*0.1914*	*0.1264*

Comment: Suggestion. To increase the 'impact' of this section and sub-model, indicate the importance of *S*. Senftenberg and that the D60 and *z*-values are realistic, and similarly that the range of D60 and *z*-values for the 'other' salmonellae are also realistic. Give references to original data or data summaries (e.g ICMSF book 5) or to prescribed time-temperature combinations considered to achieve 5D of salmonellae in meat products. (n.b. Presumably the time-temperature data presented in the Technical Appendix [Chapter 17] are 5D values for Salmonella, but this is not made explicit in the Appendix). Also indicate the generality of the relationship derived.

Response: *We agree that these changes would advance that argument. However, the argument regarding S. Seftenberg is considered adequate given that it is not a major part of the risk estimation process. No explicit factor related to the safety margin that results from designing for S. Seftenberg is included in the model. It is included to provide an example of how significantly over-designed some processes may be relative to the salmonella strains that are more likely to be there.*

Comment: Table on P. 31. The middle column is redundant because the data of interest are in the right hand column and the data in the middle column are a direct transformation of that data.

Response: *These data are presented for transparency as it is the numbers in the middle column that are used in the calculations in the Analytica model.*

Comment: Response to Question 3. P37, L11-14. I read and reread this sentence many times and still find it close to unintelligible.

Response: *This text has been made clearer. Now reads:*
"The combination of a low pathogen burden and a large safety factor, even allowing for variation in these factors, has a greater impact upon the risk associated with roast beef products than the storage of the product, and any resulting microbial growth. More specifically, although growth may occur during storage, and reheating is assumed to be rare, the contamination levels at storage will be very low due to the combination of a low pathogen burden and thermal process safety factor. Therefore, the relative safety provided by a low pathogen burden and a large safety factor dominates, making Roast Beef a relatively low risk product."

Comment: P54. What is meant by 'greater granularity"?

Response: *The sentence was not required and has been removed.*

Comment: it should be noted and emphasised that when lower lethality is modelled (e.g. 4, 3 or 2 log reductions), the assumption of a *single cell per serving surviving the process* is no longer likely to be valid. The real or potential consequences of the 'collapse' of this

assumption should be stated explicitly in the documentation accompanying the model.

Response: *The reviewer is correct with regards to the limitations of this assumption, however, as the risk management questions were refocused to only consider lethality treatments of 5, 6 and 7 this assumption is not a limitation of the model in the current context. This refocusing of risk management questions has been made more explicit in the text.*

Comment: Page 25, lines 18-19: Why was "low growth" assumed to be half of normal growth? Expert opinion? Literature data?

Response: *This was an arbitrary estimate. Although a specific datapoint might be found in the literature, the fact that there is a wide diversity of formulations representing growth inhibition, there is no way to scientifically justify the choice of any one value – this has been clarified in the text and will be investigated through sensitivity analysis and presented in the section termed "insights gained from the model" which will be added to the final draft of the document*

Comment: Binomial Lethality
The authors need to expand their explanation of this concept, as it only appears in one other document related to thermal lethality of microorganisms. Have the authors validated this model in terms of Decimal reduction values, or is this simply conjecture? There are biological factors which could bring this model into question, and therefore there needs to be some validation of this. I believe the real issue is not the "n" value, which may be inferred from data sources, but the "p" value. How does one interpret a "p" value *per gram* across a large volume of product? If the authors wish to "make a case" for binomial lethality, they had best be prepared to back it up with empirical, laboratory based data.

Response: *The text has been expanded to read:*

"The most common assumption applied in estimating the impact of thermal inactivation processes is that, for a given process, each organism has an individual and identical chance of survival in the process. In terms of D-values, the D-value is defined as the time required to reduce a microbial population by 1-log or 90%. For each organism that experiences a 1D treatment the probability that it will survive is 0.1 (or 10%). This probability, and therefore the resulting reduction obtained, is independent of the starting population size, whether it is distributed in 1 gram or 1kg or 1 Mkg, the population will be reduced to, on average, 10% of the starting population. Conversely, the probability that an organism will not survive is 0.9 (or 90%). Such a process that has only 2 discrete outcomes, organisms survive or do not survive is a binomial process, and the number of 'survivors' follows a binomial distribution.

When applying a binomial survival process across multiple production units one of the implications is that the total number of surviving organisms in the total production volume is governed by the total number of organisms in the system and the Binomial lethality parameter. In other words, when a Binomial process applies, the exact allocation of organisms among the production units before lethality does not have an impact on the total number of survivors..."

