II. HAZARD IDENTIFICATION

In the hazard identification, the known or potential health effects associated with *Listeria monocytogenes* are identified by establishing the general relationship between the pathogen, its presence in foods, and the adverse outcome (illness or death) associated with consumption of foods contaminated with *Listeria monocytogenes*. While the negative health impact of a hazard must be recognized for a risk assessment to be undertaken, the nature of the impact must be clearly defined, and specific endpoints, or health outcomes of interest, identified. Common endpoints for infectious agents are infection, disease (morbidity), death, and chronic sequelae (long-term after-effects). This risk assessment is concerned with the endpoints of serious illness and death.

Listeria monocytogenes

Listeria are short (0.5 μm in diameter by 1 to 2 μm long) gram positive, non-spore-forming rods. *Listeria monocytogenes* is one of six species are currently recognized within the genus (Rocourt, 1999). It can be isolated from numerous species of domestic and wild animals, as well as from soil, silage, and other environmental sources. *Listeria monocytogenes* can be classified into a number of subtypes using several methods. The most common is based upon recognition of antigens on the surface of the bacterium by specific antisera (Graves *et al*., 1999). Thirteen of these serotypes are associated with *Listeria monocytogenes* (1/2a, 1/2b, 1/2c, 3a, 3b, 3c, 4a, 4ab, 4b, 4c, 4d, 4e, 7). Some of these serotypes are also associated with other species of *Listeria* (1/2b, 4ab, 4c, 4d). The numbers and letters refer to specific combinations of bacterial antigens used for serotyping (Seeliger and Höhne, 1979). Serotyping is often used as a first step to type strains associated with human listeriosis, but it has relatively low discriminating power compared to molecular methods such as ribotyping or pulse field gel electrophoresis (PFGE). Ribotyping relies on separation and analysis of specific well-conserved DNA fragments and this method is often used in combination with serotyping to identify and trace a specific strain of *Listeria monocytogenes* associated with illness to a food source or to link seemingly unrelated illnesses. On the basis of ribotyping and PCR-restriction fragment length polymorphism of three virulence genes (hly, actA, and inlA), Wiedmann *et al*. (1997) separated *Listeria monocytogenes* into three lineages, which appear to have distinctive pathogenicities. Several reviews and books have

summarized the ecology, characteristics, presence in foods, and public health effects of *Listeria* (Farber *et al.*, 1996; Farber and Peterkin, 1991; Ryser, 1999a; Slutsker and Schuchat, 1999).

Listeriosis

Listeria monocytogenes is a well-known hazard for which there is extensive surveillance and outbreak data. Although rare when compared to many other foodborne diseases (Table II-1), listeriosis often leads to severe consequences, particularly in susceptible subpopulations. In 2000, *Listeria monocytogenes* caused higher rates of hospitalization than any other pathogen and caused over one-third of the reported deaths. Because listeriosis so often results in medical care, CDC believes that its surveillance system (FoodNet) misses only half of all cases, compared with 97% of missed cases for other pathogens (Mead *et al*., 1999). A description of the Foodborne Diseases Active Surveillance Network (FoodNet) is provided in Appendix 4. *Listeria monocytogenes* usually causes only flu-like symptoms in healthy people. For the purposes of this risk assessment, a distinction is made between non-invasive listeriosis with mild, flu-like symptoms (referred to as listerial gastroenteritis) and invasive listeriosis that is severe and sometimes life-threatening (referred to as listeriosis in the risk assessment).

Table II-1. Incidence of Foodborne Pathogens in the United States

Pathogen	Infections (Cases per 1,000,000 population[a])
Cyclospora	0.7
Vibrio	2.1
Listeria	3.4
Yersinia	4.4
E. coli 0157:H7	21
Shigella	79
Salmonella	144
Campylobacter	157
Total Pathogens	411.6

[a] FoodNet sites include CT, MN, GA, OR, and selected counties in CA, MD, NY, TN; Total population 30.5 million. FoodNet is the Foodborne Diseases Active Surveillance Network. (CDC, 2000a)

