Interpretive Summary:

Quantitative Assessment of the Relative Risk to Public Health from Foodborne *Listeria monocytogenes* Among Selected Categories of Ready-to-Eat Foods

Center for Food Safety and Applied Nutrition
Food and Drug Administration
U.S. Department of Health and Human Services

Food Safety and Inspection Service
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Preface

This Interpretive Summary provides an overview of the revised *Listeria monocytogenes* risk assessment. Its purpose is to briefly describe, in non-technical language, the material covered in the complete risk assessment (also referred to as the 'technical document'), including background information on *L. monocytogenes* and listeriosis, the techniques and data used to develop the risk assessment, the results of the risk assessment, and limitations and implications of those findings. In order to achieve its purpose, much of the material covered quantitatively in the complete risk assessment is described qualitatively in the Interpretive Summary. A full understanding of the risk assessment requires the reader to consider the technical document. It is recommended that those who wish to do an in-depth evaluation of the assessment read the technical document. The technical document may be found on the web at www.cfsan.fda.gov, www.fsis.usda.gov, www.foodsafety.gov, and www.foodriskclearinghouse.umd.edu. A printed copy will be provided upon request (fax request to the CFSAN Outreach and Information Center at 1-877-366-3322).

Introduction

The United States Department of Health and Human Services, 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 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.

The purpose of the assessment is to examine systematically the available scientific data and information and 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.

Listeriosis (the most significant illness induced by this pathogen) has serious public health consequences to certain susceptible groups of people. The illness occurs rarely (i.e., currently approximately 3.4 cases per million people annually), but when it does occur, it can be life threatening. In healthy people, the microorganism usually causes only a non-invasive gastrointestinal illness, with symptoms including fever, vomiting, and/or diarrhea. For the purposes of this risk assessment, a distinction is made between the mild non-invasive illness (referred to as listerial gastroenteritis) and the severe, sometimes life-threatening, disease (referred to as listeriosis). This risk assessment only considers listeriosis.

Modifications Made to the Draft 2001 Risk Assessment

A draft risk assessment was issued for public comment in January 2001. This version of the risk assessment incorporates, as appropriate, changes in response to the submitted comments and newly available data. It also contains improvements in the modeling techniques, as well as changes to the model inputs and the use of 'what-if' scenarios. These changes are listed in Summary Table 1. The combination of these changes reduced the overall uncertainty ranges for the predicted cases in most of the food categories.

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 *L. 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 *L. 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 (e.g., cheese). One food, frankfurters, may or may not be reheated prior to consumption and was considered as two separate food categories.

The models developed in the risk assessment provide predictions in two forms. The first measure is the estimated rate of a fatal infection from *L. monocytogenes* on an individual serving basis for a particular food category. This value can be considered the inherent risk associated with the manufacture, distribution, marketing, and use of the food in the category, and is reflective of the degree of *L. monocytogenes* control achieved. Examples of factors related to food that influence the "per serving" risk include the frequency of contamination, the extent of that contamination, the ability of foods in the category to support the growth of *L. monocytogenes*, the duration and temperature of refrigerated storage, and the size of the serving.

Summary Table 1. Modifications Made to the 2001 Draft *Listeria monocytogenes* Risk Assessment

Topic	Modifications
Food category changes	▪ Reorganized cheeses based on percentage of moisture ▪ Removed pickled, dried, and processed vegetables; and canned fruits and nuts ▪ Moved vegetable and fruit salads (with dressings) to Deli-type Salad food category ▪ Split frankfurters into 2 categories—reheated and not reheated ▪ Split miscellaneous dairy foods into 2 categories—Cultured Milk Products and High Fat and Other Dairy Products ▪ Increased the number of food categories from 20 to 23
New data/ information	▪ New contamination data (approximately 40 studies, various food categories) ▪ New growth data (e.g., Deli-type Salads) ▪ New information on home storage of deli meats and frankfurters ▪ Changed the storage intervals for Smoked Seafood and Fresh Soft Cheese
Modeling techniques	▪ Contamination data were weighted according to geographic area, age of the study, and size of the data set ▪ A correction factor was developed for food categories for which no recent, large-scale contamination surveys were available ▪ Default shape parameters were used to determine the spread of the contamination distribution for foods with few quantitative data ▪ Separate mortality to hospitalization ratios were calculated for each subpopulation ▪ An additional year of FoodNet surveillance data (2000) was included ▪ A 'scaling factor' was selected to adjust the uncertainty distribution for the predicted number of cases to the FoodNet estimates ▪ Model was rewritten in Visual Basic for Applications to speed up the computation time required for each run of the model and to facilitate review

The predicted relative risk per serving can be viewed as the relative risk faced by individual consumers when they 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.

The second measure is the 'per annum risk,' which is the predicted number of fatal infections per year in the United States for each food category. This value can be considered a "risk multiplier" value that 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 considered 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. Both values are needed to adequately interpret the risk assessment and evaluate the potential public health impact of different risk management strategies.

The predicted per serving and per annum relative risks were 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.

The disease end point in the risk assessment is patient fatalities, which is the most definitive measurement for this foodborne pathogen. The number of cases of listeriosis is then estimated by multiplying the predicted number of deaths by a correction factor determined from FoodNet data from 1997 to 2000. For the total United States population, the correction factor was approximately five, based on data indicating that for each death there were four additional cases of listeriosis. A specific correction factor to convert the predicted number of deaths to cases of listeriosis is used for the three subpopulations evaluated in the model.

Evaluation of sources of contamination, possible intervention steps, and potential mitigation strategies for individual foods are outside the scope of this assessment. However, the assessment and the models may serve as the basis for these types of analyses. Some examples of such applications (referred to as 'what-if' scenarios) are provided in the technical document.