Comment: While the baseline data is a reasonable starting point, it is well to keep in mind that this data is now 10 years old. There are more modern references which point to both reduced incidences of salmonellae in raw materials and to reduced populations of other pathogens, as well as to lower levels of bacteria in the finished products. These need to be taken in to account in the model. Of particular relevance are the lower incidences of salmonellae in various classes of intact and non-intact meats.

Response: *The importance of the pathogen burden estimate will be investigated in the section termed "insights gained from the model" which will be added to the final draft of the document.*

Comment: The data in the reference of: Levine et al., (2001). "Pathogen testing of ready-to-eat meat and poultry products collected at federally inspected establishments in the United States, 1990 to 1999." J Food Prot. 64(8):1188-93. Has been superseded by FSIS data from 2000 – 2004. (http://www.fsis.usda.gov/Frame/FrameRedirect.asp?main=http://www.fsis.usda.gov/ophs/rtetest/index.htm)

Response: *Note that the baseline microbiological data and the Levine paper refer to the same general timeframe. An updated comparison of both raw material quality (ideally a new baseline study with quantitative data) and updated results of finished goods testing (to which the reviewer refers) would be appropriate, but is not within the scope of this response.*

Comment: Page 31, lines 1-2. The text instructs the reader to "consult the technical appendix to review the details of the production volume estimation process." I am unable to find this information. If it is present in the appendices, it should be more obvious within the Table of Contents

Response: *The section was present in the report (Chapter 16) and is referred to in the appendix. This has been clarified in the text.*

Comment: Estimating the effect of re-heating
The effect of the simplification has to be more rigorously assessed because the number of predicted high doses, while infrequent, make the greatest contribution to the predicted risk.
the report should provide more justification that the simplification of the effects of reheating on estimated risk are valid

Response: The reviewer's instincts were quite correct. To test the impact, the effect of reheating was explicitly calculated within the storage and dose-response model. The impact of reheating was found to be much less significant than the simplified estimation process suggested. All calculations have been redone with this improved estimation process. This leads directly to higher risk estimates for certain products where reheating was a significant factor using the simplified model.

Comment: Page 53, tables: These tables might be better shown as graphs, to aid in seeing the "break point".

Response: *It is not clear which table the reviewer is referring to and what is meant by "break points"*

Comment: The predicted contamination levels in the Table on pages 23/24 should be analogous to the Levine survey results. This corresponds to an incidence of 1 in 4150 samples, or 0.02% which is below the lower incidence reported. If a composite sample is considered (say 200g) the expected incidence would increase to 0.16% which still seems low compared to that observed, particularly given that the highest contamination level was extrapolated across all products to generate this estimate.

The source of this apparent discrepancy between model predictions and available data must be addressed.

Response: *The data of Levine is derived from regulatory sampling, not statistical sampling, and*

therefore does not lend itself to characterizing the overall level of contamination on a statistical basis. The data is provided for contextual information, as opposed to validation purposes. The Levine data also includes the effect of post-process contamination (which may or may not be the dominant source of salmonellae in RTE products. Note, too, that the study is actually targeted, at least in recent years, to plants with a history of post-process contamination problems (see definition of 'high-risk' in FSIS Directive 10,240.3).

Comment: In this reviewer's opinion, another aspect that could be improved is to use more informative or intuitive names for some modules and components of the model. Some of the labels given to modules in the Analytica® main model are confusing because they do not correctly relate to the quantities that are the results of the calculations undertaken within the modules. For example, "RM Assigned Impact" ("RTE Salmonella Risk Assessment"/"Mechanics") actually represents the estimates of *Salmonella* burden per Mkg product, for the 16 RTE meat products (i.e. the same information as first Table on P.15). Similarly, the results labelled "RM Lethality Risk", "RM/COMP Risk", and "TPF Risk" do not appear to be estimates of 'risk', but predicted log concentrations of Salmonella per MKg product for each product type for various scenarios. For example, the results from "TPF Risk" are presented in the Table at the bottom of P23/top of P.24 as "Log10CFU/MKg". There are other examples in other parts of the main model, and some of the sub-models

Response: *It is agreed that this suggestion would aid users understanding of the model. Therefore, time allowing, this will be undertaken for the final draft of the Analytica model.*

Comment: The documentation states that "The model is developed with a user-interface which [*sic*] allows any of the above values (e.g. from 2.0 to 7.0 log reductions) to be considered." The Analytica model that was forwarded to this reviewer for comment does not appear to include these lethality levels. Instead, 'lethalities' of 5 or 6.5/7.0 log reductions or a mixture of the two, are the only lethality scenarios for which predictions appear to be possible (without editing of the Analytica® model).