Invasive Listeriosis

Invasive listeriosis typically has a 2 to 3 week incubation time, but can sometimes extend up to three months (Gellin and Broome, 1989). Serious conditions caused by *Listeria monocytogenes* in adults can include septicema, meningitis, enceplalitis, abortion, or stillbirth (Shelef, 1989a). Invasive diseases in nonpregenant adults can include a variety of other clinical manifestations. Endocarditis can occur in patients with underlying cardiac lesions. Cutaneous infections have been reported in persons handling animals and those exposed by accidental exposure while working in laboratories. Focal infections are rare but can include endophthalmitis, septic arthritis, osteomyelitis, pleural infection and peritonitis (Slutsker and Schuchat, 1999).

Most information on the pathogenesis of *Listeria monocytogenes* comes from studies in mice or cell biology studies using tissue culture cells (Kuhn and Goebel, 1999). When ingested, *Listeria monocytogenes* penetrates the intestinal tissue and is exposed to phagocytic cells of the immune system that function to kill microbial invaders. A portion of invading *Listeria monocytogenes* can evade the killing mechanisms, survive, and multiply within host phagocytes (macrophages). Protected within, or having escaped from these host cells, *Listeria monocytogenes* moves throughout the host via blood or lymphatic circulation to various tissues. Once in a tissue it can invade cells, multiply within them, and then use cytoskeletal acting filaments to spread to adjacent cells, without risk of exposure to humoral components of the immune system. The probability of tissue invasion depends upon the number of organisms consumed, host susceptibility, and virulence of the strain (Gellin and Broome, 1989). Most cases of listeriosis occur in fetuses or neonates and individuals with a predisposing condition that impairs the immune system (Slutsker and Schuchat, 1999).

Although *Listeria monocytogenes* is generally known to cause severe illness, there have been outbreaks in which the majority of patients only developed mild symptoms such as diarrhea, fever, headache, and myalgia (Dalton *et al.*, 1997; Salamina *et al.*, 1996; Riedo *et al.*, 1994; Aureli *et al*., 2000). 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 listeriosis.

High Risk Individuals

Two high risk (susceptible) subpopulations are considered in this risk assessment: elderly and perinatal. Persons at high risk for developing listeriosis often have deficient or immature immune systems (immunocompromised). Actual numbers of susceptible individuals are difficult to determine because these individuals belong to diverse groups including the elderly, cancer and transplant patients, and persons with immunosuppressive diseases such as AIDS (Morris and Potter, 1997). In addition, the description of an immunocompromised state is often based on qualitative or circumstantial criteria that may apply to some, but not all members of a particular group.

Susceptible subpopulations are not homogeneous with regard to susceptibility, both within and between groups. High-risk subpopulations can be separated into non-perinatal and perinatal groups. A non-pregnancy related case is a person other than a pregnant woman or her child in whom *Listeria monocytogenes* organisms are cultured from a normally sterile site. Of the non-perinatal groups, the elderly constitute the largest and most well characterized subpopulation. A case-control study revealed that of 98 cases of non-perinatal sporadic listeriosis in the United States, 98% had at least one underlying medical condition. Most (69%) of these were associated with probable immunosuppression (Schuchat *et al.,* 1992). The next largest group (33%) was associated with heart disease. Many individuals fell under more than one category. In people over the age of 60, the disease is often present with sepsis or meningitis (Schuchat *et al.*, 1991; Shelef, 1989a; Linnan *et al.*, 1988; WHO Work Group, 1988).

A perinatal infection occurs primarily as the result of transplacental transmission to the fetus following infection of the mother. The perinatal group includes fetuses or neonates from whom *Listeria monocytogenes* organisms are isolated from a normally sterile body site. Perinatal infections can occur before or after birth and outcomes include live birth of an infected neonate, stillbirth, or premature termination of pregnancy. Neonates (newborns) are defined by the American Medical Association as newborn infants from birth to one month of age. In this risk assessment, neonates are considered to be between 0-30 days of age. The term fetus is used to refer to an unborn child from 16 weeks after fertilization to birth.

