Interpretive Summary:

Draft 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

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PREFACE

The U.S. Department of Health and Human Services' Food and Drug Administration's Center for Food Safety and Applied Nutrition (DHHS/FDA/CFSAN), in collaboration with the U.S. Department of Agriculture's Food Safety and Inspection Service (USDA/FSIS) and in consultation with the Centers for Disease Control and Prevention (CDC), conducted an assessment of the relative risk of listeriosis associated with various types of ready-to-eat foods. This draft risk assessment details our current state of knowledge about this foodborne disease, and includes sophisticated models developed to estimate exposure and dose-response relationships, and the variability inherent in these estimates. For the purposes of this risk assessment, a distinction is made between *Listeria monocytogenes* infections limited to mild, flu-like symptoms (referred to as listerial gastroenteritis) and those that are severe and life-threatening (referred to as listeriosis). This risk assessment only addresses listeriosis.

This Interpretive Summary provides an overview of the draft *Listeria monocytogenes* risk assessment. Its purpose is to briefly describe, in non-technical language, the material covered in the complete risk assessment, 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. It is recommended that those who wish to do an indepth 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).

A comment period has been established during which comments, suggestions, and additional data may be submitted. Written comments should be submitted as indicated in the Federal Register Notice of Availability for this document (FDA Docket No. 99N-1168 or FSIS Docket No. 00-048N). Submit comments to the Dockets Management Branch (HFA-305), Docket No. 99N-1168, Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852, or to the FSIS Docket Clerk, Docket No. 00-048N, U.S. Department of Agriculture, Food Safety and Inspection Service, Room 102, Cotton Annex, 300 12th Street, SW., Washington DC 20250-3700.

Introduction

An estimated 76 million cases of foodborne illness occur each year in the United States. The majority of these cases are mild and cause symptoms that last for only a day or two, after which the affected individual recovers without seeking medical care. Some cases of foodborne illness are more serious. CDC estimates that each year, there are 325,000 hospitalizations and 5,000 deaths from all foodborne diseases. More serious illness tends to occur in people considered to be at higher risk, i.e., the elderly, young children, pregnant women, and those who have a preexisting illness or condition that reduces their immune system function. However, foodborne illness can also occur in healthy people, often when they consume a very high number of a pathogenic organism.

L. monocytogenes has only recently been recognized as a foodborne pathogen with major public health consequences. *L. monocytogenes* causes listeriosis, an illness that is potentially life-threatening. The microorganism also causes listerial gastroenteritis, a relatively mild flu-like disease. At least 33 states have regulations requiring health care providers to report cases of listeriosis and most cases of severe listeriosis receive medical attention. *L. monocytogenes* gained prominence in the 1980s after several large outbreaks in the United States, Canada, and Europe established conclusively that consumption of contaminated foods is the primary means by which this microorganism is transmitted to humans.

Major efforts by industry and regulatory agencies during the 1990's led to an approximate 50% reduction in the incidence of listeriosis. However, further reductions in the incidence of listeriosis have eluded the industry's food safety efforts, in part because of the unique challenges associated with controlling this pathogen and changes in the ways foods are processed, distributed, prepared, and consumed today. Reductions in the incidence of listeriosis may have continued if food buying, preparation, and consumption practices had remained unchanged. However, changes in food processing, marketing, preparation, and consumption practices have likely increased the potential for consumer exposure to *L. monocytogenes*. Today, more foods are bought already prepared from retail establishments, grocery stores, and delicatessens where adequate food safety measures may not be in place to control or prevent *L. monocytogenes* contamination. In addition, the move to increased consumption of foods prepared outside the home or ready-to-eat foods demands changes in food handling and storage practices by food manufacturers, food distributors, food preparers and consumers to minimize microbial contamination. The pathogen is 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.

The focus of this risk assessment, and the risk characterization, is on the overall burden of listeriosis on public health and includes the occurrence of both apparently sporadic illnesses (i.e., illnesses not associated with a documented outbreak) and outbreak illnesses.

Barriers to the control of *L. monocytogenes* include:

- The microorganism is commonly found in the environment, including food processing, distribution, and retail environments, and in the home.
- It primarily affects a small segment of the population that has heightened susceptibility.
- It can grow in many foods during refrigerated storage.

- It is more resistant than most bacteria to the conditions and treatments used to control foodborne pathogens.

Realizing that the gains that were achieved in reducing foodborne listeriosis have leveled off, the DHHS/FDA and other federal agencies reviewed their regulatory, outreach, and research programs to determine how to further reduce this risk to public health. This commitment to reducing foodborne listeriosis is formally recognized as a national public health goal in the Healthy People 2010 initiative coordinated by the Department of Health and Human Services. The federal government established a goal of working with industry, consumers, and the public health and research communities to achieve an additional 50% reduction in listeriosis by 2010. On May 5, 2000, President Clinton called on federal food safety regulatory agencies to consider control of listeriosis a priority initiative and to achieve the 50% reduction by 2005.

It is generally recognized that achieving additional reductions in foodborne listeriosis can only be realized by applying the best available scientific knowledge in the review of current programs and policies and developing new initiatives. During the past several years, quantitative microbial risk assessment techniques have emerged as important tools for ensuring that scientific knowledge pertinent to microbial food safety issues is systematically evaluated. Using these advanced techniques, DHHS/FDA, in collaboration with USDA/FSIS and in consultation with the CDC, conducted a quantitative microbial risk assessment of the effect of foodborne *L. monocytogenes* on public health. Federal food safety regulatory agencies will consider using the risk assessment as a tool to evaluate the effectiveness of current policies, programs, and guidance in reducing *L. monocytogenes* contamination of foods, and to identify specific areas on which to focus future initiatives. The risk assessment will be available to industry, as well as public health organizations, consumer organizations and academia.

Scope and General Approach of the *Listeria monocytogenes* Risk Assessment

The purpose of the assessment is to systematically examine available scientific data and information in order to estimate the relative risks of serious illness and death that may be associated with consumption of different types of ready-to-eat foods that may be contaminated with *Listeria monocytogenes*. Food safety regulatory agencies and others will have this evaluation available, along with the mathematical models developed during the risk assessment, to identify the scientific knowledge and information that must be harnessed to further reduce foodborne listeriosis.

This risk assessment is primarily based on contaminated foods at the retail level. The focus of the risk characterization is the overall burden of listeriosis on public health and includes both apparently sporadic illnesses (i.e., illnesses not associated with a documented outbreak) and outbreak illnesses. Illnesses attributed to documented outbreaks are 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. Assessing the likelihood that these systems will fail requires detailed information about the manufacture of individual foods that is beyond the scope of this assessment.

This risk assessment provides analyses and models that (1) estimate the potential level of exposure of three age-based population groups of U.S. consumers to *L. monocytogenes* contaminated foods in 20 food categories, and (2) relate exposure to public health consequences. The food categories include foods associated with outbreaks and individual cases of listeriosis and those for which contamination data are available. The models are used to predict the likelihood that serious illness or death will result from consuming foods contaminated with this pathogen. These predictions are used to estimate the relative risks associated with the various food categories considered in the assessment. The predictions are not intended to serve as a measure of the absolute risk to public health attributable to any particular food. Currently, the food sources are seldom identified for most cases of foodborne listeriosis. As our understanding of listeriosis increases and new contamination data become available, and as more advanced techniques are developed to trace foodborne illness outbreaks back to their source, more foods may be identified as the source of *L. monocytogenes* contamination.

