VII. INTERPRETATION AND CONCLUSIONS

This risk assessment included analysis of the available scientific information and data in the development of exposure assessment and dose-response models to predict the relative public health impact of foodborne *Listeria monocytogenes* from 23 food categories. The assessment focuses on predicting the comparative risk among ready-to-eat foods that have a history of either *Listeria monocytogenes* contamination or were implicated epidemiologically. The risk assessment demonstrates the predicted relative risk associated with these foods in relation to the overall incidence of listeriosis including both apparently sporadic illnesses and illnesses associated with outbreaks. Illnesses attributed to documented outbreaks are a small proportion of the total estimated annual cases of listeriosis. Outbreaks frequently represent a breakdown in the food safety controls that have been established to prevent such occurrences. For example, outbreaks of listeriosis have been linked to failure to protect a frankfurter processing line from environmental contamination caused by plant renovations (1998-99), use of defective processing equipment in the production of chocolate milk (1994), and inadequate pasteurization of milk used to make fresh soft Mexican-style cheese (1987). Thus, continued vigilance of current food safety control systems and the targeted initiation of new controls will likely be needed to achieve further reductions of the incidence of listeriosis.

The scientific evaluations and the mathematical models developed during the risk assessment, provide a systematic assessment of the scientific knowledge needed to assist both in reviewing the effectiveness of current policies, programs, and practices, and identifying new strategies to minimize the public health impact of foodborne *Listeria monocytogenes*. This systematic assessment provides a foundation to assist future evaluations of the potential effectiveness of new strategies for controlling foodborne listeriosis. The risk assessment provides a means of comparing the relative risks associated with these foods on a per serving and a per annum basis. However, overall interpretation of the risk assessment requires more than just a simple consideration of only the relative risk rankings associated with the various food categories. As discussed above, the results must also be evaluated in relation to the degree of variability and uncertainty inherent in the predicted relative risk, and interpreted in relation to available

scientific knowledge of the production, marketing, and consumption of the various food categories. Likewise, the results must be evaluated in relation to the available epidemiological record. A detailed consideration of the quantitative and qualitative findings for each food category is provided in the risk assessment and its appendices.

As part of the evaluation and interpretation of the predicted risk estimates and the accompanying relative risk rankings, the risk assessment considered various qualitative and quantitative methods of grouping the results that may be useful for risk management or risk communication purposes. For example, Table V-6 includes an arbitrary grouping of the per serving and per annum results into very high, high, medium, and low risk categories based on the criteria provided in the table's footnotes. In this instance, six food categories were considered to be high risk on a per serving basis: Deli Meats, Frankfurters (not reheated), Pâté and Meat Spreads, Unpasteurized Fluid Milk, Smoked Seafood, and Cooked Ready-to-Eat Crustaceans. Three food categories are considered to be moderate risk and the remaining 14 food categories are considered to be low risk on a per serving basis. On a per annum basis, the majority of the cases are predicted to be attributable to Deli Meats. The high-risk food categories included Pasteurized Fluid Milk, High Fat and Other Dairy Products, and Frankfurters (not reheated). Five food categories are considered to be moderate risks and the remaining 14 food categories are considered to be low risk on a per annum basis.

A number of methods for objectively grouping the results were evaluated, and are discussed in detail within the risk assessment. One approach that appears to be very useful for risk management/communication purposes is the evaluation of the relative risk ranking results using cluster analysis (see Appendix 12). When performed at the 90% confidence level, this analysis groups the per serving rankings into four clusters and the per annum rankings into five clusters (Table VII-1). These clusters are used, in turn, to develop a two-dimensional matrix of per serving vs. per annum rankings (see Figure VII-1) of the food categories. In this approach, the four per serving clusters were arrayed against the per annum clusters (A and B, C and D, and E). The matrix was then used to depict five overall risk designations: Very High, High, Moderate, Low, and Very Low. For example, as shown in Table VII-1, Deli Meats is included in the 'per

serving' Cluster 1 and in the 'per annum' Cluster A, so it is placed in the two-dimensional matrix cell, Very High Risk, Cluster 1-A (See Summary Figure VII-1). Frankfurters (not reheated) is in the 'per serving' Cluster 1 and in the 'per annum' Cluster B, so it is also placed in the Very High Risk cell, representing Cluster 1-B. No food categories are in the Moderate Risk cell for Clusters 3-A and 3-B because there are no foods in the 'per serving' Cluster 3 that match with the 'per annum' Cluster A or Cluster B.