Response: *This has been clarified in the text*

Comment: A problem, however, is that in the current layout of the model in that section, many of the arrows ('inferences') overlap so that it looks as though some modules are dependent on other whereas they are not. Rearranging the modules within "Mechanics" so that they are not vertically and horizontally aligned would help to alleviate this problem

Response: *The arrows connecting the nodes do overlap in some cases, however, the layout was chosen for the purpose of communicating the main stages and functionality of the model. When the nodes are moved to enable all the influences to be seen the distinct stages of the model become more difficult to identify.*

Comment: In the main model, within "Raw Material Pathogen Burden" module contains detailed calculations leading to estimates of *Salmonella* loads in ground and intact beef, pork, chicken and turkey. Those values are weighted average of contamination data etc and have no stochastic component. Thus, the "MPN as Log CFU per MKg" calculation and "MPN Calculations" module could be removed from the main model and presented as a separate sub-model consistent with the treatment given to other aspects of the model, with only summary results being used in the main model (as they currently are).

Response: *Maintaining the links between the "raw material pathogen burden" module and the main model enables the model to be easily updated with new pathogen load data which will automatically be carried through the model*

Comment: The assumptions appear to have been modeled appropriately, however, in several cases

it is not clear where a particular assumption is derived.
For example, (and as noted below) on page 22, lines 4-8 the origin of the thermal process safety factors (extra 2 and 4 log reductions) is not stated clearly. Is there any basis in expert opinion or the literature for these values? Similarly, the justification for reheating log reductions and reheating patterns for product categories are not explained.

Can the risk assessors provide justification for the assumption that beef jerky is made from "ground beef"? Changing this product to 100% intact beef has a large impact on the expected number of cases.

Response: *The thermal process safety factors and reheating log reductions are based upon assessor's estimates of what are reasonable values for these processes. The importance of the value of these factors will be explored in a section termed "insights gained from the model" which will be added to the final draft of the document*

It was found that beef jerky is a product which may be produced on a mass scale from ground beef products, but is also commonly produced from intact beef. The importance of this assumption will also be investigated in the "insights gained from the model" diction to be added to the report.

Comment: It would also be nice to quickly be able to see the source of the difference in estimated cases for "meat sticks" and "beef jerky" for example. It turns out that the two products are generally similar, except that people consume more "meat sticks" than "beef jerky", so the risk is proportionally higher

Response: *Summary graphs will be added to the report in the new section "Insights gained from the model". This is one of the points that will be discussed more fully in this new section.*

Comment: The utility of the Analytica model would be increased by adding additional text to the file. For example the "description" field of many nodes is blank. It should be noted that while this would improve utility, the documentation (in the form of the pdf file) is sufficient

Response: *It is agreed this would be useful addition to the model, however this will also be a time consuming process. Time allowing, text will be added to the model description fields.*

Comment: Page 33, First table. Cooked Poultry Deli Meat estimated at 4357 cases? In comparison to other products evaluated, this seems out of sync with reality. This also brings the response to Question 7 (page 45) into doubt

Response:

(See also earlier comment).

The reviewer has not indicated what value would be considered 'in sync'. To our knowledge the relative risks associated with these products has not been previously assessed. Note also that this refers to a scenario with only a 5-log reduction for poultry which is not the current assumed reality.

It is because of the high estimate of risk per Mkg of product compared to other products. This risk estimate is due to the assumption that poultry deli meat is rarely reheated. This relatively large estimate of risk is then further amplified as poultry deli meat has the second largest estimated consumption mass (g /day /person).

Comment: Last table on page 33 and two tables on page 34. Is the total supply risk presented in number of cases? This is not clear. If these are annual cases, these also seem to be inflated and do not appear to me to reflect reality

Response: *Noted, and clarified.*

Comment: Section 12.2 SUB-MODEL post-lethality treatment.
Number of organisms surviving the report's statement at P57, L27 – P58, L1 that the > L=2 rule is valid in 99% of cases is true. However, given the above contamination level distribution, a few servings in 10000 are expected to contain >100 MPN.g-1 or, by implication, a total load of >~10000 *Salmonella*. These cases would require a 6-D treatment to be applied for the L=2 conclusion to be true. However, the model includes scenarios in which 5-D treatments, or less, are applied. As the report is at pains to point out in other sections (e.g. *Salmonella* lethality sub-model), risk assessors must remain mindful of the fact that they are dealing with risks on logarithmic scales and that while high contamination levels are rare they have much greater *weight* in the determination of risk.