Background

Listeria monocytogenes is a bacterium that occurs widely in both agricultural (soil, plants and water) and food processing environments. Ingestion of *L. monocytogenes* can cause listeriosis, which can be a serious human illness. In 1998, among populations tracked by FoodNet, listeriosis resulted in higher rates of hospitalization than illnesses caused by any other foodborne pathogen and caused over a third of the reported deaths associated with foodborne illnesses. In 2000, the CDC reported that of all the foodborne pathogens tracked by CDC, *L. 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 of listeriosis.

Listeria monocytogenes has only recently been recognized as causing foodborne disease with major public health consequences. The pathogen gained prominence in the 1980's after several large outbreaks in the United States, Canada, and Europe established conclusively that contaminated foods are the primary means by which this microorganism affects human populations. CDC's baseline estimate (using 1996-1997 surveillance data) is that foods contaminated with *L. monocytogenes* caused approximately 2,500 cases of illness, including approximately 500 fatalities, in the United States each year. At the recommendation of CDC, the risk assessment used 2,078 cases of listeriosis and 390 fatalities as the baseline values for the national annual public health impact of the disease. These values are projected from an average of CDC's surveillance data (1997 to 2000). Nearly all cases of listeriosis are foodborne, however, in very few cases is the specific food that caused the disease identified. Identification of a specific food vehicle usually requires first that an outbreak be recognized as such and then, that the outbreak is extensively investigated. Most cases of listeriosis do not appear to be part of recognized outbreaks.

While outbreak investigations provide valuable information about potential modes of *L. monocytogenes* transmission, they do not always identify the contaminated food source. Thus, the full range of potential food vehicles of *L. monocytogenes* has most likely not been identified, and the assessment of risks among different foods cannot be based solely on the current epidemiological record. The current risk assessment relies on consumption and contamination data to estimate the United States consumer's relative risk of exposure and then to estimate the likely serious public health consequences among the various food categories.

Efforts by industry and regulatory agencies during the early 1990's resulted in approximately a 44% reduction in the incidence of listeriosis. This reduction was an outcome of various factors including research, surveillance, outbreak response, and regulatory oversight. These efforts included identification of niches, better sanitation, equipment redesign, and continual surveillance. However, further reductions in the incidence of listeriosis often eluded the industry's food safety efforts, in part because of the unique challenges associated with controlling this pathogen and changes in the way foods are distributed, prepared, and consumed today. Consumers continue to seek convenience as reflected in their food purchasing, preparation, and consumption practices. Use of ready-to-eat foods, including those with extended refrigerated shelf lives, continues to increase. Foods are increasingly bought already prepared from retail establishments, grocery stores, and deli counters where food safety measures may not be sufficient to meet the high level of sanitation needed to control or prevent *L. monocytogenes* contamination. In addition, the increased consumption of foods prepared outside the home and ready-to-eat foods presents unique challenges in food handling and storage practices by food manufacturers, food distributors, food preparers, and consumers to minimize microbial contamination. Not only is *L. monocytogenes* commonly found in food processing, distribution, and retail environments and in the home, it is more resistant than most foodborne pathogens to the treatments and conditions generally used to control microorganisms. In particular, *L. monocytogenes* can grow in many foods when stored at refrigeration temperatures.

This risk assessment focuses on the overall burden of listeriosis on public health and includes the occurrence of both sporadic illnesses (i.e., illnesses not associated with a documented outbreak) and outbreak illnesses. Illnesses attributed to documented outbreaks were a small proportion of the total estimated annual cases of listeriosis. Outbreaks frequently represent a breakdown in food production, manufacturing, or distribution systems that have been put in place to prevent *L. monocytogenes* contamination. 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 Mexican-style soft cheese (1985). Conversely, sporadic cases may reflect the occasional, chance contamination of the food in a food safety system that is otherwise "under control." In both cases, continued improvements in food safety control systems through targeted initiation of new or enhanced controls may be needed to achieve further reductions in the incidence of listeriosis.

A significant difference between this risk assessment and the approach taken by other attempts to evaluate the risks associated with ready-to-eat foods was the complexity of factors considered in the hazard characterization. In addition to establishing a general dose-response relation, models were developed for three distinct age-based subpopulations and for assessing the full range of virulence potential that is likely to occur among *L. monocytogenes* isolates. Including human susceptibility variability and pathogen virulence variability substantially reduces the estimates of risk in relation to a particular dose. It also emphasizes the fact that exposures to *L. monocytogenes* seldom lead to listeriosis, even among highly susceptible segments of the population.

Risk Assessment Framework

This risk assessment document includes an evaluation of the current scientific data and information on listeriosis and it estimates the relationship between exposure to *L. monocytogenes* and human susceptibility to illness or death from listeriosis. It follows the widely accepted framework that separates the assessment activities into four components: hazard identification, exposure assessment, hazard characterization (dose-response assessment), and risk characterization. This framework allows organization of a highly complex array of varied data, characterization of the predicted consequences, definition of uncertainties, and identification of data gaps. The following definition of terms is used:

- <u>Hazard identification</u>. Identifies known or potential health effects associated with *L. monocytogenes* by establishing the general relationship between the pathogen, its presence in foods, and the adverse outcome (illness or death) associated with consumption of contaminated foods.

- <u>Exposure assessment</u>. Estimates the frequency and level of *L. monocytogenes* ingestion from contaminated foods. Evaluates the probability that the pathogen will be present, the frequency of various levels of contamination at the time of sale, the frequency of consumption, and the impact of food handling and storage conditions on the overall potential exposure.