Table VII-1. Results of Cluster Analysis at the 0.1 Level

Risk per Serving	Risk per Annum
CLUSTER 1 　　Deli Meats 　　Frankfurters, not reheated 　　Pâté and Meat Spreads 　　Unpasteurized Fluid Milk 　　Smoked Seafood	**CLUSTER A** 　　Deli Meats
CLUSTER 2 　　Cooked RTE Crustaceans 　　High Fat and Other Dairy Products 　　Pasteurized Fluid Milk 　　Soft Unripened Cheese	**CLUSTER B** 　　High Fat and Other Dairy Products 　　Frankfurters, not reheated 　　Pasteurized Fluid Milk 　　Soft Unripened Cheese
CLUSTER 3 　　Deli-type Salads 　　Dry/Semi-dry Fermented Sausages 　　Fresh Soft Cheese 　　Frankfurters, reheated 　　Fruits 　　Preserved Fish 　　Raw Seafood 　　Semi-soft Cheese 　　Soft Ripened Cheese 　　Vegetables	**CLUSTER C** 　　Cooked RTE Crustaceans 　　Fruits 　　Pâté and Meat Spreads 　　Unpasteurized Fluid Milk 　　Smoked Seafood
CLUSTER 4 　　Cultured Milk Products 　　Ice Cream and Frozen Dairy 　　Products 　　Processed Cheese 　　Hard Cheese	**CLUSTER D** 　　Deli-type Salads 　　Dry/Semi-dry Fermented Sausages 　　Frankfurters, reheated 　　Fresh Soft Cheese 　　Soft Ripened Cheese 　　Semi-Soft Cheese 　　Vegetables **CLUSTER E** 　　Cultured Milk Products 　　Hard Cheese 　　Ice Cream and Frozen Dairy 　　Products 　　Preserved Fish 　　Processed Cheese 　　Raw Seafood

Decreased Risk per Annum →

	Clusters A and B	Clusters C and D	Cluster E	
	Very High Risk (Clusters 1-A, 1-B) Deli Meats Frankfurters (not reheated)	**High Risk (Clusters 1-C, 1-D)** Pâté and Meat Spreads Unpasteurized Fluid Milk Smoked Seafood	**Moderate Risk (Cluster 1-E)** No food categories	**Cluster 1**
	High Risk (Clusters 2-A, 2-B) High Fat and Other Dairy Products Pasteurized Fluid Milk Soft Unripened Cheese	**Moderate Risk (Clusters 2-C, 2-D)** Cooked RTE Crustaceans	**Moderate Risk (Cluster 2-E)** No food categories	**Cluster 2**
	Moderate Risk (Clusters 3-A, 3-B) No food categories	**Moderate Risk (Clusters 3-C, 3-D)** Deli-type Salads Dry/Semi-dry Fermented Sausages Frankfurters (reheated) Fresh Soft Cheese Fruits Semi-soft Cheese Soft Ripened Cheese Vegetables	**Low Risk (Cluster 3-E)** Preserved Fish Raw Seafood	**Cluster 3**
	Moderate Risk (Clusters 4-A, 4-B) No food categories	**Low Risk (Clusters 4-C, 4-D)** No food categories	**Very Low Risk (Cluster 4-E)** Cultured Milk Products Hard Cheese Ice Cream and Other Frozen Dairy Products Processed Cheese	**Cluster 4**

