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

EXECUTIVE SUMMARY

The U.S. 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 Centers for Disease Control and Prevention (CDC). 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*. This examination of current science and the models developed are among the tools that food safety regulatory agencies will consider using to evaluate the effectiveness of current policies, programs and regulatory practices to minimize the public health impact of this pathogen. While listeriosis (the illness induced by this pathogen) has serious public health consequences in certain susceptible groups of people, these manifestations of illness occur rarely (4 to 8 cases per 1,000,000 people annually). However, when listeriosis does occur, it is often serious. In 1998, when listeriosis occurred in populations tracked by FoodNet, it resulted in higher rates of hospitalization than illnesses caused by any other pathogen and caused nearly half the reported deaths. In healthy people, the microorganism usually causes only flu-like symptoms. For the purposes of this risk assessment, a distinction is made between infection limited to mild, flu-like symptoms (referred to as listerial gastroenteritis) and severe, sometimes life-threatening disease (referred to as listeriosis). The risk assessment only considers listeriosis.

This risk assessment provides analyses and models that (1) estimate the potential level of exposure of three age-based U.S. population groups to *L. monocytogenes* contaminated foods in 20 food categories and (2) relate this exposure to public health consequences. The food categories are composed of foods with a 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, and do not predict the absolute public health consequences attributable to any particular food. The foods considered in this risk assessment are ready-to-eat

foods that are generally eaten without being cooked (e.g., cheese) or are typically reheated (e.g., frankfurters) prior to consumption.

The models developed in the risk assessment provide predictions in two forms. The first is the estimated probability of a fatal infection from *L. monocytogenes* on an individual serving basis for a particular food category. The second is the predicted number of fatal infections per year in the United States for each food category. The number of cases of serious illness is then estimated by multiplying the predicted number of deaths by five, based on data indicating that for each death, 4 additional cases of listeriosis occur. The predicted relative risk per serving can be viewed as the relative risk faced by individual consumers when they consume the various foods considered in this risk assessment. The predicted per annum risk of serious illnesses for each food group can be considered the predicted relative total public health impact for each food group. These predictions were then 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 estimates the inherent variability and the uncertainty associated with these estimates.

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 in the future.

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 1999, the CDC reported that of all the foodborne pathogens tracked by CDC, *L. monocytogenes* had the second highest case fatality rate (20%) and the highest hospitalization rate (90%). 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 *in utero* exposure of the pregnant mother, causing fetal infection that leads to fetal death, premature birth, or neonatal illness and death. *L. monocytogenes* also causes milder forms of listeriosis characterized by gastrointestinal symptoms in healthy individuals. This risk assessment focuses only on the severe public health consequences.

L. 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 estimates that foods contaminated with *L. monocytogenes* cause approximately 2,500 cases of illness, including approximately 500 fatalities, in the United States each year. 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. The current risk assessment relies on contamination data to estimate the U.S. consumer's relative risk of exposure and then uses those exposure data to estimate the likely serious public health consequences among the various food categories.

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 distributed, prepared, and consumed today. The trend in reduced incidence of listeriosis may have continued had food buying, preparation, and consumption practices remained unchanged. However, consumer practices have changed, which has increased use of food purchasing, preparation, and consumption practices that have the potential to increase consumer exposure to *L. monocytogenes*. For example, imported foods constitute a larger proportion of daily diets than they did 10 years ago. Today, more foods are bought already prepared from retail establishments, grocery stores, and deli counters 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. 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.

The focus of this risk assessment is 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 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. 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).

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. It follows a framework that separates the assessment activities into four components: hazard identification, exposure assessment, dose-response assessment (hazard characterization), 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.

- Hazard identification. 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.

- Exposure assessment. Estimates the likely frequency and level of intake of the pathogen in contaminated foods. Evaluates the probability that the pathogen will be present, the frequency of various levels of contamination, and the impact of food handling, processing, and storage conditions on the overall potential exposure.

- Hazard Characterization. Estimates the relationship between the exposure level (dose) and frequency of illness or other adverse effect (response). The severity of the health effects is also evaluated, often by considering multiple biological endpoints (e.g., infection, morbidity, fatalities, and sequelae).

- Risk characterization. Estimates the likelihood of an adverse outcome from exposure to the pathogen. The exposure assessment and hazard characterizations are integrated to mathematically express 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 degree of uncertainty in relation to the results and distinguishing this from the variation that is inherent in any biological system.

Population Groups Evaluated

Based on age, three U.S. population groups that were distinguished by the FoodNet[1] surveillance data were modeled in this assessment.