- Hazard characterization. Estimates the relationship between the exposure level (dose) and frequency of severe illness or mortality (response).

- Risk characterization. The components of the model are integrated to estimate the likelihood of an adverse outcome from exposure to the pathogen. The exposure assessment and hazard characterizations are integrated to express mathematically the probability of adverse effects on given population groups as well as to provide a qualitative or quantitative estimate of the uncertainty associated with the predicted risk values. An important part of this step is determining the range of uncertainty of the predictions made and distinguishing this from the variation that is inherent in any biological system. Risk characterization includes an interpretation of the results based on both the model's quantitative predictions and the qualitative knowledge base. This includes attributes such as the production and consumption characteristics of the various food categories and the epidemiological record associated with various foods.

  The risk characterization includes an additional step wherein the relative risk rankings are determined. Conceptually, an individual risk assessment was performed for each of the 23 food categories using the four-step process described above. The results and models for each food category were obtained and then combined and contrasted to establish the relative risk among the food categories, including an evaluation of the uncertainty associated with the risk comparison.

Population Groups Evaluated

The three population groups modeled in this risk assessment are based on the FoodNet[1] surveillance data.

- Perinatal: The perinatal group includes fetuses and neonates from 16 weeks after fertilization to 30 days postpartum. The neonatal cases are assumed to be pregnancy-associated cases where exposure occurs *in utero* as a result of foodborne *L. monocytogenes* infections of the mothers during pregnancy and correspond to the FoodNet data for the age category of less than one month. Data from the County of Los Angeles Department of Health Services were used to determine mortality rates for the perinatal group. Manifestations of listeriosis for this population group include spontaneous abortions, stillbirths, and neonatal infections.
- Elderly: Individuals who were 60 or more years of age. This group was considered to have increased susceptibility to listeriosis due, in part, to physiological changes associated with the natural aging process.
- Intermediate-age group: Because there are insufficient data to separate the remaining population into discrete subgroups, this group includes the remaining population, both healthy individuals (with a substantially lower risk of severe illness or death from *L. monocytogenes*) and certain susceptible

[1] FoodNet is the Foodborne Diseases Active Surveillance Network, which conducts active surveillance for foodborne diseases and related epidemiological studies designed to help public health officials better understand the epidemiology of foodborne diseases in the United States.

subpopulation groups. These latter groups include individuals at higher risk due to underlying conditions; such as AIDS patients or individuals taking drugs that suppress the immune systems (e.g., cancer or transplant drugs), which increase their susceptibility to *L. monocytogenes*. Individuals within these susceptible subpopulations account for most of the cases of listeriosis within the intermediate-age group.

The number of predicted cases of listeriosis is estimated for the total United States population on a per serving and per annum basis for each food category.

Sources and Types of Data

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. The following types of data are used in this risk assessment:

- Consumption surveys of the kinds and quantities of foods consumed;
- Contamination data based on "presence/absence" studies and from studies involving quantitative determination of *L. monocytogenes* in foods;
- Growth and survival data for *L. monocytogenes* during refrigerated storage and thermal inactivation data under cooking or reheating conditions;
- Animal studies that address the range of virulence of *L. monocytogenes* strains and the range of susceptibility found in vulnerable population groups; and
- Information from epidemiological investigations and surveillance on the incidence of listeriosis in the three age-based human populations.

In general, there are insufficient data to model individual foods. However, even if more data were available, a model that attempts to consider individually the ready-to-eat foods would be impractical due to the increased model complexity introduced as the number of foods increases. Therefore, 23 food categories were created based on primary origin (seafood, produce, dairy, and meat), composition and processing (moisture, raw vs. cooked, pH, and salt content), available data on the prevalence of *L. monocytogenes* in the foods, and epidemiological information. The 23 food categories are listed in Summary Table 2. In a few instances, insufficient data on the frequency and extent of contamination are available for some minor foods that have been associated with *L. monocytogenes* contamination (e.g., steak tartar and bakery products) but which did not fit well in any of the food categories. These foods are not included in the risk assessment.

Summary Table 2. Food Categories Used in the *Listeria monocytogenes* Risk Assessment

SEAFOOD
Smoked Seafood (finfish and mollusks)
Raw Seafood (finfish, mollusks, and crustaceans)
Preserved Fish (dried, pickled, and marinated finfish)
Cooked Ready-to-Eat Crustaceans (shrimp and crab)
PRODUCE
Vegetables (raw)
Fruits (raw, dried)
DAIRY
Fresh Soft Cheese (queso fresco, queso de Crema, Queso de Puna)
Soft Unripened Cheese, >50% moisture (cottage cheese, cream cheese, ricotta)
Soft Ripened Cheese, >50% moisture (brie, camembert, feta, mozzarella)
Semi-soft Cheese, 39-50% moisture (blue, brick, Monterey, muenster)
Hard Cheese, <39% moisture (cheddar, Colby, parmesan)
Processed Cheese (cheese foods, spreads, slices)
Pasteurized Fluid Milk
Unpasteurized Fluid Milk
Ice Cream and Other Frozen Dairy Products
Cultured Milk Products (yogurt, sour cream, buttermilk)
High Fat and Other Dairy Products (butter, cream, other miscellaneous milk products)
MEAT
Frankfurters (reheated)
Frankfurters (not reheated)
Dry/Semi-Dry Fermented Sausages
Deli Meats (cooked, ready-to-eat)
Pâté and Meat Spreads
COMBINATION FOODS
Deli-type Salads (fruit, vegetable, meat, pasta, egg, or seafood salads)

The exposure assessment uses nutritional surveys to estimate the frequency and quantities consumed of over 640 ready-to-eat foods. Contamination data from published and unpublished sources are taken, for the most part, from food samples collected at retail. These data are assembled into a database of contamination levels in food samples; the database includes 387 studies with over 346,000 samples. The determination of the growth rate of *L. monocytogenes* in the 23 food categories is calculated from 94 studies with a total of approximately 226 individual samples. The likely contamination levels in the foods within the food categories when consumed (after storage and, in one case, reheating) are subsequently estimated using predictive microbiology models. In keeping with the goal of the Interpretive Summary, the quantitative data used in the risk assessment are provided in Summary Table 3 using qualitative terms to help clarify the type of data used in the model.