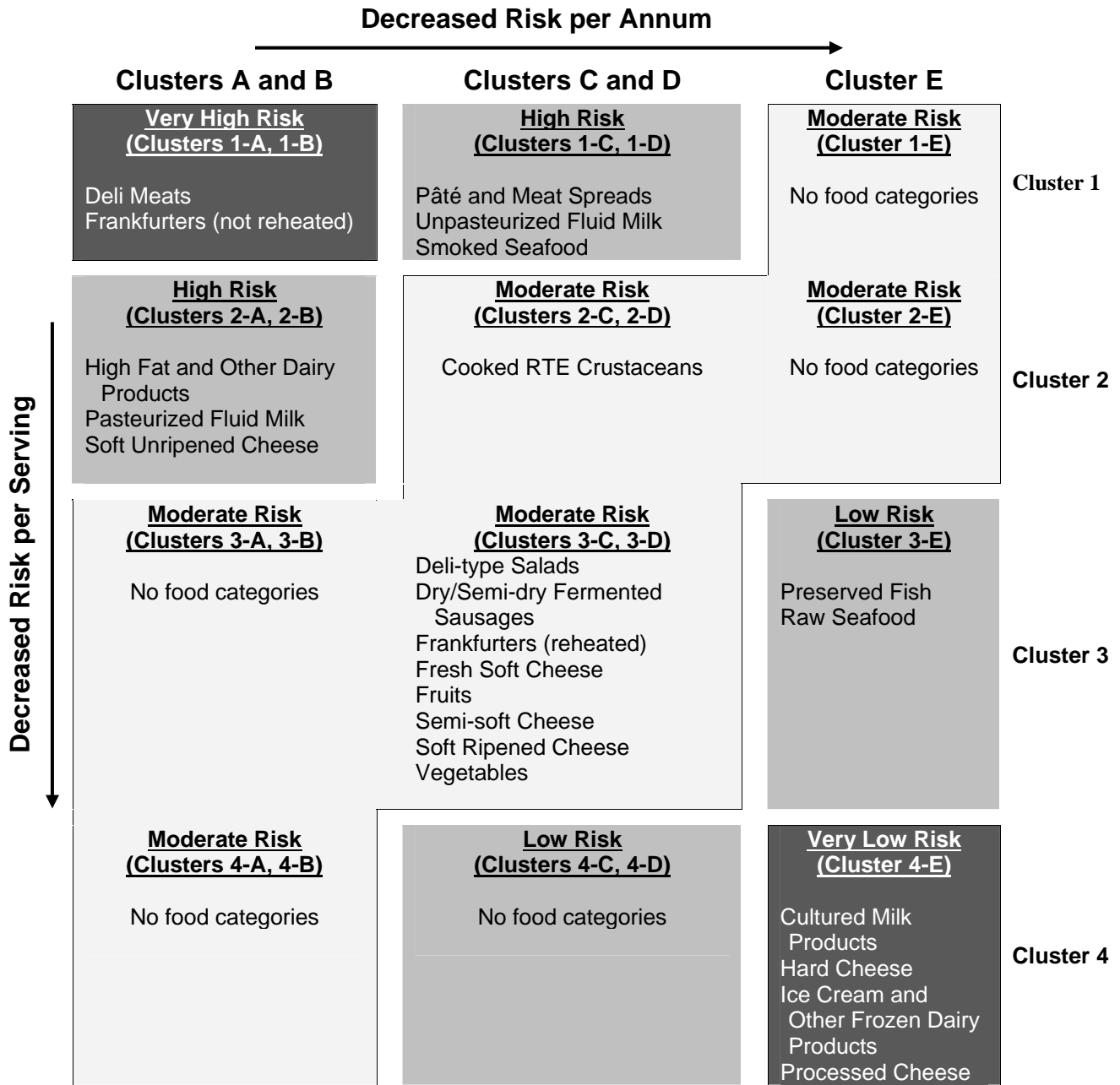**Decreased Risk per Serving** ↓ (left vertical axis)

Figure VII-1. Two-Dimensional Matrix of Food Categories Based on Cluster Analysis of Predicted per Serving and per Annum Relative Rankings
[The matrix was formed by the interception of the four per serving clusters vs. the per annum clusters A and B, C and D, and E. For example, Cluster 3-E (Low Risk) refers to the food categories that are in both Cluster level 3 for the risk per serving and Cluster level E for the risk per annum. See Table VII-1.]

The risk characterization combines the exposure and dose-response models to predict the relative risk of illness attributable to each food category. While the risk characterization must be interpreted in light of both the inherent variability and uncertainty associated with the extent of contamination of ready-to-eat foods with *Listeria monocytogenes* and the ability of the microorganism to cause disease, the results provide a means of comparing the relative risks among the different food categories and population groups considered in the assessment and should prove to be a useful tool in focusing control strategies and ultimately improving public health through effective risk management. As described above, cluster analysis techniques are employed as a means of discussing the food categories within a risk analysis framework. The food categories are divided into five overall risk designations (see Figure VII-1), which are likely to require different approaches to controlling foodborne listeriosis.

Risk Designation Very High. This designation includes two food categories, Deli Meats and Frankfurters, Not Reheated. These are food categories that have high predicted relative risk rankings on both a per serving and per annum basis, reflecting the fact that they have relatively high rates of contamination, support the relative rapid growth of *Listeria monocytogenes* under refrigerated storage, are stored for extended periods, and are consumed extensively. These products have also been directly linked to outbreaks of listeriosis. This risk designation is one that is consistent with the need for immediate attention in relation to the national goal for reducing the incidence of foodborne listeriosis. Likely activities include the development of new control strategies and/or consumer education programs suitable for these products.

Risk Designation High. This designation includes six food categories: High Fat and Other Dairy Products, Pasteurized Fluid Milk, Pâté and Meat Spreads, Soft Unripened Cheeses, Smoked Seafood, and Unpasteurized Fluid Milk. These food categories all have in common the ability to support the growth of *Listeria monocytogenes* during extended refrigerated storage. However, the foods within this risk designation appear to fall into two distinct groups based on their rates of contamination and frequencies of consumption.