Women may become infected with *Listeria monocytogenes* at any time during pregnancy, but most cases of listeriosis are reported in the third trimester (Slutsker and Schuchat, 1999). Usually three to seven days after the onset of symptoms, a woman may abort the fetus or have premature delivery (Gellin and Broome, 1989). In the first trimester, listeriosis may result in spontaneous abortion. In later stages of pregnancy, the result may be stillbirth or birth of a critically ill newborn. Listeriosis is rarely life threatening to the mother and is not known to cause increased risk in subsequent pregnancies (Skidmore, 1981; Farber and Peterkin, 1991).

Neonates may present with an early-onset or late-onset form of listeriosis. Approximately 45 to 70% of newborn cases are early-onset (Slutsker and Schuchat, 1999). Early-onset listeriosis often presents with sepsis and may progress to a syndrome known as granulomatosis infantisepticum (Gellin and Broome, 1989). This syndrome is often characterized by widely disseminated granulomas, premature birth, respiratory distress, and circulatory failure. Late-onset is defined as listeriosis in a newborn between 8 to 30 days of life. Usually late-onset neonates are born apparently healthy and at full-term. Meningitis rather than sepsis is more common in late-onset neonates (Farber, 1991a). The mothers of late-onset neonates usually have an uneventful pregnancy without illness. *Listeria monocytogenes* is rarely isolated from the mother and the source of listeriosis is often not identified in late-onset cases (Farber and Peterkin, 1991; Slutsker and Schuchat, 1999).

Non-Invasive Listeriosis (Listerial Gastroenteritis)

Gastrointestinal illness (listerial gastroenteritis) from *Listeria monocytogenes* has only recently been recognized as a distinct entity (Dalton *et al*., 1997). Typical signs and symptoms associated with the mild form of *Listeria monocytogenes* infection are primarily those associated with gastrointestinal illness: chills, diarrhea, headache, abdominal pain and cramps, nausea, vomiting, fatigue, and myalgia. A variety of foods have been implicated as the vehicle of infection. Because symptoms are mild, there is a high potential for underreporting of listerial gastroenteritis. Data are currently unavailable through foodborne surveillance mechanisms such as FoodNet to capture the incidence of listerial gastroenteritis since routine stool cultures do not include evaluation for *Listeria monocytogenes*.

Nevertheless, outbreaks of listerial gastroenteritis have been identified. Table II-2 shows reported events where most of the cases reported mild symptoms (Heitmann *et al.*, 1997; Dalton *et al.*, 1997; Salamina *et al.*, 1996; Riedo *et al.*, 1994; Aureli *et al.*, 2000). In the vast majority of these cases, there was no evidence for invasive disease beyond the intestine. Gastrointestinal and other mild symptoms were reported in individuals with no known underlying predisposition. In two of these reports, there was evidence of very high levels of food contamination. These facts suggest that, in normal individuals, listerial gastroenteritis may be associated with exposure to high levels of *Listeria monocytogenes*. It is possible that this manifestation of *Listeria monocytogenes* infection is a different disease compared to invasive and more severe listeriosis. Because modeling in this risk assessment depends on case reporting and non-invasive gastroenteritis is not likely to be reported, listerial gastroenteritis was not considered in the risk assessment model. However, the outbreaks do provide important observations related to the exposure of populations to extremely high levels of the microorganisms without identifiable cases of invasive listeriosis.

Table II-2. Reports of Outbreaks of Listerial Gastroenteritis

Location	Year	Number of Cases	Vehicle	Reference
Northern Italy	1997	1566	Tuna/Corn Salad	Aureli *et al.*, 2000
Denmark	1996	3	Unknown	Heitmann *et al.*, 1997
United States	1994	45	Chocolate Milk	Dalton *et al.*, 1997
Northern Italy	1993	18	Rice Salad	Salamina *et al.*, 1996
United States	1989	10	Shrimp	Riedo *et al.*, 1994

Asymptomatic Carriage

The large intestine may be a reservoir for *Listeria monocytogenes* in humans. Estimates of fecal carriage in various populations of healthy adults range from <1% to 21%. It has been suggested that stress can undermine resistance in fecal carriers, and may trigger listeriosis in the carrier. Several studies have looked at fecal carriage to gain insight into listeriosis. However, it is unknown how fecal carriage relates to length of incubation or occurrence of invasive disease (Skidmore 1981; Slutsker and Schuchat, 1999; Mascola *et al.,* 1992; and Schuchat *et al.,* 1991).