Response: The reviewer is quite correct that this is a valid general concern as the analysis approaches the limits of the single-cfu assumption. An earlier comment describes the relatively small increase in risk associated with larger surviving populations (more than 1 cfu). Furthermore, much of the total supply risk is associated with situation where there is considerable growth of the bacteria. In this case, the starting population becomes relatively less important, compared to variations in the extent of growth.

Comment: SUB-MODEL: Comparative Lethality (*E. coli, L. monocytogenes)*
This model and the conclusions drawn from it seem inconsistent with the approach taken in other sections of this risk assessment.

This sub-model also introduces the concept of "major" and "sub"-populations. Though not explained in the model or accompanying report, this refers to an assumption made by Juneja that the non-(log)linear inactivation kinetics he observed were due to the existence of sub-populations of different thermal tolerance within the test populations. The possible reasons for non-(log)linear inactivation kinetics have been argued in the literature for decades, but the phenomenon applies equally to inactivation kinetics of salmonellae. Elsewhere in the model and its documentation it is (implicitly) assumed that loglinear inactivation kinetics apply to salmonellae and the introduction in this sub-model of the consequences of non-loglinear inactivation kinetics as part of the justification for inability to answer Question 3 seems to this reviewer to be a spurious argument. Also it is not clear to this reviewer from the description given in the model and document how this is a 'dynamic model'.
Recommendation: Either, use the Juneja D-values based on the assumption of loglinear inactivation kinetics (Tables 2,3 and 4 in Juneja, 2003) or be prepared to explicitly include the consequences of nonloglinear inactivation kinetics of salmonellae in the other modelling presented

Response: Note that the reviewer is referring to descriptive text in the Analytica module and not to the document itself. The sub-model is included as a working module on comparative lethality. The answer to question 2 (assuming this is the question that the reviewer was referring to) was not based on the issue of non-linear inactivation kinetics. It is based on the fact that the relative inactivations achieved for different organisms are not consistent across all possible lethality processes. This is true whether linear or non-linear inactivations are assumed.

Comment: SUB-MODEL: Salmonella Lethality
Suggested Correction. It appears that the operation entitled "Mean effective probability of illness" in the "Processing" Module of the sub-model should actually be entitled "Mean effective probability of *survival*", or similar, because there is no consideration of illness at all at this stage of the model

Response: *Noted, and clarified.*

Comment: Page 27, lines 7-9 and first table on page 28. Now I am completely lost in trying to follow how the presented calculations were performed. The authors need to clarify the connection in data presented on pages 25-27 with that presented on page 28.

Response: *Text has been added to the document to clarify how these calculations were performed:*

"Applying the assumption of a single CFU per contaminated RTE serving, each CFU/Mkg in the process corresponds to one contaminated serving per Mkg. Therefore, the total risk per Mkg after considering storage and dose-response is given by the sum of the log probability of illness per serving by product type and the log contamination level predicted following the application of the thermal process safety factor. The resulting estimates of the risk of illness per Mkg are as follows:.."

Comment: Page 39, line 20. Calculations should be provided to explain the derivation of a z-value of 9.9^{o}F

Response: *This section has been expanded to include how the z-value was calculated:*
"From these values, the z-value can be calculated. From a plot of the log_{10} of the D-value against temperature, the z-value is the reciprocal of the slope.

Comment: Page 47+, Question Eight, Nine and Ten. The authors clearly define "effective lethality" and the need to look further than a weighted average. However, this portion of the manuscript is going to be a "hard sell" since most readers will have in mind that survivors will not be equally distributed among product, but be weighted toward product from the smaller volume producers. The authors could make this portion of the manuscript stronger by including more example calculations to guide the reader's thought process.

Response: *While we agree with the notion, the answers to these questions are not meant to be anything more than hypothetical. The fact that these are hypothetical scenarios is made much clearer throughout these scenarios.*

Comment: Page 45: A short background paragraph on the current state of the regulations would clarify this section for those not familiar with the regulations: i.e. what do the regulations currently require and for which products?