- Pâté and Meat Spreads, Smoked Seafood, and Unpasteurized Fluid Milk have relatively high rates of contamination and thus high predicted per serving relative risks. However,

these products are generally consumed only occasionally in small quantities and/or are eaten by a relatively small portion of the population, which lowers the per annum risk. All three products have been associated with outbreaks or sporadic cases, at least internationally.

These foods appear to be priority candidates for new control measures (i.e., Smoked Seafood, Pâté and Meat Spreads) or continued avoidance (i.e., Unpasteurized Fluid Milk).

- High Fat and Other Dairy Products, Pasteurized Fluid Milk, and Soft Unripened Cheeses have low rates of contamination and corresponding relatively low predicted per serving relative risks. However, these products are consumed often by a large percentage of the population, resulting in elevated predicted per annum relative risks. In general, the predicted per annum risk is not matched with an equivalent United States epidemiologic record. However, the low frequency of recontamination of individual servings of these products in combination with their broad consumption makes it likely that these products are primarily associated with sporadic cases and normal case control studies would be unlikely to lead to the identification of an association between these products and cases of listeriosis.

  These products (High Fat and Other Dairy Products, Pasteurized Fluid Milk, and Soft Unripened Cheeses) appear to be priority candidates for advanced epidemiologic and scientific investigations to either confirm the predictions of the risk assessment or identify the factors not captured by the current models that would reduce the predicted relative risk.

Risk Designation Moderate. This risk designation includes nine food categories (Cooked Ready-to-Eat Crustaceans, Deli Salads, Dry/Semi-Dry Fermented Sausages, Frankfurters-Reheated, Fresh Soft Cheese, Fruits, Semi-soft Cheese, Soft Ripened Cheese, and Vegetables) that encompass a range of contamination rates and consumption profiles. A number of these foods include effective bactericidal treatments in their manufacture or preparation (e.g., Cooked Ready-to-Eat Crustaceans, Frankfurters-Reheated, Semi-soft Cheese) or commonly employ

conditions or compounds that inhibit the growth of *Listeria monocytogenes* (e.g., Deli Salads, Dry/Semi-dry Fermented Sausages). The risks associated with these products appear to be primarily associated with product recontamination, which in turn, is dependent on continued, vigilant application of proven control measures.

It is worth noting that two food categories, Fresh Soft Cheese and Soft Ripened Cheese, were previously classified as higher risk products in the draft 2001 version of the risk assessment. This change reflects the acquisition of extensive new exposure data that indicate a significant reduction in contamination rates. The changes in contamination rates, in turn, appear to be the result of increased use of pasteurized or otherwise heat-treated milk, and reflect how relative risk can change as a result of effective food safety control programs.

Risk Designation Low. This risk designation includes two food categories, Preserved Fish and Raw Seafood. Both products have moderate contamination rates but include conditions (e.g., acidification) or consumption characteristics (e.g., short shelf-life) that limit *Listeria monocytogenes* growth and thus limit predicted per serving risks. The products are generally consumed in small quantities by a small portion of the population on an infrequent basis, which results in low predicted per annum relative risks. Exposure data for these products are limited so there is substantial uncertainty in the findings. However, the current results predict that these products, when manufactured consistent with current good manufacturing practices, are not likely to be a major source of foodborne listeriosis.

Risk Designation Very Low. This risk designation includes four food categories: Cultured Milk Products, Hard Cheese, Ice Cream and Other Frozen Dairy Products, and Processed Cheese. These products all have in common the characteristics of being subjected to a bactericidal treatment, having very low contamination rates, and possessing an inherent characteristic that either inactivates *Listeria monocytogenes* (e.g., Cultured Milk Products, Hard Cheese) or prevents its growth (e.g., Ice Cream and Other Frozen Dairy Products, Processed Cheese). This results in a very low predicted per serving relative risks. The predicted per annum relative risks are also low despite the fact that these products are among the more commonly consumed ready-

to-eat products considered by the risk assessment. The results of the risk assessment predict that unless there was a gross error in their manufacture, these products are highly unlikely to be a significant source of foodborne listeriosis.

The following conclusions are provided as an integration of the results derived from the models, the evaluation of the variability and uncertainty underlying the results, and the impact that the various qualitative factors identified in the hazard identification, exposure assessment, and hazard characterization have on the interpretation of the risk assessment.

- The risk assessment reinforces past epidemiological conclusions that foodborne listeriosis is a moderately rare although severe disease. United States consumers are exposed to low to moderate levels of *Listeria monocytogenes* on a regular basis.