Segments of the Population Evaluated

This risk assessment considers three age-based groups of people, based on the data available from FoodNet[1]. These groups are:

- Perinatal: This group includes fetuses and newborns from 16 weeks after fertilization to 30 days after birth. These are pregnancy-associated cases where the mother experiences a foodborne *L. monocytogenes* infection during pregnancy, exposing her fetus to the pathogen.

- Elderly: This group includes people 60 or more years of age. This group is considered to have increased susceptibility to listeriosis due, in part, to physiological changes associated with the natural aging process.

- Intermediate-age: Because there are insufficient data to separate the remaining population into healthy and susceptible groups, this group includes the entire remaining population. Healthy people appear not to be very susceptible to severe illness or death from *L. monocytogenes*. However, there are certain subpopulations within this age group that are more susceptible to listeriosis, such as AIDS patients or individuals taking drugs that suppress the immune systems (e.g., cancer or transplant patients). Individuals within these subpopulations account for most of the cases of listeriosis within the intermediate-age group.

The *L. monocytogenes* risk assessment follows the generally accepted framework for microbial risk assessments. This framework divides the risk assessment into four distinct components: (1) hazard identification, (2) exposure assessment, (3) hazard characterization, and (4) risk characterization. The first of these components defines the food safety hazard posed by *L. monocytogenes*. The latter three components use available data and, where necessary, science-

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

based assumptions, to develop mathematical models that estimate how often consumers eat food contaminated with *L. monocytogenes,* the number of the bacteria likely to be in that food, and the risk of serious illness or death to the age-based groups when they are exposed to the hazard.

A number of factors were considered in assessing the risk of listeriosis to the public health. These include the severity of the illness caused by *L. monocytogenes,* the likelihood of *L. monocytogenes* (the hazard) being present in a serving of food, the probability that an exposure to the hazard will cause an adverse health effect, the variation in how the population responds to the hazard (variability), and the limitations of the current state of knowledge (uncertainty).

As part of this risk assessment, a mathematical model was developed, based on all of the information gathered. The results of the risk assessment are expressed in three forms. The first is a general description of the characteristics common to foods that have a higher relative risk of being a source of foodborne *L. monocytogenes*. The second is the predicted relative risk of severe illness (listeriosis) that an individual consumer faces when they consume one serving of a particular food. The third is the "most likely" predicted annual impact on U.S. public health, in general, of listeriosis attributable to each of the 20 food categories. Understanding the three types of information is important for the risk assessment to be useful to industry, public health agencies, food safety regulatory agencies, consumers, and the scientific community.

A risk assessment can include both qualitative (descriptive) and quantitative (numerical) data. The factors considered in this risk assessment relied on contamination data that were quantitative, where specific numerical measurements were taken during scientific studies or surveys. Some of the available data, however, were qualitative: many studies of *L. monocytogenes* contamination in foods recorded only the presence or absence of *L. monocytogenes* without determining the number of bacteria present. These presence/absence data were converted to numerical values and were included in the model by assigning the lowest possible contamination level that could be detected by the laboratory methods used. In keeping with the goals of the Interpretive Summary, the quantitative data used in the risk assessment are summarized in Table 1 using qualitative terms to help clarify the types of data used in the model.

Table 1. Qualitative Summary of Data Used to Model *Listeria monocytogenes* Exposure for Each Food Relative to Other Food Categories

Food Category	**Number of Annual Servings** Low = ≤5 x 10^8 Mod = >5x10^8 to <1x10^{10} High = ≥1x10^{10}	**Median Amount Consumed** Low = ≤45 g Mod = >45g to <100 g High = ≥100 g	**Contamination Frequency** Low = ≤4% Mod = >4% to <10% High = ≥10%	**Predicted Contamination Level at Retail (Servings at 10^6 to 10^9 cfu)** Low = <0.1% Mod = ≥0.1% to <1.0% High = ≥1.0%	**Growth Rate During Storage** Low = ≤0.1 Mod = >0.1 to <0.2 High = ≥0.2	**Most Likely Storage Time** Short = ≤ 2 days Mod = >2 days to < range [6 to 10 days] Long = ≥ range [6 to 10 days]
SEAFOOD						
Smoked Seafood	Low	Moderate	High	High	Moderate	Long
Raw Seafood	Low	Low	Moderate	Low	Moderate	Short
Preserved Fish	Low	Moderate	High	Moderate	—[a]	—[a]
Cooked Ready-to-Eat Crustaceans	Moderate	Moderate	Low	Low	High	Short
PRODUCE						
Vegetables	High	Low	Moderate	Low	Low	Moderate
Fruits	High	High	High	Low	Low	Moderate
DAIRY						
Soft Mold-Ripened and Blue-Veined Cheese	Low	Low	Moderate	Moderate	Moderate	Long
Goat, Sheep, and Feta Cheese	Low	Low	Moderate	Moderate	Low	Long
Fresh Soft Cheese (e.g., queso fresco)	Low	Low	High	High	Moderate	Long
Heat-Treated Natural Cheese and Processed Cheese	High	Low	Low	Low	Moderate	Long
Aged Cheese (semi-soft, hard)	High	Low	Low	Low	Low	Long
Fluid Milk, Pasteurized	High	High	Low	Low	High	Moderate
Fluid Milk, Unpasteurized	Low	High	Moderate	Low	High	Moderate
Ice Cream and Frozen Dairy Products	High	High	Low	Low	—[a]	—[a]
Miscellaneous Dairy Products	High	Low	Low	Low	Low	Long
MEATS						
Frankfurters	Moderate	Moderate	Moderate	Low	Moderate	Moderate
Dry/Semi-Dry Fermented Sausages	Moderate	Moderate	Moderate	Moderate	—[a]	—[a]
Deli Meats	High	Moderate	Moderate	Moderate	High	Moderate
Pâté and Meat Spreads	Low	Moderate	Moderate	Moderate	High	Long
COMBINATION FOODS						
Deli Salads	Moderate	High	Moderate	Moderate	High[b]	Moderate

[a] A no-growth food category; growth rates and storage times are not applicable. [b] No data for this food category; surrogate data used from deli meats.

During the collection and evaluation of data for this risk assessment, instances were encountered where certain data were lacking. In such circumstances, data that were reasonably similar were substituted. For instance, data for the levels of *L. monocytogenes* in soft ripened cheese made from unpasteurized milk were used in part for the Fresh Soft Cheese food category. For some of the contamination survey data used, the samples were collected at the manufacturer or processing plant. These contamination data were adjusted to reflect anticipated levels at retail. In addition, no data were found that fully characterize consumer storage practices. In that case, values were estimated by DHHS/FDA and USDA/FSIS scientists and compared to the ranges of storage times recommended by USDA to maintain the quality of various products. DHHS/FDA and USDA/FSIS are interested in receiving additional data on consumer storage practices.

Hazard Identification

The first reported case of foodborne listeriosis occurred in 1953, when the stillbirths of twins were linked to the mother's consumption of unpasteurized milk from a cow with listerial mastitis. The significance of foods as a primary route of transmission for human exposure to *L. monocytogenes* was recognized when several large, common-source outbreaks of listeriosis occurred in the United States, Canada, and Europe during the 1980s. While *L. monocytogenes* can be transmitted several ways–from mother to child, contact from animal to man, and hospital acquired–most cases of human listeriosis involve foodborne transmission.