An underlying assumption of the risk assessment is that all the cases of listeriosis are attributed to the foods in these 23 categories. This allows the risk assessment to be 'anchored' to the U.S. 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 additional cases.

The hazard characterization uses data from epidemiological studies, health statistics, outbreaks, and scientific investigations with animal models. Due to the lack of data on the rates of symptomatic versus asymptomatic *L. monocytogenes* infections in humans, the dose-response models used in the risk assessment are based on the likelihood that a foodborne *L. monocytogenes* infection would lead to death. The rate of severe cases of listeriosis requiring hospitalization is then estimated based on medical records of the number of additional cases of listeriosis for every death for the specific subpopulations. The dose-response model used in the risk assessment is based on integrating epidemiological data with the characteristics of the pathogen in an animal model.

Exposure Assessment

The purpose of the exposure assessment is to estimate how often consumers eat food contaminated with *L. monocytogenes* and the number of the bacteria likely to be in that food. The contamination data used were primarily from food samples collected in the marketplace (retail). In the few instances where data collected at the processing or manufacturing plant are employed, the data are adjusted to reflect anticipated *L. monocytogenes* levels at retail. *Listeria monocytogenes* can grow during refrigerated storage and is destroyed by heating. Therefore, it is necessary to estimate levels of contamination at consumption. The exposure assessment model estimates the changes in contamination levels during refrigerated storage and reheating in the home. The exposure assessment assumes that the food categories contribute to listeriosis through direct consumption. While epidemiologic investigations suggest in some instances that cross contamination could play a role in the transmission of *L. monocytogenes* during preparation or storage, insufficient data are available to consider this possibility.

Food Consumption. Data from two large, nationwide U.S. food consumption surveys are used to estimate exposure to *L. monocytogenes*. The Continuing Survey of Food Intakes by Individuals (CSFII 1994-96) is the latest survey conducted by the Agricultural Research Service of the USDA. Data from the food intake component of the Third National Health and Nutrition Examination Survey (NHANES III) (1988-94), conducted by the National Center for Health Statistics in the Centers for Disease Control and Prevention (CDC/NCHS) of the Department of Health and Human Services (DHHS), are also used. The CSFII and NHANES III surveys gather information on dietary intake by surveying a sample of consumers over one or two days. Based on the survey data, the consumption patterns for a larger population over one or two days can be estimated, but this information may not predict consumption patterns of individuals or the larger group over an entire year. This contributes to the uncertainty in the model.

Summary Table 3. Summary of Data Used to Model *Listeria monocytogenes* Exposure for each Food Relative to Other Food Categories

Food Category	**Number of Annual Servings** Low = ≤1x10^9 Mod = >1x10^9 to <1x10^{10} High = ≥1x10^{10}	**Median Amount Consumed** Low =≤40g Mod =>40 to <90 g High = ≥90g	**Contamination Frequency** Low =≤2% Mod =>2 to <5% High= ≥5%	**Contamination Level at Retail (% of servings at 10^3 to 10^6 cfu)** Low =<0.1 Mod =>0.1 to <0.6 High= ≥0.6	**Growth Rate During Home Storage (log cfu/day)** Low =≤0.1 Mod =>0.1 to <0.2 High = ≥0.2	**Most Likely Home Storage Time** Short =≤2 days Mod =>2 to 5 days Long = ≥ range 6 to 10 days
SEAFOOD						
Smoked Seafood	Low	Moderate	High	High	Moderate	Moderate
Raw Seafood	Low	Low	High	High	Moderate	Short
Preserved Fish	Low	Moderate	High	Moderate	—[a]	—[a]
Cooked Ready-to-Eat Crustaceans	Low	Moderate	Moderate	Moderate	High	Short
PRODUCE						
Vegetables	High	Low	Moderate	Low	Low	Moderate
Fruits	High	High	High	Low	Low	Moderate
DAIRY						
Fresh Soft Cheese	Low	Low	Low	Low	Low	Moderate
Soft Unripened Cheese, >50% moisture	Moderate	Low	Moderate	Moderate	Low[b]	Long
Soft Ripened Cheese, >50% moisture	Moderate	Low	Moderate	Low	Low[b]	Long
Semi-soft Cheese, 39-50% moisture	Moderate	Low	Moderate	Low	Low[b]	Long
Hard Cheese, <39% moisture	Moderate	Low	Low	Low	Low[b]	Long
Processed Cheese	High	Low	Low	Low	Low[b]	Long
Pasteurized Fluid Milk	High	High	Low	Low	High	Moderate
Unpasteurized Fluid Milk	Low	High	Moderate	Moderate	High	Moderate
Ice Cream and Frozen Dairy Products	High	High	Low	Low	—[a]	—[a]
Cultured Milk Products	Moderate	High	Low	Low	Low[b]	Long
High Fat and Other Dairy Products	High	Low	Low	Low	Moderate	Long
MEATS						
Frankfurters, reheated	Moderate	Moderate	Moderate	High	Moderate	Moderate
Frankfurters, not reheated	Low	Moderate	Moderate	High	Moderate	Moderate
Dry/Semi-dry Fermented Sausages	Moderate	Moderate	High	Moderate	Low[b]	Long
Deli Meats	High	Moderate	Moderate	Low	High	Long
Pâté and Meat Spreads	Low	Moderate	High	Moderate	High	Long
COMBINATION FOODS						
Deli-type Salads	High	High	Moderate	Low	Low	Moderate