Approximately 1 to 5% of normal asymptomatic carriers shed *Listeria monocytogenes* bacteria in the feces (Hof, 2001). *Listeria monocytogenes* was isolated from 2 of 100 colon biopsy

specimens from patients with colon cancer; however, neither patient exhibited signs of listeriosis (Hof, 2001).

In a retrospective study of the outbreak in 1985 that was linked to Hispanic-style fresh soft cheese, outbreak-related listeriosis patients and matched controls were asked to participate in a study of stool carriage of *Listeria monocytogenes* (Mascola *et al*., 1992). Fecal carriage incidence was also determined for employees of the cheese plant and their household contacts. Stool specimens from 8% of those tested were positive for *Listeria monocytogenes*. The highest rate of recovery of the organism from stool samples was from employees of the cheese plant and their household contacts. It was found that the occurrence of listerial gastroenteritis or listeriosis was not associated with fecal carriage of *Listeria monocytogenes,* and was actually more common for persons with negative stool samples.

Between January 1990 and December 1991, as part of a multistate active surveillance project on sporadic listeriosis, a study was conducted to evaluate the fecal carriage of *Listeria monocytogenes* among household contacts of patients with invasive listeriosis (Schuchat *et al.*, 1993). The authors determined that the rates of carriage did not vary significantly by sex but were significantly higher in younger persons. The organism was isolated from 32% of those <30 years of age, compared to 7% from older persons. Nearly 20% of household contacts of patients with sporadic listeriosis had asymptomatic carriage of the strain associated with illness. The authors suggested that carriage of *Listeria monocytogenes* is more common in persons that have been in contact with listeriosis patients and that it was difficult to compare the fecal carriage rate in this study group to the population at large.

Epidemiological Patterns of Listeriosis: Sporadic versus Outbreak-Associated Cases

The Centers for Disease Control and Prevention (CDC) has estimated that approximately 2,500 cases of listeriosis occur annually in the United States (Mead *et al*., 1999). The overall annual incidence of listeriosis in the United States has been estimated to range from 3.4 per million (CDC, 2000) to 4.4 per million (Tappero *et al*., 1995). The incidence of listeriosis reported from other countries vary substantially, for example 3.5 per million persons in Bristol, England; 1.8 per million persons in England, Wales and Northern Ireland; and 6 to 7 per million persons in Denmark (Slutsker and Schuchat, 1999).

Most cases of human listeriosis occur sporadically although much of what is known about the epidemiology of the disease has been derived from outbreak-associated cases. However, it is unclear what percentage of sporadic cases may actually represent unrecognized, temporally or geographically diffuse outbreaks. Case-control studies are often used to elucidate risk factors for both outbreak-associated and sporadic cases. Investigations of outbreaks have provided much of our knowledge of the etiology of this disease organism, particularly in relation to isolation of *Listeria monocytogenes* from both the case patient and the implicated food. Investigation of sporadic cases of listeriosis often does not lead to this direct product isolate-human isolate link. Therefore, studies of sporadic cases are more likely to identify a food group, such as soft cheese, as a risk factor rather than a specific brand of soft cheese, the latter to be more likely in an outbreak investigation. Also, outbreaks of listeriosis are often associated with a processing or production failure (Slutsker and Schuchat, 1999) whereas this has been less evident among sporadic cases (Barnes *et al*., 1989).

Sporadic Listeriosis

In 1988, a microwave reheated turkey frank, consumed by an immunocompromised woman, was among the first microbiological food isolates from an RTE product associated with sporadic clinical listeriosis in the United States. Food isolates of *Listeria monocytogenes*, of the same serotype with the same electrophoretic enzyme type as the clinical isolate, were identified from both opened and unopened turkey franks from the same manufacturer (Barnes *et al*., 1989).