<u>Listeriosis</u>

Listeriosis is a relatively rare disease in North America and Western Europe, with an incidence rate typically in the range of 4 to 8 cases per 1,000,000 individuals. In the United States, approximately 2,500 persons become seriously ill with listeriosis each year, and approximately 500 of these individuals die. A person infected with *L. monocytogenes* usually displays initial symptoms of fever, muscle aches, and sometimes gastrointestinal symptoms such as nausea or diarrhea. If the bacteria enter the bloodstream, septicemia (characterized by chills, fever, rapid heart rate and breathing, possibly followed by a drop in blood pressure and damage to organs) may result. If infection spreads to the nervous system, symptoms such as headache, stiff neck, confusion, loss of balance, or convulsions can occur. There can be a substantial delay (one to six weeks) between the time of ingestion of a contaminated food and the onset of serious symptoms.

In most individuals, infections with *L. monocytogenes* either do not cause obvious symptoms or are limited to flu-like conditions. In general, most cases that are reported to medical authorities are severe infections requiring medical care. The terms "severe infection," "severe listeriosis," or "invasive listeriosis" are commonly used to describe life-threatening, systemic infections such as perinatal listeriosis and septicemia. The term "listeriosis" is used in this risk assessment to refer to these severe forms of the disease.

Listeriosis most often occurs in people with increased susceptibility. This includes people with preexisting illnesses that reduce their immune system function (such as AIDS or diabetes) or an impaired immune system resulting from age or immunosuppressive treatments (such as treatments for cancer or kidney disease, or use of steroid medications). Pregnant women, or more correctly, their fetuses and newborns, are at higher risk of listeriosis. Infected pregnant women generally only experience a mild, flu-like illness; however, infection during pregnancy can lead to miscarriage, premature delivery, infection of the newborn with serious long-term consequences, or even stillbirth. Children older than 1 month and healthy adults are not particularly susceptible to developing listeriosis.

In addition to listeriosis, there have been several reports of outbreaks of *Listeria*-induced illness where symptoms were limited to mild gastroenteritis. The frequency of these types of outbreaks is unknown because most cases of listerial gastroenteritis are not reported to public health officials. For this reason, this risk assessment is restricted to severe cases of disease, i.e., listeriosis.

Many healthy people carry *L. monocytogenes* in their intestinal tract at some time in their lives. This suggests that people are routinely exposed to *L. monocytogenes*. This also suggests that exposure rarely leads to serious illness, given the low number of reported cases.

<u>*Listeria monocytogenes*</u>

Listeria monocytogenes is commonly found in soil and water, and it has been isolated from a wide range of domestic and wild animals. Vegetables and fruits can become contaminated from the soil or from manure used as fertilizer. Animals can carry the bacteria without appearing ill, and can contaminate foods of animal origin such as meats and dairy products. *L. monocytogenes* has been found in raw foods, such as uncooked meats, vegetables, fruits, and dairy products made from unpasteurized milk.

L. monocytogenes is killed by pasteurization and by the heating methods used to prepare ready-to-eat processed meats. However, *L. monocytogenes* has been found in a wide variety of processed foods that included a pasteurization step in the production process, such as soft cheese and frankfurters, indicating that these foods became contaminated after processing. Post-process contamination can occur because the microorganism can readily adapt to and live in the environment of food processing, distribution, and retail facilities. Unless process controls are strictly followed, processed foods can become re-contaminated.

L. monocytogenes can survive longer under adverse environmental conditions than many other non-spore forming bacteria of food safety concern. Unlike most foodborne pathogens, it can grow at refrigeration temperatures in many foods. It can also tolerate and grow in relatively acidic foods, in foods with relatively low moisture content, and in foods with high salt concentration. This ability to persist in the food environment makes *L. monocytogenes* a particularly difficult microorganism to control.

<u>*Food Category Identification*</u>

A review of the scientific and medical literature identified foods that are historically associated with contamination by *L. monocytogenes.* This review included data from outbreaks, sporadic cases, and contamination studies from the U. S. and other countries. Foods selected for inclusion in the exposure assessment included different types of ready-to-eat foods that are eaten without further cooking and foods that have been cooked but are likely to be cooled and stored before eating, thereby allowing for possible recontamination. Since frankfurters are typically reheated just prior to consumption (although they are fully cooked by the processor), they are modeled both as reheated and not reheated. Because sufficient data on the frequency and extent of contamination were not available, some minor foods that have been associated with *L. monocytogenes* contamination (e.g., hummus) were not included in the risk assessment. Consideration of individual foods would have made the risk assessment overly complex, so the foods were grouped into 20 food categories (Tables 1 and 2). The food categories are further grouped under the general headings of Seafood, Produce, Dairy, Meats, and Combination Foods (i.e., foods composed of a mixture of ingredients, such as salads containing meat, poultry, egg, seafood, pasta, or cheese as the primary ingredient).

Exposure Assessment

The purpose of the exposure assessment was to estimate how often consumers eat food contaminated with *L. monocytogenes* and the number of the bacteria likely to be in that food. Unlike other microbial risk assessments, this risk assessment did not attempt to consider how a food became contaminated or the effects of changes in manufacturing procedures on the amount of *L. monocytogenes* in a food as it is consumed. The reason is that the contamination data used were primarily from food samples collected in the marketplace (retail). Data collected at the processing or manufacturing plant were adjusted to reflect anticipated *L. monocytogenes* levels at retail. *L. monocytogenes* can grow during refrigerated storage and is destroyed by heating. Therefore, it was necessary to estimate levels of contamination at consumption. Thus, a major portion of the exposure assessment was to model 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 earlier epidemiologic investigations suggested that cross contamination could play a role in the transmission of *L. monocytogenes* during preparation or storage, insufficient data were available to consider this possibility.

Food Consumption

Data from two large, nationwide U.S. food consumption surveys were 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. This database contains sufficient data on 18 of the 20 food categories to provide nationally representative estimates of the consumption of foods in those categories. Data from 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), were used for two food categories that had small (less than 30 servings) sample sizes in the CSFII survey. Neither food consumption survey reports the consumption of unpasteurized milk. Thus, it was assumed that consumers who drink unpasteurized milk drink the same amount as those who drink pasteurized milk. On the other hand, we assumed that the annual number of servings of unpasteurized milk is a very small proportion (0.5%) of the annual servings of pasteurized milk.

These two food consumption surveys were designed primarily to gather nutritional information about the foods Americans eat, not for use in a microbial exposure assessment. The surveys did not collect information on aspects of food consumption affecting food safety. For example, the surveys did not determine whether a cheese was made from unpasteurized milk, if milk or juice was pasteurized or unpasteurized, if smoked seafood was hot- or cold-smoked, if luncheon meats were prepackaged or sliced and packaged in a deli; or if steamed shrimp and crabs were eaten immediately after cooking or allowed to cool before eating. Factors such as these could influence the risk of listeriosis associated with a food category, but this specific information was not available for use in this risk assessment.

In addition, dietary information was limited or lacking for many of the age-based groups of concern. Food consumption information was available for the non-institutionalized elderly and women of childbearing age (although very limited for pregnant women and lacking for institutionalized elderly people). Data were also not available to differentiate specific dietary habits associated with other susceptible groups, such as the immunocompromised, who are considered to be at increased risk for serious *L. monocytogenes* infections.

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.

