

***Listeria monocytogenes* Risk Assessment: Executive Summary**

FDA/Center for Food Safety and Applied Nutrition

USDA/Food Safety and Inspection Service

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Background

The U.S. Department of Health and Human Service, Food and Drug Administration's Center for Food Safety and Applied Nutrition (DHHS/FDA/CFSAN) conducted this risk assessment in collaboration with the U.S. Department of Agriculture's Food Safety and Inspection Service (USDA/FSIS) and in consultation with the DHHS Centers for Disease Control and Prevention (CDC). The purpose of the assessment is to examine systematically the available scientific data and information to estimate the relative risks of serious illness and death associated with consumption of different types of ready-to-eat (RTE) foods that may be contaminated with *Listeria monocytogenes*. This examination of the current science and the models developed from it are among the tools that food safety regulatory agencies will consider when evaluating the effectiveness of current and future policies, programs, and regulatory practices to minimize the public health impact of this pathogen.

The Healthy People 2010 goals for national health promotion and disease prevention called on federal food safety agencies to reduce foodborne listeriosis by 50% by the end of the year 2005. Preliminary FoodNet data on the incidence of foodborne illnesses for the United States in 2001 indicated that the incidence of infection from *Listeria monocytogenes* decreased between 1996 and 2001 from 0.5 to 0.3 cases per 100,000 people per year. The level then reached a plateau. In order to reduce further the incidence to a level of 0.25 cases per 100,000 people by the end of 2005, it became evident that additional targeted measures were needed. The *Listeria monocytogenes* risk assessment was initiated as an evaluation tool in support of this goal.

Listeria monocytogenes is a bacterium that occurs widely in both agricultural (soil, plants and water) and food processing environments. Ingestion of *Listeria monocytogenes* can cause listeriosis, which can be a life-threatening human illness. In 2000, the CDC reported that of all the foodborne pathogens tracked by CDC, *Listeria monocytogenes* had the second highest case fatality rate (21%) and the highest hospitalization rate (90.5%). Serious illness almost always occurs in people considered to be at higher risk, such as the elderly and those who have a pre-existing illness that reduces the effectiveness of their immune system. Perinatal listeriosis results from foodborne exposure of the pregnant mother leading to *in utero* exposure of the fetus, resulting in fetal infection that leads to fetal death, premature birth, or neonatal illness and death. *Listeria monocytogenes* also causes listerial gastroenteritis, a syndrome typically associated with mild gastrointestinal symptoms in healthy individuals. This risk assessment focuses on the severe public health consequences.

Scope and General Approach

This risk assessment provides analyses and models that (1) estimate the potential level of exposure of three age-based population groups and the total United States population to *Listeria monocytogenes* contaminated foods for 23 food categories and (2) relate this exposure to public health consequences. The food categories consist of foods with a documented history of *Listeria monocytogenes* contamination. The models provide a means of predicting the likelihood that severe illness or death will result from consuming foods contaminated with this pathogen. These

predictions are interpreted and used to estimate the relative risks among the food categories. The foods considered in this risk assessment are ready-to-eat foods that are eaten without being cooked or reheated just prior to consumption. One food, frankfurters, may or may not be reheated prior to consumption and was considered as two separate food categories. The working assumption is that all the cases of listeriosis are attributed to the foods in 23 categories, so that the risk assessment could be 'anchored' to the United States public health statistics. However, it is recognized that additional foods or cross-contamination from raw foods before cooking to other RTE foods may also contribute to additional cases.

The published scientific literature, government food intake surveys, health statistics, epidemiological information, unpublished food product surveys acquired from state and federal public health officials and trade associations, and surveys specifically designed to augment the data available for the risk assessment are the primary sources of data used in this document. Expert advice on scientific assumptions was actively sought from leading scientists from academia, industry, and government. This included two formal reviews of the underlying model structure and assumptions by the United States National Advisory Committee on Microbiological Criteria for Foods. In addition, the risk assessment was initially published in draft form and public comments sought for six months.

While the risk assessment purposely did not look into the pathways for the manufacture of individual foods, the risk assessment model developed can be used to estimate the likely impact of control strategies by changing one or more input parameters and measuring the change in the model outputs. This process, referred to as conducting 'what-if' scenarios, can be used to explore how the components of a complex model interact. Several 'what-if' scenarios are detailed within the risk assessment to evaluate the impact of refrigerator temperature, storage times, and reduction of the number of organisms in foods at before it is sold, and reduction in the contamination levels in foods that support growth.

Results

The relative risk rankings, along with the corresponding risk estimates expressed in terms of both the predicted number of cases per serving and per annum, are provided in Summary Table 1. Both measures are important in understanding and interpreting the risks associated with foodborne listeriosis. The per serving value can be considered the inherent risk associated with the manufacturing, distribution, marketing, and use of the food category, and is reflective of the degree of *Listeria monocytogenes* control achieved. Examples of factors that influence the 'per serving' risk include the frequency of contamination, the extent of that contamination, the ability of the food category to support the growth of *Listeria monocytogenes*, the duration and temperature of refrigerated storage, and the size of the serving. The predicted relative risk per serving can be viewed as the relative risk faced by individual consumers when he/she consume a single serving of the various foods considered in this risk assessment. The 'per serving' risk is typically the value upon which risk management decisions related to a specific product are based.