Likely dietary risk factors for sporadic cases of listeriosis have been identified through two case-control studies conducted by the CDC. Case-patients were identified through active surveillance conducted by CDC, and controls were selected and matched on age, geographic location, socioeconomic status, and underlying health conditions. The first case-control study of sporadic cases of listeriosis enrolled 82 patients and 239 controls from 1986 to 1987. Non-reheated frankfurters and undercooked chicken were found to have an attributable risk of 15% and 6%, respectively. These were the only foods that were statistically significantly associated with sporadic cases of listeriosis. In the subsequent and larger case-control study conducted by CDC from 1988 to 1990, 165 patients and 376 controls were enrolled in the study of sporadic listeriosis cases. This study also included a microbial assessment of patient-consumed foods.

Case-patients were significantly more likely to have consumed foods bought at a deli or to have eaten soft cheeses (Schuchat, *et al.*, 1992). Food samples were collected from 123 (75%) of patients' refrigerators and assayed for presence of *Listeria monocytogenes*. The organism was isolated from at least 1 food item in 64% of refrigerators. *Listeria monocytogenes* was found in 7.6% of ready-to-eat samples including processed meats, leftovers, cheeses, and raw vegetables. These ready-to-eat food items, as well as other food samples containing the 4b serovar of the organism, were significantly more likely to be associated with disease (Pinner *et al*., 1992). The contamination rates, by type of food are presented in Table II-3.

The FoodNet Listeria Case-Control Study was initiated in 2000 and will be completed in 2003 (Varma, 2003). The goal of the case-control study is to further characterize established risk factors and identify other potential risk factors for *Listeria* infection. Nine FoodNet sites have enrolled cases and controls and interviewed subjects with a standardized questionnaire that explores more than 400 different dietary, behavioral, and environmental risk factors.

Table II-3. Isolation of *Listeria Monocytogenes* In Food Specimens Collected from the Refrigerators of Patients with Listeriosis

	Number of Samples	
Type of Food	**Positive samples**	**Total tested**
Beef	50	140
Poultry	33	108
Pork	26	95
Deli Meats	18	98
Seafood	7	57
Vegetables	72	683
Fruit	5	155
Dairy	9	533
Other[b]	6	144
Total	226	2,013

[a]Source: Pinner *et al*., 1992.
[b]Included bread, pasta, eggs, lamb, and miscellaneous mixtures of food.

Outbreak-Associated Listeriosis

Reported outbreak-associated listeriosis cases represent a small proportion of the annual number of listeriosis cases estimated to occur in the United States (Mead *et al*., 1999). However, data collected during outbreak investigations provide important information about both the vehicle of transmission and the mechanism by which the food contamination occurred. Published and

unpublished outbreak investigation reports for the period 1970 through 2000 were reviewed. Seventeen (32.7%) of the outbreaks occurred in the United States, with the remaining 37 outbreaks occurring outside the United States. Of the 17 domestic outbreaks, one or more contaminated food vehicles were identified in 13 (76.5%) outbreaks; in the remaining four outbreaks the source of the outbreak was not identified. In two (13.3%) outbreaks, the majority of cases were classified as having listerial gastroenteritis. Of the 37 international outbreaks, one or more vehicles were identified in 22 (59.5%) outbreaks. In all but one of the outbreaks in which no vehicle was identified, the events occurred prior to 1988. In four (10.8%) outbreaks, the majority of cases were classified as having listerial gastroenteritis.

Outbreaks in the United States. A total of 466 cases of listeriosis occurred during 12 severe listeriosis outbreaks in the United States between 1970 and 2002 (Table II-4). The mean number of cases per outbreak was 39 (median, 24.5; range 2 to 142 cases). Only two outbreaks had more than 100 associated cases, and these occurred over an extended time period. Eleven of the outbreaks involved RTE products and an outbreak of two cases involved raw eggs. Mexican-style soft cheese was the identified vehicle for the largest reported outbreak of 142 cases of which 93 (65.5%) were perinatal cases. A total of 48 perinatal and non-perinatal deaths (37.5%) were attributed to this outbreak. The second largest outbreak of 101 cases (with 21 deaths) involved two products, frankfurters and deli meats, both of which were produced by the same manufacturing establishment. During the course of the outbreak, the plant was noted to have widespread environmental disruption (with major construction being done), a known risk factor for post-kill-step recontamination of RTE products (Mead, 1999).