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 was assigned a contamination level of 0.04 organisms per gram of the food. This most likely underestimates contamination levels. The second type of data is enumeration data, which is the number of *L. monocytogenes* organisms that were measured in a food sample. Specific enumeration data for one food category (Fresh Soft Cheese) were lacking, however, so data from a similar category (soft ripened cheese made from unpasteurized milk) were used.

Most of the contamination studies used 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 representative of the U. S. food supply. However, the globalization of the marketplace and the increased number of imported foods that are a routine component of American diets lead to the assumption that the frequency and level of contamination around the world, especially in foods of the U. S. and Western Europe, do not vary significantly for a given food category. The occurrence data from different countries did not seem to differ greatly on an order of magnitude basis. This observation is reinforced by the similarity of data on the incidence of listeriosis in Europe and North America. All foods within a category were assumed to have a similar pattern of contamination. Less than 1% of milk consumed in the U.S. is imported. Therefore, for milk, all available data (North American and European) were used to develop the distribution of contamination; however, only the North American data were used in the model to estimate prevalence.

Most of the studies used in the risk assessment were published from 1986 to 1999. 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. Examination of the studies, by year of publication, overall indicated no significant differences in contamination levels before and after 1993. However, differences in pre-1993 and post-1993 contamination frequencies were observed with certain food categories. This was considered when evaluating the uncertainty of the relative risk estimates for the various food categories.

There are relatively few quantitative or numerical data on *L. monocytogenes* in foods. This is, in part, because the occurrence of *L. monocytogenes* in food is infrequent, but also because most surveys of the occurrence of *L. monocytogenes* in food did not measure the number of organisms in positive samples, but instead used qualitative, presence/absence assays. There was also a large degree of variation, between studies, in the occurrence of high numbers of *L. monocytogenes*. The extent to which this variation reflects true variation in a particular food is not known.

Post-Retail Growth of Listeria

A number of factors affect the level of *L. monocytogenes* in foods that become contaminated. Even when *L. monocytogenes* is initially present at a low level in a contaminated 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.

The growth module of this risk assessment included a number of factors that affect post-retail growth: the initial number of *L. monocytogenes* in the foods when purchased from a retail store, 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. Data on some of these factors were limited or lacking, and additional research in those areas would strengthen this risk assessment. Data on the maximum *L. monocytogenes* growth levels that a food would support under retail conditions were obtained from published laboratory trials in which foods were inoculated with *L. monocytogenes* and growth followed throughout storage at retail conditions.

Some foods are consumed on the day of purchase, and others remain in the home refrigerator for a lengthy period. However, comprehensive studies on the length of time foods are stored in the home were not available. Therefore, the range of storage periods used, including variation and uncertainty, were estimated and these storage times were compared to ranges of storage times recommended by FSIS to maintain the quality of various products to determine whether they were consistent. Recognizing that, in many instances, a food is kept beyond its recommended storage time, estimates of this possibility were included as well. An exception was Frankfurters for which some storage time data were available.

Data on consumer food preparation and eating practices are also limited. Related factors include the time a food is kept after the original package is opened (particularly if it is a vacuum or modified atmosphere package), and likely cross-contamination at the retail level such as sales, or in the home refrigerator or kitchen.

Hazard Characterization

Hazard characterization describes the adverse health effects of a particular substance, organism, or other entity. It is the portion of the risk assessment where a cause-effect or 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 is a function of the number of *L. monocytogenes* consumed and how virulent they are, the effects of the food that the pathogen is in, and the relative susceptibility to listeriosis of the person consuming the contaminated food.

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 relation between the number of *L. monocytogenes* consumed (the dose) and the likelihood of illness occurring, in combination with the severity of the illness resulting from that dose (the response), is not well understood. This is primarily because clinical studies involving human subjects have never been conducted due to the potential for fatal outcomes in susceptible individuals. As a result, most of the data used in the dose-response module were derived from laboratory experiments with rodents and then modified to fit human epidemiological data.

The mouse has been the animal most often used to study *L. monocytogenes*, with infection and death as the two responses most frequently measured. However, it is difficult to correlate infection in mice (as determined by isolating the microorganism from the spleen or liver) with observable symptoms in humans, such as fever, diarrhea, or meningitis. As a result, death was modeled in the risk assessment. Since the human fatality rate for serious *L. monocytogenes* infections has been consistently about 20%, modeling death also provided a means of estimating cases of listeriosis. However, extrapolation from animal data to the human disease response still required several factors to be taken into consideration related to the inherent differences between animal species and humans, and how these differences interact with specific aspects of listeriosis.

The relationship between the number of *L. monocytogenes* consumed and the occurrence of death was modeled by using data obtained from mice exposed to a single strain of *L. monocytogenes*. The mouse model is primarily used to establish the overall pattern of the dose-response relationship. This basic model was then modified to account for variation in virulence among *L. monocytogenes* strains, differences in human susceptibility, and differences in susceptibility between laboratory mice and humans. In order to ensure that extrapolation of animal data to human illness provided results that were realistic, the dose-response curves included an adjustment factor that assured that the predicted numbers of fatalities were in reasonable agreement with the public health statistics available for listeriosis.

One potential source of bias involves the use of mice that were not previously exposed to *L. monocytogenes* in laboratory experiments. In humans, both food contamination data and fecal carriage studies suggest that exposure to *L. monocytogenes* is relatively common among humans. Comparison of dose-response in these unexposed mice with humans that had been exposed is therefore a source of uncertainty. However, this may have minimal impact on the interpretation of the risk assessment because most cases of listeriosis involve individuals with suppressed immune systems. In many ways, these individuals could be considered immunologically naïve (not unlike the mice) despite their prior exposure to *L. monocytogenes*.

Human Susceptibility

Immunological and physiological factors in humans play a role in determining the distribution of 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 was 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 indicates that different strains of *L. monocytogenes* vary in their ability to cause illness. Animal surrogate studies also show a range of virulence among *L. monocytogenes*. It is possible that small genetic differences in strains account for variability in virulence, or that there are virulence factors that have not yet been identified. Another consideration is the various factors that affect the survival and occurrence of disease-producing strains. This variability influences the number of organisms required to produce illness and possibly the severity or symptoms of illness. A large number of potential human virulence factors have been described and seem to occur in essentially all of the human and environmental isolates which have been studied. Data from mouse lethality studies were used to model the range of strain virulence that may be encountered.

Food Composition

The composition of a food, referred to as the food matrix, has been demonstrated to affect the ability of other pathogens to survive inside the body and express virulence. Food matrix effects are also likely to play a role in listeriosis. Possible factors include the fat, water, or salt content of the food. However, no quantitative data specifically related to *L. monocytogenes* were available, so this factor was not included in the current model.

Dose-Response Model Adjustment

A dose-response adjustment factor was applied to the dose-response model to align the range of predicted numbers of deaths with the current epidemiological information. Without the adjustment, when the mouse dose-response model is coupled with the human exposure assessment model, the model can overestimate the incidence of lethal infections in humans from *L. monocytogenes* by a factor of over one million. One possible reason for this large overestimation is that healthy human beings may be much less susceptible to *L. monocytogenes* than the laboratory mice used in experiments. There are a number of possible reasons for the lower susceptibility of humans, any or all of which may contribute.