- The risk assessment supports the findings of epidemiological investigations of both sporadic illness and outbreaks of listeriosis that certain foods are more likely to be vehicles for *Listeria monocytogenes*.

- Three dose-response models were developed that relate the exposure to different levels of *Listeria monocytogenes* in three age-based subpopulations [i.e., perinatal (fetuses and newborns), elderly, and intermediate-age] with the predicted number of fatalities. These models were used to describe the relationship between levels of *Listeria monocytogenes* ingested and the incidence of listeriosis. The dose of *Listeria monocytogenes* necessary to cause listeriosis depends greatly upon the immune status of the individual.

  1. Susceptible subpopulations (such as the elderly and perinatal) are more likely to contract listeriosis than the general population.

  2. Within the intermediate-age subpopulation group, almost all cases of listeriosis are associated with specific subpopulation groups with increased susceptibility (e.g., individuals with chronic illnesses, individuals taking immunosuppressive medication).

3. The strong association of foodborne listeriosis with specific population groups suggests that strategies targeted to these susceptible population groups, i.e., perinatal (pregnant women), elderly, and susceptible individuals within the intermediate-age group, would result in the greatest reduction in the public health impact of this pathogen.

- The dose-response models developed for this risk assessment considered, for the first time, the range of virulence observed among different isolates of *Listeria monocytogenes*. The dose-response curves suggest that the relative risk of contracting listeriosis from low dose exposures could be less than previously estimated.

- The exposure models and the accompanying 'what-if' scenarios identify five broad factors that affect consumer exposure to *Listeria monocytogenes* at the time of food consumption.

  1. Amounts and frequency of consumption of a ready-to-eat food

  2. Frequency and levels of *Listeria monocytogenes* in a ready-to-eat food

  3. Potential of the food to support growth of *Listeria monocytogenes* during refrigerated storage

  4. Refrigerated storage temperature

  5. Duration of refrigerated storage before consumption

Any of these factors can affect potential exposure to *Listeria monocytogenes* from a food category. These factors are 'additive' in the sense that factors where multiple factors favor high levels of *Listeria monocytogenes* at the time of consumption are typically more likely to be riskier than foods where a single factor is high. These factors also suggest several broad control strategies that could reduce the risk of foodborne listeriosis such as reformulation of products to reduce their ability to support the growth of *Listeria monocytogenes* or encouraging consumers to keep refrigerator temperatures at or below 40 ºF and reduce refrigerated storage times. For example, the 'what-if' scenarios using Deli Meats predicts that consumer education and other

strategies aimed at maintaining home refrigerator temperatures at 40 ºF could substantially reduce the risks associated with this food category. Combining this with pre-retail treatments that decrease the contamination levels in Deli Meats would be expected to reduce the risk even further.

The models generated as the basis for this risk assessment can be used to further evaluate the impact of listeriosis on the public health. For example, the FAO/WHO risk assessment on *Listeria monocytogenes*, which is largely based on the approaches used in the current risk assessment, is being developed to consider several risk management questions posed by Codex Alimentarius. It is anticipated that additional risk assessments on individual foods within specific food categories will be conducted to help answer specific questions about how individual steps in their production and processing impact public health, including the likely effectiveness of different preventive strategies. The models may also be used to evaluate the expected public health impact of preventative controls such as storage limits, sanitation improvements, or new processing technologies. Sources of contamination during food production and retail conditions can also be added to the model to provide more detailed examination of factors contributing to the risk of listeriosis from the final product. For example, the FSIS *Listeria* Risk Assessment in Deli Meats, used portions of the exposure and dose-response models from the current risk assessment to develop information about the effects of combining testing, sanitation, and post-lethality processing interventions to reduce cases of listeriosis.

The models may also be used to evaluate the impact of hypothetical changes in a process such as limits on storage time or temperature to provide insight in how the different components of the model interact. The 'what if' scenarios modeled in this risk assessment provide insight to the impact on public health of limiting storage times, avoiding high temperature refrigeration storage, and reducing contamination levels. Scenario testing emphasizes that the results of any risk assessment are influenced by the assumptions and data sets that were used to develop the exposure assessment and hazard characterization. The results of this revised *Listeria monocytogenes* risk assessment, particularly the predicted relative risk ranking values, could

change as a result of the availability of new information, changes in scientific approaches, or data.

This risk assessment significantly advances our ability to describe our current state of knowledge about this important foodborne pathogen, while simultaneously providing a framework for integrating and evaluating the impact of new scientific knowledge on public health enhancement.