Among the eight outbreaks for which mortality data were available, there were 121 deaths among 466 cases (26 %) and ranged within the outbreaks from 11.1 to 44.4 %. A total of 130 (36.9%) of 352 cases occurred in a fetus or neonate (perinatal listeriosis), in nine outbreaks for which perinatal infection data were available. The serotype was reported for eight outbreaks, of which serotype 4b was responsible for seven (87.5%) outbreaks (Table II-4).

A total of four food categories were implicated in the 12 outbreaks of listeriosis listed in Table II-4. Nine outbreaks were associated with only one type of food vehicle each. A dairy product

was implicated in four outbreaks, meat was implicated in three, and one outbreak each was attributed to eggs and vegetables. The specific food vehicles included pasteurized milk, Mexican-style cheese, butter, eggs (raw), deli turkey meat, pâté, and vegetables. Considering only those outbreaks in which a single vehicle was identified, the numbers of cases by food vehicle were dairy, 309 (63.75%); meat, 103 (33.3%); vegetables, 7 (2.3%); and eggs, 2 (0.6%). More than one vehicle was implicated in three outbreaks involving a total of 157 cases. The largest outbreak involved RTE meats produced in the same processing establishment.

Table II-4. Outbreaks of Listeriosis in the United States (1970-2002) with Known Food Vehicle(s)

Year	Food Vehicle	State	Cases	Perinatal cases (% of total)	Deaths (% of total)	Serotype	Reference
1979	Raw vegetables or cheese	MA	20	0 (0)	3 (15.0)	4b	Ho, 1986
1983	Pasteurized fluid milk	MA	32	7 (21.9)	14 (43.8)	4b	Fleming, 1985
1985	Mexican-style cheese (raw milk)	CA	142	93 (65.5)	48 (33.8)	4b	Linnan, 1988
1986-1987	Ice cream, salami, brie cheese	PA	36	4 (11.1)	16 (44.4)	4b,1/2b, 1/2a	Schwartz, et al., 1989
1986-1987	Raw eggs	CA	2	Unknown	Unknown	4b	Schwartz, et al., 1988
1987	Butter	CA	11	Unknown	Unknown	Unknown	Ryser, 1999a
Not specified	Frozen vegetables	TX	7	3 (42.9)	Unknown	4b	Simpson, 1996
1998-1999	Hot dogs, deli meats	22 states	101	Unknown	21 (20.8)	4b	Mead, 1999
1999	Pâté	CT, MD, NY	11	2 (18.2)	unknown	1/2a	Carter, 2000
2000	Deli turkey meat	10 states	29	8 (27.6)	7 (24.1)	unknown	CDC, 2000b
2000-2001	Homemade Mexican-style cheese (raw milk)	NC	12	10 (83.3)	5 (41.7)	unknown	CDC, 2001
2002	Deli turkey meat, sliceable	8 North Eastern states	63	3 (4.8)	7 (11.1)	unknown	CDC, 2002b
Total			466				

Outbreaks outside the United States. A total of 1,058 listeriosis cases occurred during 18 listeriosis outbreaks outside the United States between 1970 and 2000 (Table II-5). The mean number of cases per outbreak was 59 (median, 24; range 4-355 cases). All of the reported outbreaks outside the United States in which a vehicle was identified occurred in so-called "developed" countries. Five (27.8%) outbreaks occurred in France, five (27.8%) in Oceania (Australia and New Zealand), two (11.1%) in England, and one (5.6%) each in Austria, Canada, Denmark, Finland, Sweden, and Switzerland.

Information on the number of deaths was available for 18 outbreaks. A total of 257 (24.3%) of 1,058 persons who were ill died. The number of hospitalized cases was available for five outbreaks; 91 (42.9%) of 212 cases were hospitalized. Thirteen reports contained information about the number of perinatal cases; 477 (49.1%) of 972 cases were perinatal. The serotype was reported for 15 outbreaks, of which, 9 (60.0%) were caused by serotype 4b (Table II-5).