The adjustment factor is presently used to account for all of the possible known factors, as well as unknown factors, that may influence virulence. In the future, it may be possible to account for additional factors such as food matrix effects or the development of immunity. Because the dose-response adjustment factor was selected to make the rest of the model consistent with existing public health data, new information about initial *L. monocytogenes* contamination levels, growth rates, strain virulence, host susceptibility, foods implicated in listeriosis cases, or the annual number of reported cases could affect the magnitude of the adjustment factor.

Dose-Response Model

Susceptibility and virulence data were combined with the mouse studies to generate a dose-response model to predict the percentage of the three age-based subpopulations that would become ill after being exposed to a particular dose. The dose-response model can thus predict the number of deaths for any level of exposure, but a single exposure level can also be used to compare the three age-based groups. One billion microorganisms is a relatively high dose, and rarely encountered, but can serve as a reasonable example for comparison.

For every 100 million servings, each containing one billion *L. monocytogenes*, the model predicted that the most likely number of deaths in the intermediate-age group (which includes immunocompromised individuals) would be 103. However, given the degree of uncertainty in the model, this prediction could also have ranged from a low value of less than one death to a high value of about 1,190 deaths. For perinatal cases, the subpopulation that was the most sensitive to *L. monocytogenes*, the model predicted the most likely number of deaths to be 14,000, with a range from 3,125 to 781,250 deaths. For the elderly, who fall in between the other two groups in terms of sensitivity, the model predicted that exposure to one billion *L. monocytogenes* would most likely cause 332 deaths. The range was from a low of about one death to a high value of about 2,350 deaths.

Clearly, variability and uncertainty play a large role in the dose-response model, and any additional knowledge that reduced the uncertainty would help narrow the range of predictions.

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 judgement.

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 were combined to provide an estimate of risk on a per serving basis and on a per annum basis. This was done using a technique referred to as a two-dimensional Monte Carlo simulation. This involves solving the model 30,000 times and integrating the results to produce a "simulation." The process was 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 was a critical component in establishing and interpreting the relative risk of an individual food category causing listeriosis in relation to the other 19 food categories.

The second phase of the risk characterization was the development of a "relative risk ranking." This ranks the foods in relation to each other. The relative risk ranking values ranged from 1 to 20, with 1 being the food category with the greatest predicted relative risk and 20 having the lowest predicted relative risk. This was again accomplished using computer simulation techniques where the "most likely" relative risk ranking for each of the food categories was generated for 4,000 simulations. This allowed the predicted relative risk ranking for a food category to be accompanied by a measure of the uncertainty associated with that ranking. This provided a means of interpreting the ranking in relation to the degree of confidence associated with the predicted ranking.

A key determinant in characterizing the risk to the consumer is the predicted relative risk per serving of food, i.e., the probability that consuming one serving of a food will lead to listeriosis to the individual consumer. The predicted risk for the 20 food categories is depicted graphically in Figure 1, which compares the predicted number of listeriosis cases per 100 million servings of a food category. A more detailed table describing the predicted relative risk on a per serving basis is provided in the full risk assessment document.

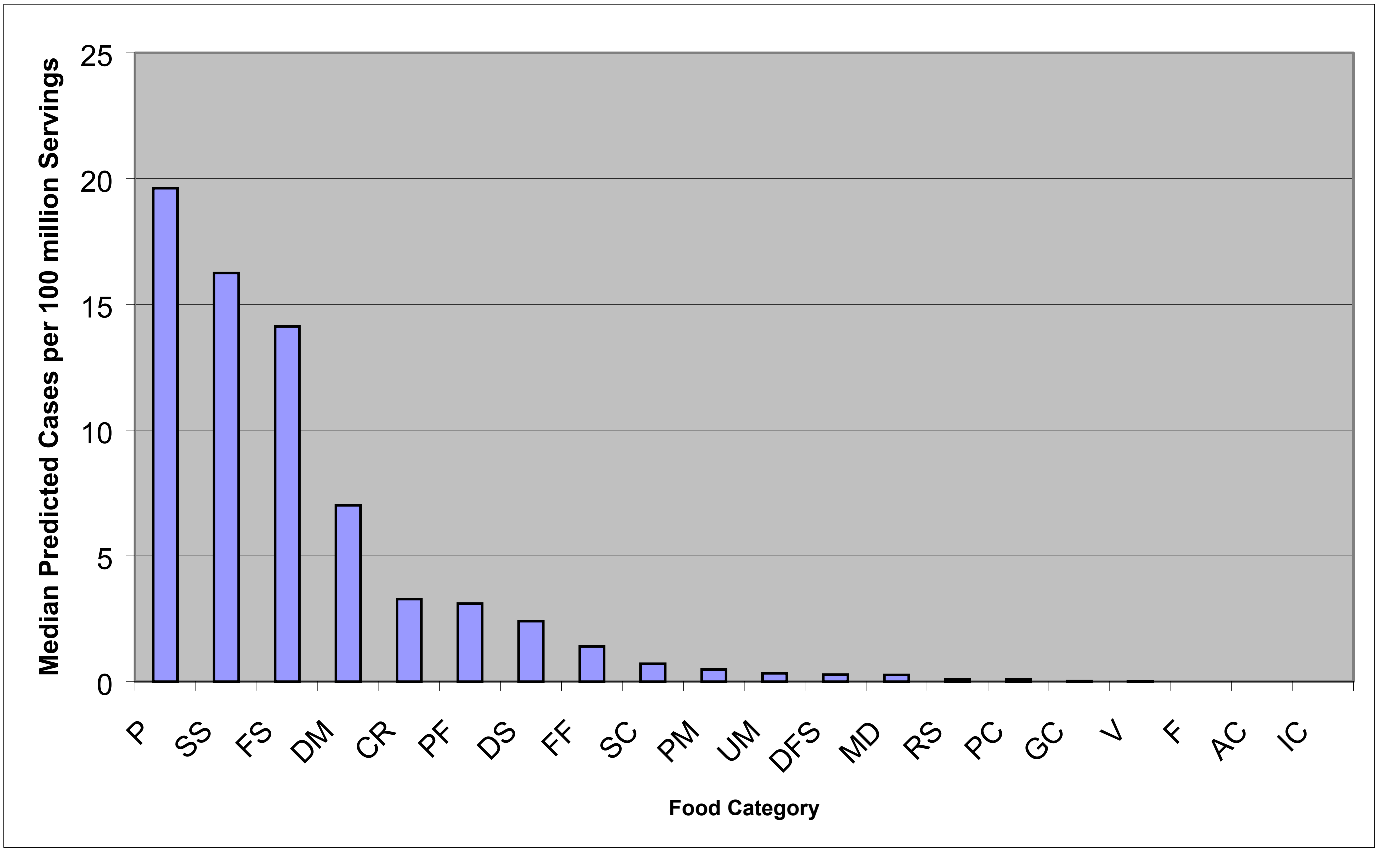

Figure 1. Predicted Relative Risks Associated with Food Categories for the Total Population based on the Median Predicted Cases of Listeriosis per 100 million Servings.

P= Pátê and Meat Spreads; SS= Smoked Seafood; FS = Fresh Soft Cheese; DM = Deli Meats; CR = Cooked Ready-To-Eat Crustaceans; PF= Preserved Fish; DS = Deli Salads; FF= Frankfurters (reheated and non-reheated); SC = Soft Mold-Ripened and Blue-Veined Cheese; PM = Pasteurized Fluid Milk; UM= Unpasteurized Fluid Milk; DFS= Dry/Semi-Dry Fermented Sausages; MD= Miscellaneous Dairy Products; RS = Raw Seafood;
PC = Heat-Treated Natural Cheese and Processed Cheese; GC = Goat, Sheep, and Feta Cheese; V= Vegetables; F= Fruits; AC= Aged Cheese; IC= Ice Cream and Frozen Dairy Products.