- Perinatal: This group includes fetuses and neonates from 16 weeks after fertilization to 30 days postpartum. These are pregnancy-associated cases where exposure occurs most often *in utero* as a result of foodborne *L. monocytogenes* infections of the mothers during pregnancy. Manifestations include spontaneous abortions, stillbirths, and neonatal infections.
- Elderly: Individuals who are 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 group: Because there are insufficient data to separate the remaining population into discrete subgroups, this group includes the remaining population, both healthy individuals (with very low risk of severe illness or death from *L. monocytogenes*) and certain susceptible population groups. The population groups include individuals with increased susceptibility to listeriosis, such as AIDS patients or individuals taking drugs that suppress the immune systems (e.g., cancer or transplant drugs). Individuals

[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 U.S.

within these susceptible population groups account for most of the cases of listeriosis within the intermediate-age group.

Sources and Types of Data

The published scientific literature, national government food intake surveys, health statistics, epidemiological information, and personal communications with state and federal public health officials and trade associations were the primary sources of data used in this document. The public was invited to submit scientific data and information for use in this risk assessment in the *Federal Register* (US DHHS, 1999a). The following types of data were 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, survival and thermal inactivation data for *L. monocytogenes* under refrigeration, storage and 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.

The exposure assessment used contamination data from published and unpublished sources that, for the most part, were taken from food samples collected at retail. The likely contamination levels in the foods when consumed (after storage and, in one case, reheating) were subsequently estimated using predictive microbiology models. In general, there were insufficient data to model individual foods. Therefore, 20 food categories were created based on: primary origin (seafood, produce, dairy and meat); composition and processing (raw, cooked, pH and salt content); available data on the prevalence of *L. monocytogenes* in the foods; and epidemiological information. The 20 food categories are listed in Summary Table 1.

Summary Table 1: Food Categories Used in the *Listeria monocytogenes* Risk Assessment

SEAFOOD
Smoked Seafood (finfish and mollusks)
Raw Seafood (finfish and mollusks)
Preserved Fish (dried, pickled, and marinated finfish)
Cooked Ready-to-Eat Crustaceans (shrimp and crab)
PRODUCE
Vegetables (raw, dried, and vegetable salads)
Fruits (raw, dried, fruit salads, and nuts)
DAIRY
Soft Mold-Ripened and Blue-Veined Cheese
Goat, Sheep, and Feta Cheese
Fresh Soft Cheese (e.g., queso fresco)
Heat-Treated Natural Cheese and Processed Cheese (mozzarella, cottage, cream cheese, and cheese spreads)
Aged Cheese (hard and semi-soft cheese)
Pasteurized Fluid Milk
Unpasteurized Fluid Milk
Ice Cream and Frozen Dairy Products
Miscellaneous Dairy Products (butter, yogurt, cream)
MEAT
Frankfurters
Dry/Semi-Dry Fermented Sausages
Deli Meats (cooked, ready-to-eat)
Pâté and Meat Spreads
COMBINATION FOODS
Deli Salads (cooked seafood, meat, poultry, egg, and cheese and/or pasta as primary salad ingredients.)

The hazard characterization used 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 were based on the likelihood that a foodborne *L. monocytogenes* infection would lead to death. The rate of listeriosis could then be determined based on the worldwide observation that there are approximately four additional cases of listeriosis for every death. The dose-response model used in the risk assessment was based on a combination of epidemiological data and data acquired from studies using animal models.

Reliability of Results and the Role of Uncertainty and Variability

The risk assessment evaluated available data to describe, as accurately as possible, the current state of scientific knowledge related to human listeriosis associated with different types of ready-to-eat foods. In doing so, the assessment has attempted to capture both the inherent variability associated with the incidence of foodborne listeriosis and the uncertainty that arises from less than ideal data. Two examples of factors that resulted in risk estimates that spanned a large range were 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 increased the range of the risk estimates. Thus, to more accurately depict 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 can be evaluated by examining the ranges of predicted values or the levels of certainty associated with different estimates. If data used in the model reflect numerous studies that were consistent in their findings, the degrees of uncertainty associated with the risk estimates are relatively small. Conversely, if the data were meager or inconsistent, the resulting estimates of risk have wide ranges. In addition to these quantitative estimates, the variability and uncertainty associated with each food group are evaluated and discussed in relation to the interpretation of the results for each food group.

The nature of the data and the structure of the models used in this risk assessment lead to conclusions with varying degrees of certainty. 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, future 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 largely limits the interpretation of the current results to a consideration of the relative risk among the 20 food groups considered.

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 of 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.