[a] A nongrowth food category; growth rates and storage times are not applicable. [b] Includes probabilities that *L. monocytogenes* numbers will decline during storage

Food Contamination. There is no systematic, quantitative survey for levels of *L. monocytogenes* in the U.S. food supply. As a result, contamination data were primarily gathered from published scientific literature, and published and unpublished government and industry documents. Most of these data were obtained from samples of foods collected at retail or during storage before sale. Two types of data on the levels of *L. monocytogenes* contamination in foods were found for most of the food categories. The first type is presence/absence data (whether the sample contains *L. monocytogenes* or not). These data were converted to numerical data and included in the model by assigning the lowest possible contamination level that can be detected by laboratory methods (generally 0.04 organisms per gram of food). So, if *L. monocytogenes* was detected in a food, but the number of organisms was not measured, the sample is assumed to contain at least 0.04 organisms per gram of the food. The second type of data is enumeration data, in which the actual numbers of *L. monocytogenes* were measured in a food sample. Enumeration studies with multiple observations that could be used to characterize the *L. monocytogenes* distribution over a wide range of concentrations are not available for many food categories. The shape of the distribution for these foods is derived by analogy using data from other similar foods.

Most of the contamination studies were conducted in the industrialized countries of Western Europe and North America. It is possible that the studies of foods from other countries, even other industrialized ones, may not be fully representative of the U. S. food supply. A three-tiered system of weighting is used based on the geographical location of the study. While all data are included data from developing countries are given less weight for the purpose of constructing an *L. monocytogenes* distribution for the United States.

Studies used in the risk assessment were published from 1986 to 2002. However, many of the contamination data were collected from 1986 through 1991 (and reported through 1993), before substantial worldwide efforts were made to reduce *L. monocytogenes* contamination. It is possible that older data may unduly bias an estimate of the current rate of contamination. Therefore, the contamination data are also weighted based on the age of the study.

Post-Retail Growth of Listeria. Even when *L. monocytogenes* is initially present at a low level in a food, the microorganism can multiply during storage, including storage at refrigeration temperatures. Some foods are known to support growth of *L. monocytogenes* better than others. In addition, consumer storage practices and conditions vary. Some foods are subject to cooking or reheating before consumption, which can greatly reduce contamination levels. This risk assessment addresses, to the extent possible, each of those factors.

Each food category has a "growth module" appropriate for its characteristics to consider post-retail growth. These modules are used to estimate the numbers of *L. monocytogenes* in the foods at the time of consumption. Examples of factors considered in the growth modules are refrigerator temperatures during storage, the rate of *L. monocytogenes* growth that a food will support, the estimated length of time that food is stored, and the maximum number of microorganisms that a food can support.

Hazard Characterization

Hazard characterization describes the adverse health effects of a particular substance or microorganism. It is the portion of the risk assessment where a dose-response relationship is described, usually as a percentage of the population that will become ill after being exposed to a particular dose or level of contamination. In this risk assessment, the dose-response relationship is based on the number of *L. monocytogenes* consumed, their virulence, and the relative susceptibility of an individual to listeriosis.

For *L. monocytogenes*, the overall incidence of severe illness and the differences in risk to susceptible groups (e.g., the elderly vs. intermediate-age groups) are well characterized. However, the relationship between the number of *L. monocytogenes* consumed (the dose) and the likelihood of illness occurring (response), in combination with the severity of the illness resulting from that dose are not well understood. As a result, the dose-response modules are derived from laboratory experiments with rodents and then modified to fit human epidemiological data.

The occurrence of death is modeled in the risk assessment as a clear, distinct biological endpoint for which there is definitive epidemiological data. The number of serious cases (i.e., those requiring hospitalization) is then estimated from the mortality rate using the CDC data. However, extrapolation from animal data to the human disease response still required several factors to be taken into consideration. These factors are related to the inherent differences between animal species and humans, and how these differences interact with specific aspects of listeriosis. This was accomplished by applying a ‘scaling’ parameter to tie the dose-response relationship from the animal data to the human epidemiological data from CDC. Thus, the dose-response curves include adjustment factors that assure that the predicted numbers of fatalities are in reasonable agreement with the public health statistics available for listeriosis.

Human Susceptibility. Immunological and physiological factors in humans play a role in determining the susceptibility that may be found throughout a population. The probability of death is described for the three different age-based groups of people. As indicated above, epidemiological information is used to adjust the dose-response model to fit the number of listeriosis fatalities observed in FoodNet and to develop the dose-response model for each of these groups.

Virulence. Epidemiological information and laboratory studies indicate that different strains of *L. monocytogenes* vary in their ability to cause illness. This variability influences the number of organisms required to produce illness and possibly the severity of symptoms of illness. A large number of potential human virulence factors have been described that seem to occur in essentially all of the human and environmental isolates that have been studied. Data from mouse lethality studies are used to model the range of strain virulence that may be encountered.

Risk Characterization

Risk characterization combines the results of the exposure assessment and the hazard characterization to produce an estimate of the likelihood of adverse health effects associated with the hazard. It also provides estimates of the variability and uncertainty associated with the predictions of relative risk and the contributing factors. This information is critical to the correct interpretation of the results of a risk assessment. In a quantitative risk assessment, such as this, the risk characterization is developed using computer simulation modeling techniques and then interpreted in relation to available scientific and medical data and expert scientific judgment.