A single food vehicle was identified in 17 outbreaks involving 1,030 cases. Dairy products were implicated in six (35.3%) outbreaks, meat products in five (29.4%) outbreaks, seafood products in four (23.5%) outbreaks, and vegetables in two (11.8%) outbreaks. The specific food items included cheese (four outbreaks), two outbreaks each for pâté, pork tongue, and smoked mussels, one outbreak each for cold-smoked trout, pasteurized cream, butter, rillettes (a RTE product made of ham cooked with fat), raw fish, cabbage, and raw vegetables. Considering only those outbreaks in which a single food vehicle was identified, the number of cases by food group were: meat, 710 (68.9%); dairy, 228 (22.1%); vegetables, 53 (5.1%); and fish, 39 (3.8%). In one outbreak in Austria in 1978, multiple food vehicles were identified during the epidemiologic investigation (unpasteurized milk, vegetables).

Examples of using outbreak information in developing dose-response curves is presented in Appendix 9 using the 1985 Mexican-style cheese outbreak and Finish butter outbreak.

Table II-5. Outbreaks of Listeriosis Outside the United States (1970-2000) with Known Food Vehicle

Year	Food Vehicle	Country	Cases	Perinatal cases (% of total)	Deaths (% of total)	Serotype	Reference
1978-1979	Vegetables (raw)	Australia	12	Unknown	0 (0)	Unknown	Le Souëf and Walters, 1981
1980	Raw seafood (finfish and mollusks)	New Zealand	22	22 (100.0)	6 (27.3)	1b	Lennon *et al*., 1984
1981	Miscellaneous Dairy Products	England	11	Unknown	5 (45.5)	1/2a	Ryser, 1999a
1981	Vegetables (raw)	Canada	41	34 (82.9)	17 (41.5)	4b	Schlech, *et al*., 1983
1983 - 1987	Vacherin Mont d'Or cheese	Switzer-land	122	65 (53.3)	31 (25.4)	4b	Bille, 1990; Bula *et al*., 1995
1986	Unpasteurized milk, organic vegetables	Austria	28	24 (85.7)	5 (17.9)	Unknown	Allerberger and Guggenbichler 1989
1987-1989	Pâté and meat spreads	England	355	185 (52.1)	94 (26.5)	4b	McLaughlin *et al.,* 1991
1989 - 1990	Semi-soft Cheese (blue)	Denmark	23	Unknown	0 (0)	4b	Jensen, 1994
1990	Pâté and meat spreads	Australia	11	11 (100.0)	6 (54.5)	1/2a	Ryser, 1999a
1991	Smoked mussels	Tasmania, Australia	4	0 (0)	0 (0)	1/2a	Mitchell, 1991; Misrachi *et al*., 1991
1992	Smoked mussels	New Zealand	4	0 (0)	0 (0)	1/2	Brett, *et al*., 1998
1992	Pork tongue in jelly	France	280	93 (33.2)	63 (22.5)	4b	Jacquet *et al*., 1995
1993	Rillettes	France	38	31 (81.6)	11 (28.9)	4b	Goulet, 1998
1994-1995	Smoked Seafood (finfish and mollusks)	Sweden	9	3 (33.3)	2 (22.2)	4b	Ericsson *et al*., 1997
1995	Soft Ripened Cheese, >50% moisture (brie, camembert, feta, mozzarella)	France	33	9 (45.0)	4 (20.0)	4b	Goulet *et al*., 1995; Jacquet *et al*., 1995
1997	Pon l'Eveque cheese	France	14	Unknown	0 (0)	4b	Ryser, 1999a
1998-1999	Butter	Finland	25	0 (0)	6 (0)	3a	Lyytikainen *et al*., 2000
1999-2000	Pigs tongue in aspic	France	26	Unknown	7 (0)	Unknown	Dorozynski, 2000
Total			1058				

All outbreaks combined. Data from outbreaks from within and outside the United States were collectively summed by number of outbreaks and number of cases and each food group was ranked accordingly (Table II-6). When ranked by number of associated outbreaks, dairy

products ranked highest, followed by meat products, then seafood and finally, produce. When number of outbreak-associated cases are ranked, meat products were first and dairy products were second. Contaminated meat and dairy products were responsible for more than 90% of cases. In addition, dairy and meat products were implicated in three other outbreaks with multiple food vehicles. Serotype 4b was found in 16 (72.7%) of 22 outbreaks; 1/2a was found in four (18.0%) outbreaks (Tables II-4 and II-5).