These results reinforce a number of general concepts brought out by other evaluations of the risks associated with foodborne listeriosis. As expected, the risk assessment indicates that none of the food categories are risk-free as long as there is a potential for a food to become contaminated with *L. monocytogenes*. However, this risk assessment also demonstrates that there are substantial differences in the relative risk among the different food categories. Further, the risk assessment clearly indicates that listeriosis on a per serving basis is a moderately rare event.

In certain instances, the per serving relative risk rankings were subdivided to better determine how specific practices impact relative risk. For example, two per serving relative risk rankings for frankfurters were determined by considering unheated product only and by estimating the percentage of the product that was reheated prior to consumption. This demonstrated that adequate reheating greatly decreased the relative risk per serving associated with this product (predicted per serving relative risk rankings of 8 and 1, respectively).

As described above, the predicted relative risk values were used to generate the per serving predicted relative risk rankings for each of the three age-based groups (Table 2). Accompanying those predictions is a "latitude array," an example of which is presented in Figure 2. This represents the frequency of a food category's predicted relative risk rankings (based on the total population) when the model was run 4,000 times. As would be expected from the range of parameters covered by the risk assessment, the specific ranking for a food category varies within a range that reflects the uncertainty associated with the ranking. The predicted relative risk rankings should be interpreted in combination with the detailed uncertainty evaluation, which is provided in the full risk assessment, on a per food category basis. In addition, to the latitude array, the qualitative factors identified in the risk assessment but not included in the models must be considered in interpreting the predicted rankings. The consideration of the predicted relative risk ranking in relation to the variability and uncertainty associated with the predictions provides the basis for the conclusions reached by the risk assessment (see Interpretation and Conclusions).

Table 2. Predicted Relative Risk Rankings For Listeriosis among Food Categories for Three U.S. Age-Based Subpopulations Using Median Estimates of Predicted Relative Risks for Listeriosis on a Per Serving Basis

Food Categories[a]	Subpopulation		
	Intermediate Age[b]	Elderly[b]	Perinatal[b]
SEAFOOD			
Smoked Seafood	3	3	3
Raw Seafood	14	14	14
Preserved Fish	7	7	6
Cooked Ready-to-Eat Crustaceans	6	5	5
PRODUCE			
Vegetables	17	17	17
Fruits	18	18	18
DAIRY			
Soft Mold-Ripened & Blue-Veined Cheese	9	9	9
Goat, Sheep, and Feta Cheese	16	16	16
Fresh Soft Cheese (e.g., queso fresco)[c]	2	1	1
Heat-Treated Natural/Process Cheese	15	15	15
Aged Cheese	19	19	19
Fluid Milk, Pasteurized[d]	10	10	10
Fluid Milk, Unpasteurized[d]	11	11	11
Ice Cream and Frozen Dairy Products	20	20	20
Miscellaneous Dairy Products	12	13	13
MEATS			
Frankfurters			
All frankfurters[e]	8	8	7
Only reheated frankfurters[f]	[15]	[15]	[15]
Only non-reheated frankfurters[f]	[1]	[2]	[2]
Dry/Semi-Dry Fermented Sausages	13	12	12
Deli Meats	4	4	4
Pâté and Meat Spreads	1	2	2
COMBINATION FOODS			
Deli Salads	5	6	8

[a] Food categories are grouped by type of food but are not in any particular order.
[b] A ranking of 1 indicates the food category with the greatest predicted relative risk per serving of causing listeriosis and a ranking of 20 indicates the lowest predicted relative risk of causing listeriosis.
[c] Data from soft ripened cheese made from unpasteurized milk were used in the modeling to define the shape of the distribution of contamination data for fresh soft cheese.
[d] All available data for this food category were used in the modeling to define the shape of the distribution for this food category but only contamination data from North America were used to determine the frequency of contamination.
[e] This ranking is based on the assumption that 1% to 14 % of frankfurters are consumed without reheating and the remainder are assumed to be adequately heated before consumption.
[f] The bracketed values reflect the ranking of frankfurters, reheated and not reheated, when modeled independently. The rankings of the other food categories would be adjusted accordingly. For example, for the intermediate age, the predicted risk ranking is 1 for non-reheated frankfurters and would be 2 for Pâté and Meat Spreads.

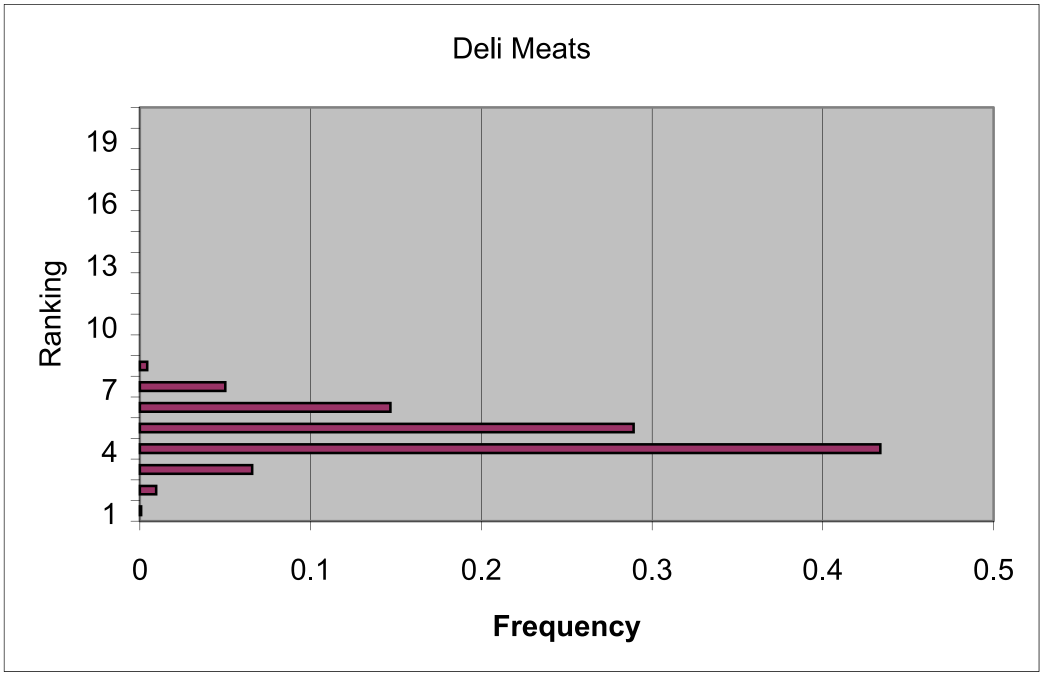

Figure 2. Example Latitude Graph: Rankings of total predicted listeriosis cases per serving for Deli Meats. [The figure depicts that when the relative risk ranking simulation was run 4,000 times, deli meats ranked 7th about 5% of the time, 6th about 15% of the time, 5th about 29% of the time, etc.]