Summary Table 4. Relative Risk Ranking and Predicted Median Cases of Listeriosis for the Total United States Population on a per Serving and per Annum Basis

Relative Risk	Predicted Median Cases of Listeriosis for 23 Food Categories	
	Per Serving	Per Annum Basis ^b

Ranking	Basis ^a					
	Food	Cases	Food		Cases	
1	High Risk	Deli Meats	7.7×10^{-8}	Very High	Deli Meats	1598.7
2		Frankfurters, not reheated	6.5×10^{-8}	High Risk	Pasteurized Fluid Milk	90.8
3		Pâté and Meat Spreads	3.2×10^{-8}		High Fat and Other Dairy Products	56.4
4		Unpasteurized Fluid Milk	7.1×10^{-9}		Frankfurters, not reheated	30.5
5		Smoked Seafood	6.2×10^{-9}	Moderate Risk	Soft Unripened Cheese	7.7
6		Cooked Ready-to-Eat Crustaceans	5.1×10^{-9}		Pâté and Meat Spreads	3.8
7	High Fat and Other Dairy Products	2.7×10^{-9}	Unpasteurized Fluid Milk		3.1	
8	Moderate Risk	Soft Unripened Cheese	1.8×10^{-9}	Cooked Ready-to-Eat Crustaceans	2.8	
9		Pasteurized Fluid Milk	1.0×10^{-9}	Smoked Seafood	1.3	
10		Low Risk	Fresh Soft Cheese	1.7×10^{-10}	Low Risk	Fruits
11	Frankfurters, reheated		6.3×10^{-11}	Frankfurters, reheated		0.4
12	Preserved Fish		2.3×10^{-11}	Vegetables		0.2
13	Raw Seafood		2.0×10^{-11}	Dry/Semi-dry Fermented Sausages		<0.1
14	Fruits		1.9×10^{-11}	Fresh Soft Cheese		<0.1
15	Dry/Semi-dry Fermented Sausages		1.7×10^{-11}	Semi-Soft Cheese		<0.1

16		Semi-soft Cheese	6.5×10^{-12}		Soft Ripened Cheese	<0.1
17		Soft Ripened Cheese	5.1×10^{-12}		Deli-type Salads	<0.1
18		Vegetables	2.8×10^{-12}		Raw Seafood	<0.1
19		Deli-type Salads	5.6×10^{-13}		Preserved Fish	<0.1
20		Ice Cream and Other Frozen Dairy Products	4.9×10^{-14}		Ice Cream and Other Frozen Dairy Products	<0.1
21		Processed Cheese	4.2×10^{-14}		Processed Cheese	<0.1
22		Cultured Milk Products	3.2×10^{-14}		Cultured Milk Products	<0.1
23		Hard Cheese	4.5×10^{-15}		Hard Cheese	<0.1

^a Food categories were classified as high risk (>5 cases per billion servings), moderate risk (≤ 5 but ≥ 1 case per billion servings), and low risk (<1 case per billion servings).

^b Food categories were classified as very high risk (>100 cases per annum), high risk (>10 to 100 cases per annum), moderate risk (≥ 1 to 10 cases per annum), and low risk (<1 cases per annum).

The second measure, the 'per annum risk,' is the predicted number of fatal infections per year in the United States for each food category. This value takes into account the number of servings of the food category that are consumed. The predicted per annum risk of serious illnesses for each food category can be thought of as the predicted relative total public health impact for each food category. Since the 'per annum' risk is derived from the 'per serving' risk, there is generally a higher degree of uncertainty associated with the former. The predicted per serving and per annum relative risks are used to develop risk rankings to compare the various food categories. In addition to presenting the 'most likely' relative risk rankings for the different population groups and food categories, the risk assessment provides the inherent variability and the uncertainty associated with these rankings.

Evaluation and Interpretation

The overall interpretation of the risk assessment requires more than just a simple consideration of the relative risk rankings associated with the various food categories. First, the interpretation of the results requires an appreciation of the fact that the values being compared are the median values of distributions that may be highly skewed (i.e., not evenly distributed). The use of median values was selected as being the appropriate method for comparing the overall relative risks among the different food categories. The quantitative results must be considered in relation to the associated variability and uncertainty (i.e., the confidence intervals surrounding the median) and interpreted in the context of both the epidemiologic record and how the food categories are manufactured, marketed, and consumed. A detailed consideration of the

quantitative and qualitative findings for each food category is provided in the risk assessment and its appendices.

A number of methods for objectively grouping the results were evaluated, and are discussed in detail within the risk assessment. One approach is cluster analysis. When performed at the 90% confidence level, this analysis groups the per serving rankings into four clusters and the per annum rankings into five. These clusters are used, in turn, to develop a two-dimensional matrix of per serving vs. per annum rankings of the food categories (Summary Figure 1). In this approach, the 'per serving' clusters are arrayed against the 'per annum' clusters. The matrix is then used to depict five risk designations: Very High, High, Moderate, Low, and Very Low.

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 Summary Figure 1), which are likely to require different approaches to controlling foodborne listeriosis.

		Decreased Risk per Annum →		
		Clusters A and B	Clusters C and D	Cluster E
Decreased Risk per Serving ↓	Cluster 1	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 2	High Risk (Clusters 2-A, 2-B) High Fat and Other Dairy Products Pasteurized Fluid	Moderate Risk (Clusters 2-C, 2-D) Cooked RTE Crustaceans	Moderate Risk (Cluster 2-E) No food categories

		Milk Soft Unripened Cheese		
	Cluster 3	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 4	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

Summary Figure 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.]

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 relatively 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, 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.

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.

Conclusions

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 foods 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 °F 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 °F 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.

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.