In this assessment, the risk characterization was developed using a two-step computer modeling process. In the first step, the results of the exposure assessment and hazard characterization are combined to provide estimates of risk on a per serving basis and on a per annum basis. This is done using a technique referred to as a two-dimensional Monte Carlo simulation. This involves running the model 30,000 times and integrating the results to produce a "simulation." The process is then repeated to obtain 300 simulations. In addition to providing "most likely" results, this technique allows the variability and uncertainty of the estimates to be evaluated. Consideration of variability and uncertainty associated with the exposure assessment and hazard characterization is a critical component in establishing and interpreting the relative risk of an individual food category causing listeriosis relative to the other food categories.

The second step of the risk characterization is the development of a 'relative risk ranking.' This ranks the foods in relation to each other. The relative risk ranking values range from 1 to 23, with 1 being the food category with the greatest predicted relative risk and 23 the food category with the lowest predicted relative risk. This is again accomplished using computer simulation techniques where the 'most likely' relative risk ranking for each of the food categories is generated for 4,000 simulations. This allows the predicted relative risk ranking for a food category to be accompanied by a measure of the uncertainty associated with that ranking. This provides a means of interpreting the ranking in relation to the degree of confidence associated with the predicted ranking.

Reliability of Results and the Role of Uncertainty and Variability

The risk assessment evaluates available data to describe, as accurately as possible, the current state of scientific knowledge about human listeriosis associated with different types of ready-to-eat foods. In doing so, the assessment attempts to capture both the variability inherent in the incidence of foodborne listeriosis and the uncertainty associated with the data analysis. Two examples of factors that result in risk estimates with wide confidence intervals are the propensity for *L. monocytogenes* to affect only a small segment of the population and the extreme range of levels of *L. monocytogenes* that occur in different foods. Likewise, limits in the availability of data for certain foods and the need to consider how this could affect the final risk estimates increase the associated confidence intervals. Thus, to depict the current knowledge about the risks associated with *L. monocytogenes* contamination of the foods included in this risk assessment, the models developed portray the predicted variability in the occurrence of illness and death and the uncertainty associated with those predictions. The impact of the uncertainties captured by the risk assessment is evaluated by examining the ranges of predicted values or the levels of certainty associated with different estimates. If data used in the model reflect consistency among numerous studies, the degrees of uncertainty associated with the risk estimates are relatively small even if the biological phenomenon might be highly variable. Conversely, if data are meager or inconsistent, the resulting uncertainty estimates have wide ranges. In addition to these quantitative estimates, the variability and uncertainty associated with each food category was evaluated and is discussed in the interpretation of the results.

The nature of the data and the structure of the model used in this risk assessment lead to varying degrees of certainty in the results for each food category and subpopulation. In general, the additional data and modeling techniques employed in revising the risk assessment has lead to a substantial reduction in uncertainty for most food categories. Whether or not the degree of certainty in the risk assessment is sufficient to justify a particular risk management decision will likely depend upon the food and course of action being considered. The accumulation of additional data from research and surveillance, as well as industry-collected data, could potentially reduce the uncertainty associated with the risk assessment's predictions. However, acquisition of additional or better data may or may not change the estimated risk values because of the high degree of inherent variability. The inherent variability associated with this microorganism and its disease potential in humans will always be a critical part of translating the results of this risk assessment into effective risk management strategies.

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 4. Both measures are important in understanding and interpreting the risks associated with foodborne listeriosis. The per serving estimate measures the inherent risk faced by the consumer when he/she consumes an individual serving of that product. This estimate reflects the degree of control achieved by current food safety risk management systems for that product and, as such, is the primary value for assessing which foods are likely to be amenable to further risk reduction efforts. The per annum value can be viewed as a "risk multiplier" which takes the per serving value and accounts for the number of servings that are consumed in the United States each year. This value can be viewed as the predicted total public health burden. Thus, a food that is inherently risky but is consumed only to a highly limited degree would have a high per serving risk but a low per annum risk. Conversely, a food that is manufactured under a rigorous control program may have a low per serving risk but, if consumed daily by most consumers, the food may have a significant per annum risk.

The interpretation of the results also 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. However, these values must be considered in relation to the associated variability and uncertainty (i.e., the confidence intervals surrounding the median). These analyses are provided in detail within the body and appendices of the risk assessment.

The results clearly predict that the risk of listeriosis on both per serving and per annum basis varies greatly among the various food categories. For example, the differential between per serving risks associated with Deli Meats (relative risk rank of 1) and Hard Cheeses (relative risk rank of 23) is almost 10,000,000-fold.