Response: Noted, this may be clarified in a document for public consumption.

Comment: Page 6, Line 30. While the units "pathogen contamination on a concentration basis, expressed in units of colony-forming units per million kilograms (CFU/Mkg)", may make sense from a risk assessment standpoint, I am personally unaware of any other literature which uses this notation. I would encourage the authors to present the data as both log cfu/MKg and log cfu/g. Presenting the data solely as log cfu/MKg will likely lead to confusion and misinterpretation

Response: *Key tables are now presented in both log cfu/MKg and log cfu/g*

Comment: Page 9, Table beginning with "Controllability" The authors may wish to clarify this notation. The term "very high" may be interpreted as "very high controllability" (which I believe was the intent), but others may interpret this as "very high *variability*". I believe that a minor clarification would solve this. The authors may also want to clarify the "medium" and "low" rankings. In my experience, all of these processes are very controllable; the variability comes in the wide variety of individual practices employed at various meat processing establishments. For example, the salt cured/dried process is quite controllable in a laboratory environment. However, there is considerable variability in actual practice within the industry. I do not think that any of this changes the intent of

the authors text, but it may help in the interpretation of the report by a wider audience.

These same comments may be applied to "relative margin of safety"

Response: *The text has been clarified to read*
"Controllability –each risk category is assigned a degree of controllability related to the ability to manage the primary control mechanism (note this does not refer to the potential variability that may be inherent in the control mechanisms applied"

Comment: Page 11, Table 2.1.2. Most cooked ham is in fact cured. There is very little cooked fresh ham that moves in commerce

Response: *The inclusion of cooked ham here is merely to illustrate the types of product that this product category would encompass. The amount of these types pf product actually in commerce is accounted for when consumption estimates are incorporated into the model.*

Comment: Page 11, lines 18 – 20. While the microbiological baselines are an important reference, the data is now 10 years old. Recent trends in the incidence of salmonellae, as reported by FSIS, show significant declines in incidence. Unfortunately, the new data does not include population data on positive samples. Somehow, the reduced incidence should be factored into the calculations, even if it is just the population distributions from the (old) baselines are applied to the new incidence data. Although the discussion in the following pages tends to address this, one thing is clear. Sampling and analytical methods have improved over the last ten years, and even with the improvements in sampling and testing, FSIS is reporting a clear reduction in the incidence of salmonellae in raw meats

Response: *The importance of the estimated pathogen burden in predicting the final estimates of risk will be presented in a new section to be added to the final draft of the document named "insights gained from the model".*

Comment: Page 13, "Summary of *Salmonella spp.* Burden Results for Ground Raw Materials " A classically trained food microbiologist will be expecting to see a value expressed as "log cfu/g". I have already mentioned the issue of cfu/MKg units. Perhaps the authors could add a third column to the tables, showing log CFU/g. While this will be expressed as a negative number, this will not be inconsistent with information published by the ICMSF (see ICMSF Book 7). For example, log 8.7 cfu/MKg is equivalent to log -0.3 cfu/g. This does not change the intent of the authors text, but simply aids in the interpretation by a broader audience

Response: *Key results are now presented in both cfu/Mkg and cfu/g*

Comment: Page 16, Table on Simplified Post-lethality surviving pathogen burden

This table will be widely misinterpreted in its present form. When expressed as log cfu/MKg, the table appears to suggest only a modest margin of safety with a 6.5 lethality standard, and in fact an apparent risk at a 5 log lethality standard. This is simply an inaccurate interpretation. Based on the data used in this simplified calculation, a 5 log lethality standard would in fact reduce a "worst case" meat product from a theoretical 0.001 cell per gram (-2.7 cfu/g or 6.3 cfu/MKg) to $2 * 10^{-8}$ cfu/gram (-7.7 cfu/g or 1.295 cfu/MKg).
I would strongly encourage the authors to present the table in both log cfu/MKg *AND* log cfu/g to avoid this potential misinterpretation. This does not change the calculations, but simply presents the data in a format which is far more common

Response: *This table, and others are now presented in both cfu / g and cfu / Mkg*

Comment: Page 17, lines 9-15. Compliance with lethality standard
Although the RTI expert elicitation report was released in 2004, the elicitation itself came shortly after the changes in USDA-FSIS regulations, at a time when many small and very small establishments were still struggling to interpret and apply the regulations to their own processes. Since that time, industry trade associations and university extension personnel have worked with these establishments, such that the numbers are now much closer to 100% in all categories. This is a challenge to address, because the industry changes rapidly, and a survey that is more than a year old is probably out of date