In addition to the relative risk per serving determinations, the risk assessment also considered the predicted relative risk of the food categories contributing to the incidence of listeriosis on a per annum basis (Table 3). These values were derived using the computer simulation modeling techniques described above, but also took into account the number of servings of the food categories consumed each year. The results were then transformed to predicted relative risk rankings. If the per serving predicted relative risk ranking provides a measure of the risk to the individual consumer, then the per annum predicted relative risk ranking provides a measure of the risk to the total U.S. population. Thus this risk assessment suggests that for foods that are consumed in higher amounts, such as frankfurters, the predicted number of listeriosis cases per annum is higher than for other foods that are consumed in low amounts, such as pâté. For example, in Table 2, the predicted relative risk per serving for pâté is 1 (for intermediate age) but because so few servings of this food are consumed, the predicted relative risk per annum is 8 (for intermediate age). However, the per annum predicted relative risk rankings generally have a greater degree of uncertainty than the corresponding per serving rankings. In a few instances such as for pasteurized milk and vegetables, when high consumption rates are combined with uncertainty in frequency or contamination levels, there is significant impact on the uncertainty associated with the predicted per annum risk ranking. For example the per annum ranking for pasteurized milk has a great deal of uncertainty due to the lack of sufficient data on contamination levels in combination with high consumption (high number of annual servings and large serving sizes). Again, the variability and uncertainty underlying these rankings were evaluated for each food category (see the technical risk assessment document for details), in order to interpret the results which provide the basis for the interpretation and conclusions described later.

Table 3. Predicted Relative Risk Rankings for Listeriosis among Food Categories for Three U.S. Age-Based Subpopulations Using Median Estimates of Relative Predicted Risks for Listeriosis on a Per Annum Basis

Food Categories[a]	**Subpopulation**		
	Intermediate Age[b]	**Elderly**[b]	**Perinatal**[b]
SEAFOOD			
Smoked Seafood	6	6	7
Raw Seafood	17	20	17
Preserved Fish	13	13	13
Cooked Ready-to-Eat Crustaceans	9	8	9
PRODUCE			
Vegetables	11	9	11
Fruits	16	14	14
DAIRY			
Soft Mold-Ripened and Blue-Veined Cheese	14	15	15
Goat, Sheep, and Feta Cheese	18	17	18
Fresh Soft Cheese (e.g., queso fresco)[c]	7	11	6
Heat-Treated Natural/Process Cheese	10	10	10
Aged Cheese	19	18	19
Fluid Milk, Pasteurized[d]	3	2	2
Fluid Milk, Unpasteurized[d]	15	16	16
Ice Cream and Frozen Dairy Products	20	19	20
Miscellaneous Dairy Products	5	4	5
MEATS			
Frankfurters[e]	4	5	4
Dry/Semi-Dry Fermented Sausages	12	12	12
Deli Meats	1	1	1
Pâté and Meat Spreads	8	7	8
COMBINATION FOODS			
Deli Salads	2	3	3

[a] Food categories are grouped by type of food but are not in any particular order.
[b] A ranking of 1 indicates the food category with the greatest predicted relative risk per annum of causing listeriosis and a ranking of 20 indicates the lowest predicted relative risk of causing listeriosis.
[c] Data from soft ripened cheese made from unpasteurized milk were used in the modeling to define the shape of the distribution of contamination data for fresh soft cheese.
[d] All available data for this food category were used in the modeling to define the shape of the distribution for this food category but only contamination data from North America were used to determine the frequency of contamination. Also see text for a discussion of the effects of uncertainty on the ranking for pasteurized milk and other foods that are consumed in high amounts.
[e] This ranking is based on the assumption that 1% to 14 % of frankfurters are consumed without reheating and the remainder are adequately heated before consumption.

Risk Assessment As A Tool For Identifying Information and Research Needs

Several gaps in data and information were identified during the risk assessment. Filling these gaps with new information about *L. monocytogenes* and listeriosis would be useful to refine and improve the accuracy of this risk assessment. In addition, new information about *L. monocytogenes* and new data associated with specific food categories will facilitate the development of product-specific risk assessments. The increased accuracy of *L. monocytogenes* risk assessments will provide federal food safety regulatory agencies, public health organizations and industry with information to assist with risk management decisions and developing preventive intervention programs. Among the types of information needed are the following:

- Investigative techniques and efforts need to be enhanced, both in surveillance and outbreak investigation. Outbreak investigations need to explore the kinds and amounts of food consumed by each patient and the frequency of consumption, as well as the number of *L. monocytogenes* in the food. The total number of individuals exposed to the food would allow calculation of the attack rate.

- Delineation of sick and exposed individuals by relevant characteristics would also be informative. Future *L. monocytogenes* risk assessments might also include the CDC Pregnancy Nutrition Surveillance Survey. Additional studies specifically comparing diets of pregnant women to women of childbearing age would also be helpful.

- It is unclear whether consumption by the elderly has been adequately represented in the food consumption surveys: data are not available to characterize the consumption by elderly living in nursing homes or other forms of assisted living outside of the home.

- In addition, information is needed about the health status of consumers that would adequately delineate those individuals who are immunocompromised, and to better characterize the consumption patterns of all susceptible groups.

- Although this risk assessment assumed that overall consumption does not change significantly over a year, a better understanding of consumption patterns for the subpopulations would strengthen the risk assessment.

- Data on consumer food preparation, storage, and eating practices are needed. Related factors include the time after opening the original package (particularly if it is a vacuum or modified atmosphere package) and likely cross-contamination in the home refrigerator or kitchen.

- Information about the reheating practices for frankfurters and deli meats before consumption is needed.

- Additional studies are also needed on selected foods to determine *L. monocytogenes* growth in the presence of competing microbes and to model actual growth conditions. These studies should also document the physical properties of the food (acidity, salt, moisture) and identify the *L. monocytogenes* strain used. Use of a single, well-characterized *L. monocytogenes* strain is recommended so that the results of different studies can be compared. This should include consideration of what impact food composition and handling have on the expression of virulence factors by the microorganism.

- Typical systems to classify *L. monocytogenes* strains (serotyping, phagetyping, ribotyping) are valuable epidemiological tools for identifying and tracking outbreaks, but they are not mechanistically related to virulence. Development of rapid methods to identify high and low virulence strains would allow more effective assessment of the public health threat of *L. monocytogenes* found in food.

- Most data on *L. monocytogenes* contamination of foods were presence/absence data. More quantitative contamination data are needed.

- Studies are needed to determine the occurrence and growth of *L. monocytogenes* in specific foods during storage (identified as high risk products by this risk assessment or by epidemiologic information) and to relate those new data to shelf-life and dating recommendations of manufacturers.

- Data are needed on the effects of various interventions such as irradiation, organic acids, modified atmosphere, etc., on the control of *L. monocytogenes* contamination and growth in products.

- Data are needed on retail practices, including at deli counters, and the occurrence or potential occurrence of cross-contamination.

Interpretation and Conclusions

This risk assessment included analysis of the available scientific information and data in the development of exposure assessment and dose-response models to predict the relative public health impact of foodborne *L. monocytogenes* from 20 food categories. The assessment focuses on predicting the comparative risk among ready-to-eat foods that have a history of either *L. monocytogenes* contamination or were implicated epidemiologically. The risk assessment focuses on the predicted relative risk associated with these foods in relation to the overall incidence of listeriosis including both apparently sporadic illnesses and illnesses associated with outbreaks. Illnesses attributed to documented outbreaks are a small proportion of the total estimated annual cases of listeriosis. Outbreaks frequently represent a breakdown in the food safety controls that have been established to prevent such occurrences. For example, outbreaks of listeriosis have been linked to failure to protect a frankfurter processing line from environmental contamination caused by plant renovations (1998-99), use of defective processing equipment in the production of chocolate milk (1994), and inadequate pasteurization of milk used to make fresh soft Mexican-style cheese (1987). Therefore, maintenance of food safety control systems and either initiating new or strengthening existing controls will contribute to reduction of the incidence of listeriosis.