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 Ranking	Per Serving Basis[a]			Per Annum Basis[b]		
		Food	Cases		Food	Cases
1	High Risk	Deli Meats	$7.7x10^{-8}$	Very High	Deli Meats	1598.7
2	High Risk	Frankfurters, not reheated	$6.5x10^{-8}$	High Risk	Pasteurized Fluid Milk	90.8
3	High Risk	Pâté and Meat Spreads	$3.2x10^{-8}$	High Risk	High Fat and Other Dairy Products	56.4
4	High Risk	Unpasteurized Fluid Milk	$7.1x10^{-9}$	High Risk	Frankfurters, not reheated	30.5
5	High Risk	Smoked Seafood	$6.2x10^{-9}$	Moderate Risk	Soft Unripened Cheese	7.7
6	High Risk	Cooked Ready-to-Eat Crustaceans	$5.1x10^{-9}$	Moderate Risk	Pâté and Meat Spreads	3.8
7	Moderate Risk	High Fat and Other Dairy Products	$2.7x10^{-9}$	Moderate Risk	Unpasteurized Fluid Milk	3.1
8	Moderate Risk	Soft Unripened Cheese	$1.8x10^{-9}$	Moderate Risk	Cooked Ready-to-Eat Crustaceans	2.8
9	Moderate Risk	Pasteurized Fluid Milk	$1.0x10^{-9}$	Moderate Risk	Smoked Seafood	1.3
10	Low Risk	Fresh Soft Cheese	$1.7x10^{-10}$	Low Risk	Fruits	0.9
11	Low Risk	Frankfurters, reheated	$6.3x10^{-11}$	Low Risk	Frankfurters, reheated	0.4
12	Low Risk	Preserved Fish	$2.3x10^{-11}$	Low Risk	Vegetables	0.2
13	Low Risk	Raw Seafood	$2.0x10^{-11}$	Low Risk	Dry/Semi-dry Fermented Sausages	<0.1
14	Low Risk	Fruits	$1.9x10^{-11}$	Low Risk	Fresh Soft Cheese	<0.1
15	Low Risk	Dry/Semi-dry Fermented Sausages	$1.7x10^{-11}$	Low Risk	Semi-Soft Cheese	<0.1
16	Low Risk	Semi-soft Cheese	$6.5x10^{-12}$	Low Risk	Soft Ripened Cheese	<0.1
17	Low Risk	Soft Ripened Cheese	$5.1x10^{-12}$	Low Risk	Deli-type Salads	<0.1
18	Low Risk	Vegetables	$2.8x10^{-12}$	Low Risk	Raw Seafood	<0.1
19	Low Risk	Deli-type Salads	$5.6x10^{-13}$	Low Risk	Preserved Fish	<0.1
20	Low Risk	Ice Cream and Other Frozen Dairy Products	$4.9x10^{-14}$	Low Risk	Ice Cream and Other Frozen Dairy Products	<0.1
21	Low Risk	Processed Cheese	$4.2x10^{-14}$	Low Risk	Processed Cheese	<0.1
22	Low Risk	Cultured Milk Products	$3.2x10^{-14}$	Low Risk	Cultured Milk Products	<0.1
23	Low Risk	Hard Cheese	$4.5x10^{-15}$	Low Risk	Hard Cheese	<0.1

Predicted Median Cases of Listeriosis for 23 Food Categories

[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).

‘What-If’ Scenarios

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. Scenarios were run to allow comparison of baseline calculations to new situations that might arise as a result of potential risk reduction strategies. Several ‘what-if’ scenarios are detailed within the risk assessment.

- <u>Refrigerator Temperature Scenario</u>. One example of a ‘what-if’ scenario considered was the impact that assuring that home refrigerators do not operate above either 45 ºF or 41 ºF would have on the total number of cases of listeriosis. In this example, the predicted number of cases of listeriosis would be reduced approximately 69% (from 2105 to 656) by assuring that all home refrigerators temperatures operated at 45 ºF or less. The predicted number of cases was further reduced to 28 per year (>98%) when the distribution of home refrigerator temperatures did not exceed 41 ºF.

- <u>Storage Times Scenario</u>. Storage affects the amount of possible growth in a food. The impact of reducing the maximum storage time (e.g., by labeling food with “consume-by” dates) is evaluated. Limiting the storage time for Deli Meat, for example, from the maximum 28 days estimated to 14 days reduces the median number of cases of listeriosis in the elderly population from 228 to 197 (13.6% reduction). Shortening storage time to 10 days further reduces the cases to 154 (32.5% reduction). Another ‘what-if’ scenario explores how extended shelf life affects the predicted risk of listeriosis in Smoked Seafood. Increasing the storage time from a maximum of 30 days to a maximum of 45 days more than doubled the predicted median number of cases of listeriosis for the elderly subpopulation (0.8 vs. 2.1). Storage times and temperatures interact to affect the amount of growth that could occur in a food.

- <u>Reduction of the Number of Microorganisms Scenario</u>. Interventions designed to reduce the number of *L. monocytogenes* in food before it is sold could impact risk. For example, the cooking or pasteurization of a product in its final package will reduce the level of contamination and if the magnitude of the reduction is large enough, it will also reduce the frequency of contaminated packages. The effects of such interventions are typically expressed in relation to the extent of the surviving microbial population as measured by the number of log reductions achieved. Thus, there is 10% survival with a 1-log reduction, 1% survival with a 2-log reduction, etc. To model the effect of such interventions, scenarios were run to calculate the predicted reduction in the number of cases in the elderly population attributable to Deli Meats after different levels of treatment (e.g., 1-log, 2-log). The storage times and temperatures were not truncated so re-growth in Deli Meats, foods that typically support the rapid growth of *L. monocytogenes* and have extended refrigerated storage times, could occur in packages that contained surviving cells. The modeling predicts that the inclusion of a treatment that produced a 1-log reduction in contamination at retail would reduce the number of predicted cases in the elderly population by 50%, from 227 to 120, and a 2-log treatment would result in a 74% reduction. Further analysis of the results of the scenario (see the “Contamination Level Scenario” below) suggests that these reductions are largely attributable to those instances where either the initial levels in the product were low enough or the extent of the treatment was greatest such that there was an effective reduction in the frequency of contaminated packages. This reflects the fact that in packages where there were surviving *L. monocytogenes*, the pathogens were likely to re-grow during the normal shelf life of the product. Even greater reductions in relative risk would be expected with food categories that do not support the growth of *L. monocytogenes.* In those products the lack of potential re-growth would result in both a reduction in the frequency of contaminated packages and a reduction in the levels of the pathogen in packages still containing viable *L. monocytogenes* at the time of consumption.