Response: *The importance of the level of compliance with the lethality standard applied in the model will be presented in the "insights gained from the model" section of the report.*

Comment: Page 21, lines 21-25
I would disagree with these statements. There are many engineers with expertise in heat transfer coefficients which could provide a basis for estimating the lethality and heat transfer properties associated with "typical" processed meat products. Many non-intact products (frankfurters, deli meats) are produced in relatively standard product diameters, and estimating the lethality would be reasonably straight forward. Most major meat processors have already done these calculations. Although there is more variability in intact products (roast beef, ham), most large processors have performed these calculations and could provide an estimate of potential lethality. I would recommend that the authors approach the trade associations for the meat industry, who could in all likelihood solicit this information in an anonymous form from their members. Lacking that, it is likely that the Food Research Institute at the University of Wisconsin would have at least some basic data to work with. I do not mean this to be as harsh a criticism as it possibly sounds, but this risk assessment will likely be publicly criticized if this issue is not addressed, which will ultimately damage the credibility of an otherwise fundamentally sound document

Response: *The aim here is to simplify the model. There may be information available for some products, and some products may be characterized, perhaps to a very detailed degree in terms of their associated thermodynamics, however this is unlikely to be the case for all products under consideration. The net effect of this process is therefore summarized through the use of safety factors – sensitivity analysis will be used to investigate the importance of the application, and magnitude of these factors on insights gained from the risk assessment.*

Comment: Page 21, lines 38-42. The concept of integrated lethality is widely understood and applied in the canning industry. The fact that it has not been applied in a regulatory sense to the meat industry does not change the fundamental science of integrated lethality

Response: *Not clear what the reviewer is suggesting be changed in the document.*

Comment: Page 22 – 23 Safety Factor Level. The authors may wish to clarify their ranking of some of these products. For example, "meat sticks" moving in interstate commerce in all likelihood have a "high" safety factor level, while those produced and sold solely for intra-state commerce have considerably more variability in their safety factor level

Response: *While this may be true, in the absence of some evidence of this phenomenon, this assumption will not be made or described.*

Comment: Page 26, unlabelled table at top of page
If the numbers in the table are intended to be the % of product which falls into a given category, then the authors need to re-think their approach. For example, the pathogen which is the basis for the lethality standards (salmonellae) does not grow, or grows very

erratically, below 10°C. Growth rates in the 10 – 13 °C are extremely slow. Since these are perishable products, holding at high refrigeration temperatures (10 – 13 C) results in rapid spoilage of the product. I would re-classify the Fully cooked, uncured, non-shelf-stable category to the low growth, refrigerated category

Also:

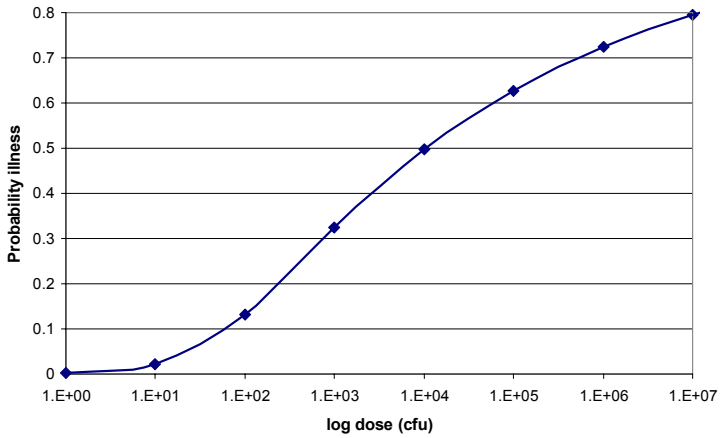
Page 37, storage and growth risk. As indicated in the comments on Question 1 (Page 26, unlabelled table), salmonellae does not grow at what are commonly assumed to be refrigeration temperatures (<10C). To place the storage and growth risk at "higher risk" assumes that most of the product produced is exposed to temperature abuse before consumption. I am not certain that that is a justifiable assumption

Response: *The reviewer has misinterpreted what the growth category classification means. The classification of products to storage and growth patterns is based upon a consideration of the RELATIVE level of growth that might be expected for the different products when they are held under the same conditions (for example temperature and time). The actual time and temperature conditions for which products are stored are variables in the model (based upon data on consumer practices) and are applied to all products to predict the extent of growth that occurs. It is not assumed that products that would allow growth under some conditions, will necessarily always exhibit growth. Low temperatures are factored in to limit the amount of growth for refrigerated products.*

Comment: Page 26 Probability of illness per surviving pathogen.
The authors need to include more detail on how these number were determined. If I interpret the table correctly, there will be 0.055 illnesses per surviving pathogen for fully cooked uncured not shelf stable product. This apparently assumes growth during storage, which is unlikely. Where does the calculation of infectious dose enter in?