Table II-6. A Comparative Ranking of Types of Food Vehicles by Outbreaks and Cases with Combined United States and International Outbreak Data

Type of Food Vehicle	Ranking Order by the Number of Outbreaks or Cases	
	Outbreaks	Cases
Dairy	1	2
Meat	2	1
Seafood	4	4
Produce	3	3

Dairy and RTE meat products were most often implicated in domestic and international outbreaks. The most commonly implicated dairy product was soft (fresh and mold-ripened) cheese. A variety of meat products have been involved in listeriosis outbreaks including all RTE meats, such as frankfurters, deli meat, pâté and pork tongue. These findings are similar to those from case-control studies of sporadic listeriosis, in which un-reheated frankfurters, undercooked chicken, soft cheeses and foods purchased at a deli counter were associated with listeriosis (Schwartz *et al*., 1988; Schuchat *et al*., 1992). "Foods purchased at a deli counter" as a food group is not specific, but a subset of case-patients identified RTE meats as the only item they had purchased at a deli counter prior to becoming ill with listeriosis. The results of this case-control study were corroborated by Pinner *et al.* (1992), who found that the foods most likely to cause listeriosis were RTE foods, foods with a high concentration of *Listeria monocytogenes*, and foods from which serotype 4b was isolated. In this analysis of outbreaks, serotype 4b was found in almost 70% of the outbreaks.

The proportion of fatal cases was similar for domestic (26%) and foreign (24%) outbreaks and agreed with other sources (Slutsker and Schuchat, 1999). A somewhat lower fatality rate has been reported (i.e., 20%) when sporadic outbreak cases were considered (Mead *et al*., 1999).

The proportion of outbreak associated perinatal (prenatal and neonatal) cases was approximately similar (40 to 50%) between outbreaks in the United States and outside the United States. In many reports, information about the number of perinatal cases and hospitalized cases was incomplete; therefore, the proportion of perinatal cases and hospitalized cases reported are probably underestimated. For international outbreaks 42.9% of cases were reportedly hospitalized. This proportion substantially underestimates the findings reported by Mead *et al*. (1999), in which 92.2% of persons with culture confirmed listeriosis required hospitalization.

The epidemiology of listeriosis outbreaks occurring within the United States appears to be similar to outbreaks occurring outside the United States. Outbreaks appear to have disproportionately higher frequency of serotype 4b. The reported median number of cases per outbreak are 24.5 and 24, respectively; however, the means are not similar. The proportion of fatal cases (26% and 24.3%), and the food groups implicated in causing outbreaks are also similar. Therefore, it appears valid to generalize the results from international (developed countries) listeriosis outbreaks to the United States.

Outbreaks due to dairy products were most often the result of raw milk being present in a product such as soft (fresh and mold-ripened) cheese, or from post-pasteurization contamination. Dairy products were incriminated in nine outbreaks, including five due to contaminated soft (fresh and mold-ripened) cheese. Post-processing contamination of butter was blamed for an outbreak in Finland (Lyytikainen *et al*., 2000). A 1983 outbreak in Massachusetts was epidemiologically linked to pasteurized milk, suggesting that *Listeria monocytogenes* can survive the pasteurization process (Fleming *et al*., 1985); however, Ryser (1999c) has raised doubts about this conclusion, citing studies that have shown *Listeria monocytogenes* is unlikely to survive pasteurization. Schuchat and colleagues (1992) proposed that contamination of the implicated milk have occurred post-pasteurization. The source of contamination implicated in this outbreak has been frequently debated without a definitive conclusion. A Danish case-control study found unpasteurized milk to be a risk factor for sporadic listeriosis (Jensen *et al*., 1994). Additional foods associated with sporadic cases of listeriosis are discussed in earlier in this chapter in the section titled ‘Sporadic Listeriosis.’