- Contamination Level Scenario. The effect on interventions that reduce the frequency and extent of contamination on the risk of foodborne listeriosis was further characterized by a second 'what-if' scenario that considered the impact of limiting the maximum levels of *L. monocytogenes* that occur in retail foods. Deli Meats, which support the rapid growth of the pathogen and can have extended refrigerated storage times, was again examined. The scenario was performed by using single contamination levels instead of a distribution of contamination levels without altering the distribution of storage times and temperatures. This 'what-if' scenario predicts that reducing *L. monocytogenes* in this food category from 1000 to 100 and even down to 1 cfu/g reduces the risk about 30% for each log decrease in contamination level. When the contamination level was decreased to less than one *L. monocytogenes* per serving of Deli Meats, the risk decreased in proportion to the frequency of contamination. This is interpreted as indicating that for foods, such as Deli Meats, that can support the rapid growth of *L. monocytogenes* to high levels during their normal shelf-life, reducing contamination levels by itself would not have a major effect on reducing risk until reductions in contamination levels are large enough to affect the frequency of contamination. Thus, the risk reductions observed in the "Reduction of the Number of Organisms Scenario" above are largely attributable to reductions in the frequency of contaminated servings. This scenario further suggests that, in order for Deli Meats treatments that reduce the levels of *L. monocytogenes* without reducing the frequency of contamination to be effective in reducing the risk of listeriosis, the treatments would have to be coupled with other interventions that limit re-growth (e.g., inclusion of inhibitors, reducing the time and temperature of refrigerated storage). Again, the effect of reducing the levels of contamination in foods that do not support the growth of the pathogen would be expected to have a more substantial impact on reducing the relative risk associated with those food categories since re-growth cannot occur.

The following two scenarios were developed to serve as focused sensitivity analyses directed towards two particular issues.

- Fresh Soft Cheese Made from Unpasteurized Milk Scenario. Unlike the 2001 draft risk assessment, the revised risk assessment indicates that the risk from Fresh Soft Cheese is low. This change is largely attributable to the inclusion of additional retail data indicating a very low prevalence rate in this food category. However, there is a strong epidemiological correlation between Hispanic-style fresh soft cheese (Queso Fresco) and listeriosis. A likely explanation for this discrepancy is that the data collected for this category represents commercially produced cheese whereas the cheeses linked to the disease have often been associated with non-commercially produced cheese, and in some cases illicitly distributed fresh soft cheese made from raw, unpasteurized milk. To characterize the risk from Queso Fresco made from raw milk, the exposure model is constructed using contamination data representative of raw milk. The estimated risk per serving was 43 times greater for the neonatal population and 36 times greater for the elderly population when these cheeses were assumed to be made from unpasteurized milk compared to manufacture with pasteurized milk. This suggests that decreasing the consumption of Fresh Soft Cheese made from unpasteurized milk could reduce the risk associated with this food category.

- Pasteurized Fluid Milk Scenarios. The primary intervention for fluid milk is pasteurization. Requirements for pasteurization can vary from country to country. As with other food categories, the available exposure data were weighted both geographically and temporally. To better understand the possible impact of including contamination data from other countries and data for chocolate milk, scenarios were run using domestic milk only with and without the inclusion of chocolate milk. Excluding non-U.S. milk and chocolate milk had little impact on the predicted number of cases of listeriosis attributed to Pasteurized Fluid Milk on both a per serving and per annum basis.

Evaluation and Interpretation

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 *L. 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 technical risk assessment document.

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, Summary Table 4 includes an arbitrary grouping of the per serving and per annum results into very high, high, moderate, 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 include 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. When performed at the 90% confidence level, this analysis groups the per serving rankings into four clusters and the per annum rankings into five (see Summary Table 5). These clusters are used, in turn, to develop a two-dimensional matrix of per serving vs. per annum rankings (see Summary Figure 1) of the food categories. In this approach, the four per serving clusters are arrayed against three groups of per annum clusters (A and B, C and D, and E). The matrix is then used to depict five overall risk designations: Very High, High, Moderate, Low, and Very Low. For example, as shown in Summary Table 5, 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 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.

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 *L. 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.

Summary Table 5. 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 Other 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 Other Frozen Dairy Products Preserved Fish Processed Cheese Raw Seafood

Decreased Risk per Annum →

Decreased Risk per Serving ↓

	Clusters A and B	Clusters C and D	Cluster E
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 Milk Soft Unripened Cheese	**Moderate Risk (Clusters 2-C, 2-D)** Cooked RTE Crustaceans	**Moderate Risk (Cluster 2-E)** No food categories
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. three groups of 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 Summary Table 5.]

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 *L. 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 *L. 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 U.S. 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-type 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 *L. 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 *L. 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 *L. 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 *L. 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 *L. monocytogenes*.

- Three dose-response models were developed that relate the exposure to different levels of *L. 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 *L. monocytogenes* ingested and the incidence of listeriosis. The dose of *L. 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 *L. 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 *L. monocytogenes* at the time of food consumption.

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

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

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

    4. Refrigerated storage temperature

    5. Duration of refrigerated storage before consumption

Any of these factors can affect potential exposure to *L. monocytogenes* from a food category. These factors are 'additive' in the sense that foods where multiple factors favor high levels of *L. 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 *L. 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 predict 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 Food and Agricultural Organization/World Health Organization (FAO/WHO) risk assessment on *L. 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 preventative strategies. The models may be used to evaluate the expected public health impact of preventive 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 to 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 *L. 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.