Page 27, Lines 7 – 9 "Applying the assumption of a single CFU per contaminated RTE serving, each CFU/Mkg in the process corresponds to one contaminated serving per Mkg." While this assumption may simplify the assessment, it ignores the biology of salmonellae, which is the organism designed to be controlled by the lethality standard. A single cfu is not an infectious dose. A more likely estimate, which would still be very conservative, is an infectious dose of 10- 100 cfu per serving

Response: *Using growth models and data regarding storage temperature and time profiles the growth that would result from the contamination of a serving with 1 cfu is estimated for each of the growth scenarios (low-survival, no growth, low growth refrigerated, and growth refrigerated). Using this predicted dose as an input, a dose response model is used to estimate the probability of illness that results from exposure at the levels predicted following growth. The model adopted is a Beta-Poisson model which assumes that the presence of a single cfu can cause illness, although at a low probability of occurrence with the probability that 1 cfu causes infection estimated to be 0.0025 . The probability of illness then increases as the level of exposure increases, following the dose response model. As such no assumption regarding an infectious dose is made. The relationship between the dose and probability of illness is shown in the below figure. This is the accepted method of dose-response modeling for bacterial pathogens.*



Comment: Page 28, Unlabelled table at top of page.
Which lethality standard is being applied? The authors have discussed a 5 log, a split, and a 6.5/7 log reduction

Response: *These results are for the split lethality scenario. This table has been updated in the text to include risk in both grams and Mkg and all 3 lethality scenarios..*

Comment: What is "log risk/MKg"? Is this the probability of a single contaminated serving per MKg

Response: *Risk is defined as illness; therefore log risk/Mkg is the number of illnesses that occur per Mkg of product. This has been made clearer in the text*

Comment: Page 32 Relative Product Risk – Again, this is an undefined term, although the text states that it is "proportional" to the cases per MKg. Can the authors simply give a table of estimated cases per MKg? Also, does a larger number suggest a larger risk?
I believe that much of this confusion could be solved by simply inserting text and/or a formula on page 30, lines 2-3, explaining the "log risk" factor

Response: *The product risk per Mkg can be interpreted as the estimated number of cases of illness per Mkg of product. This has been clarified in the text.*

Comment: Page 33, Table 2.10
I believe that the authors need to add information to the Table. I believe the numbers in the table are "cases per year". If so, this simply needs to be stated
Also if "The total supply risk is simply the sum of the individual product risks", then the numbers in table preceding table 2.10 do not add up to the numbers in the numbers in this table

Response: *It has been made clearer that the table presents the number of cases per year.*
The number in the preceding table correspond to the numbers for 'Include reheating =yes" and "Include thermal process safety factors = yes"

Comment: Summary:

The biological issues which have not been adequately addressed relate to the infectious dose (see comments page 27, lines 7 – 9) and an adequate understanding of what the performance standards really mean. A 5 $\log_{10}$ reduction, or a "5D" reduction, is based on a per gram assumption. That is, a 5D performance standard means that a process sufficient to destroy 5 $\log_{10}$ of a given pathogen has been applied to every gram of

product, irrespective of production lot size. Although this is never discussed in the text, I am not certain that the authors fully understand this concept

Response: *The reviewer, on this point, is repeatedly mistaken. The reviewer misinterprets the results of lethality calculations when the final average concentration is, for example,.1 cell per 1000 grams. This does not constitute zero risk.*

Also the use of the concept of infectious dose is not considered to be an appropriate biological model of the reality of these pathogens (see WHO hazard characterization guidelines).