The scientific evaluations and the mathematical models developed during the risk assessment, provide a systematic assessment of the scientific knowledge needed to assist both in reviewing the effectiveness of current policies, programs, and practices, and identifying new strategies to minimize the public health impact of foodborne *L. monocytogenes*. This systematic assessment provides a foundation to assist in 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, considering only the simple ranking of the relative risk associated with the various food categories is not sufficient. 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 pertaining to the production, marketing, and consumption of the various food categories.

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. Although the exposure assessment suggests that U.S. consumers are exposed to low levels of *L. monocytogenes* on a regular basis, the likelihood of acquiring listeriosis is very small.

- The risk assessment also supports the findings of epidemiological investigations of both sporadic illness and outbreaks of listeriosis that certain foods, e.g., pâté, soft cheeses, smoked seafood, frankfurters, and some foods from delicatessen counters, are potential vehicles of listeriosis for susceptible populations.

- New case control studies are needed to reflect changes in food processing, distribution patterns, preparation, and consumption practices.

- From the exposure models, it is apparent that five factors affect consumer exposure to *L. monocytogenes* at the time of food consumption.

    1. Amounts and frequency of consumption of a food
    2. Frequency and levels of *L. monocytogenes* in ready-to-eat food
    3. Potential to support growth of *L. monocytogenes* in food 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;" food categories in which more than one of these factors affects the food favor a greater risk of higher levels of *L. monocytogenes* contamination and are the foods more likely to increase consumers' risk of listeriosis.

- Three dose-response models were developed that predict the number of deaths that are likely to be caused by exposure to different levels of *L. monocytogenes* in three age-based subpopulations; perinatal (fetuses and newborns), the elderly, and intermediate-age. These models are used to describe the relationship between levels of *L. monocytogenes* ingested and the incidence of serious listeriosis. From this hazard characterization, it is concluded that the dose of *L. monocytogenes* necessary to cause listeriosis depends greatly upon the immune status of the individual.

    1. Susceptible subpopulations (the elderly and perinatal) are more likely to contract listeriosis from a specific exposure to *L. monocytogenes* than the intermediate-age group (general population).

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

    3. The strong association of foodborne listeriosis with specific groups suggests that reducing the public health impact of this pathogen would benefit from strategies targeted to susceptible subpopulations, i.e., perinatal (pregnant women), elderly, and susceptible individuals of the intermediate-age group.

- The dose-response models developed for this risk assessment considered, for the first time, the range of virulence of different isolates of *L. monocytogenes*. In addition to more accurately describing the likelihood of *L. monocytogenes* causing disease, the dose-response curves suggest that the relative risk of contracting listeriosis from low exposures is less than previously calculated.

- The risk characterization combines the exposure and dose-response models to predict the relative risk of illness attributable to each food category. Although a substantial degree of variability and uncertainty exists around the models' predictions, the results provide a means of comparing the relative risks among the different food categories and subpopulations considered in the assessment and should be useful in focusing control strategies.

- Extensive research has demonstrated that for products that receive a treatment that inactivates *L. monocytogenes,* the risk of listeriosis is determined to a large extent by the potential for recontamination. There is a need for increased awareness of the potentially important role refrigerated storage conditions and shelf-life have on the risks associated with products that support the growth of *L. monocytogenes.*

    1. New strategies are needed (a) to decrease the rates of recontamination during the manufacturing and marketing of ready-to-eat foods, (b) to estimate the impact of

storage times and temperatures on the potential levels of *L. monocytogenes* when the microorganism is present, and (c) to ensure that adequate information related to storage conditions and safe handling practices is available.

2. Industry and regulatory agencies should identify the key aspects of sanitation standard operating practices, good manufacturing practices, and other process control and process verification systems, such as Hazard Analysis Critical Control Point (HACCP), that prevent the recontamination of ready-to-eat foods, particularly those that support the growth of *L. monocytogenes* at refrigerator temperatures.

3. New strategies are needed to ensure that consumers receive sufficient product safety information about the storage and shelf-life of refrigerated products, so that consumers can store them properly and use or discard when the shelf-life expires.

4. New strategies are needed to educate consumers to pay strict attention to manufacturer safety information about the storage and shelf-life of refrigerated products, storing them properly and using or discarding when the shelf-life expires.

- The following food categories warrant identification of new approaches for reducing the potential for *L. monocytogenes* contamination:

  Pâté and Meat Spreads; Fresh Soft Cheese, such as queso fresco (particularly those made with unpasteurized milk); Smoked Seafood; Deli Meats; and Deli Salads. Unpasteurized Fluid Milk is also included in this group because in addition to being a moderate relative risk from direct consumption, it is also a primary ingredient in products that have a higher degree of relative risk or that have been epidemiologically linked to listeriosis (e.g., Fresh Soft Cheese).

- This risk assessment indicated that a number of the food categories have either a high degree of variability associated with their potential to contribute to foodborne listeriosis or a higher degree of uncertainty associated with their predicted relative risk ranking. These food categories need to be examined on an individual basis to determine if the appropriate means for reducing their predicted relative risk is through the establishment of control strategies (variability) or whether ranking will be affected by acquisition of additional data (uncertainty). Food categories that require such an evaluation are:

  Preserved Fish; Dry/Semi-Dry Fermented Sausages; Cooked Ready-to-Eat Crustaceans; Miscellaneous Dairy Products; and Vegetables.

- Some food categories have a potentially low relative risk due to the inclusion of a "listericidal treatment" in the manufacturing or preparation of the foods. Over 15 years of scientific investigations have indicated that the primary determining factor affecting the presence of *L. monocytogenes* in these products is the likelihood that they will be recontaminated. Thus, the low relative risk associated with these foods is dependent on manufacturers', distributors', food service and retailers', and consumers' continued vigilance in producing, preparing, and storing these products. The importance of this continuing vigilance is emphasized by the fact that several of these foods have been implicated in outbreaks of listeriosis. This group of food categories is:

Frankfurters (when adequately reheated); Heat-Treated Natural Cheese and Processed Cheese; Pasteurized Fluid Milk; and Soft Mold-Ripened and Blue-Veined Cheese.

- Some food categories have low predicted relative risk due to inherent characteristics associated with the food. In addition this group of food categories appears to represent substantially less relative risk in terms of either cases or outbreaks of foodborne listeriosis. This group of food categories is:

  Ice Cream and Frozen Dairy Products; Aged Cheese; Fruits; Goat, Sheep, and Feta Cheese; and Raw Seafood.

The models generated as the basis for this risk assessment can be used in the future to further evaluate the impact of listeriosis on the public health. It is anticipated that additional risk assessments on individual foods within specific food categories will be conducted to help answer specific questions about how individual steps in their production and processing impact public health, including the likely effectiveness of different preventive strategies. The models may 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.

The results of this *L. monocytogenes* 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 draft risk assessment, particularly the predicted relative risk ranking values, could change as a result of the DHHS/FDA and USDA/FSIS actively seeking new information, scientific opinions, or data during the public comment period.

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 enhancing public health.