Comment: Page 35, lines 27-34 These statements are in fact false. The canning and medical device industries have effectively used surrogate organisms for *Clostridium botulinum* and other spore forming human pathogens for more than 50 years. Simply because this has not been previously applied in the meat industry does not mean that the biological science is incorrect

Response: *The text has been clarified. The intent was to convey issues regarding the wide variability in the manner in which a lethality might be applied across the range of products considered. This variability makes it intractable to predict the effect upon other organisms, as the way in which organisms will respond will be specific to the exact mechanism by which the lethality standard is implemented.*

Comment: Page 36, lines 10-12 There is a consensus on this subject, and it is in fact well documented in the literature. I would suggest that the authors review the documentation which FSIS has used to promulgate regulations, especially the documentation surrounding 9 CFR part 430

Response: The reference to an “unwritten” consensus has been removed.

Comment: Page 41 lines 6 – 27 This text gives the impression that the existing 5 log performance standard is in fact a much higher standard because of the overall lethality of the process. This certainly is true, as irrespective of how fully cooked beef patties are prepared commercially, the integrated lethality is greater than 5 logs. However, to state that “Given the binomial survival assumptions stated earlier in this document, this would increase the corresponding public health risk by several logs compared to the impact of the current prescribed guidelines” seems misleading. If a 5 log reduction is justifiable from a public health perspective, then any method which achieves a 5 log reduction, including an integrated lethality calculation, should achieve the public health objective. What we have now, based on the regulations of times at end point temperatures, is a *de facto* performance standard which is in fact considerably greater than 5 logs. The fundamental question seems to be, is the 5 log performance standard justifiable from a public health perspective, or do we in fact need a higher performance standard? If the 5 log reduction performance standard is in fact justifiable from a public health perspective, then integrated lethality calculations should be justifiable. The FSIS regulations on cooked intact beef seem to bear this out, as the “safe harbor” guidelines in FSIS Directive 7370.2 have times and temperatures considerably lower than those in 9 CFR 318.23

Response: The question being answered is not whether the standard is justifiable, or whether the calculation approach is justifiable. The question being answered is what would be the impact of changing from a ‘safe harbor’ assumption where the lethality is assessed only at one time interval, versus one in which the lethality is considered over the complete heating process. The second process would result in much less total lethality being required to comply with the 5-log requirement. This lower total lethality would, inevitably, lead to more surviving pathogens. This is the extent of the argument presented. The use of Integrated lethality calculations may still be justifiable, but that is a different question.

Comment: Page 48, table Using production Fractions for Poultry (or meat)

The authors should clarify that these tables are examples only, and not the actual fact. My concern is that these tables will be used to generate a sound byte that says “Small meat and poultry processors account for 75-80% of the public risk for food borne disease from meat and poultry”. In fact, such a statement would be indefensible. These tables are included in the text as examples, to exercise the model, and not to address a specific policy issue. Arbitrarily assigning the lethality standards is an expedient for modeling purposes, but these do not represent the reality of poultry or meat processing today.

Page 49 The previous comments apply to these tables. Hypothetical examples should be clearly labeled as such

Response: *The text has been updated to make clear that these are hypothetical examples.*

Comment: Q9 Page 50 Given that the assumptions for Question 8 are speculative, the section on question 9 simply multiplies the error. The large and small poultry establishments are already operating at the 7 log standard, so a more likely scenario is that “Year 0” is 6,7,7 which is a combination not currently in the table. The statement that this “shift will reduce the risk associated with this product by a factor of 100” may be technically true from a modeling standpoint, but represents neither the industry practice nor a true impact on public health. Again, my primary concern is that these tables will be extracted from the report and presented as absolute fact, when they are simply examples of ways to exercise the model

Response: *The text has been updated to make clear that these are hypothetical examples.*

Comment: Page 53 The authors either confuse the standards, or simply are using examples for demonstration purposes. The regulations for a 5 log performance standard are for fully cooked RTE poultry *patties* (9 CFR 318.23 Heat-processing and stabilization requirements for uncured meat patties). It is doubtful that there are many (or any) poultry establishments with fewer than 50 employees which are producing this type of product. This tends to be a specialized type of manufacturing process, and even if produced in “small” establishments, they would rarely if ever be produced in establishments which were not operated by very large, multi-national companies. Also, many if not all of the establishments which manufacture pre-cooked poultry patties are operating at or above the 5 log standard. The tables on page 54 are misleading, in the sense that they are hypothetical models, and not based on actual fact.

These same comments apply to fully cooked meat patties

Response:	*The text has been updated to make clear that these are hypothetical examples for demonstration purposes, not based on evidence of relative performance by plant size.*