II. HAZARD IDENTIFICATION

In the hazard identification, the known or potential health effects associated with *L. 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 *L. 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 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

L. monocytogenes is a short (0.5 μm in diameter by 1 to 2 μm long) gram positive, non-spore-forming rod that is part of the lactobacilli family along with genera such as *Lactobacillus* and *Streptococcus* (Rocourt, 1999). It can be isolated from numerous species of domestic and wild animals, as well as from soil, silage, and other environmental sources. *L. 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 *L. monocytogenes* (1/2a, 1/2b, 1/2c, 3a, 3b, 3c, 4a, 4ab, 4b, 4c, 4d, 4e, 7). Some 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 Hohne, 1979). Serotyping is often used as a first step to type strains in 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 *L. monocytogenes* associated with illness to a food source or to link seemingly unrelated illnesses. Several reviews and books have summarized the microorganism's ecology, characteristics, presence in foods, and public health effects (Farber *et al.*, 1996; Farber and Peterkin, 1991; Slutsker and Schuchat, 1999).

Listeriosis

L. monocytogenes is a well-known hazard for which there is extensive surveillance and outbreak data. Although rare when compared to many other foodborne diseases (see Table II-1), listeriosis often leads to severe consequences, particularly in susceptible subpopulations. In 1998, *L. monocytogenes* caused higher rates of hospitalization than any other pathogen and caused nearly half 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 3. *L. 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 severe, sometimes life-threatening listeriosis (referred to as listeriosis in the risk assessment).

Table II-1. Incidence of Foodborne Pathogens, FoodNet, 1999

Pathogen	Number of Infection Cases per 1,000,000 population[a]
Vibrio	2
Listeria	5
Yersinia	6
E. coli 0157:H7	20
Shigella	40
Salmonella	177
Campylobacter	148
Total Bacterial Pathogens	398

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

Invasive Listeriosis

Invasive listeriosis can have a long (up to three months) incubation time (Gellin and Broome, 1989) and a wide range of symptoms. A partial list of serious conditions caused by *L. monocytogenes* includes bacteremia, bacterial meningitis, conjunctivitis, central nervous system infection, cutaneous

infection, encephalitis, endocarditis, meningoencephalitis, miscarriage, neonatal disease, osteomyelitis, peritonitis, pleural infection, pneumonia, premature birth, septicemia, and stillbirth.

Most information on the pathogenesis of *L. monocytogenes* comes from studies in mice, or cell biology studies using tissue culture cells (Kuhn and Goebel, 1999). Ingested *L. 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 *L. monocytogenes* can evade the killing mechanisms, survive, and multiply within host phagocytes (macrophages). Protected within, or having escaped from these host cells, *L. 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 actin 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 listeriosis occurs in fetuses or neonates and individuals with a predisposing condition that impairs the immune system (Slutsker and Schuchat, 1999).

Although *L. 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 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 *L. 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 U. S., 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 *L. 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 *L. monocytogenes* at any time during pregnancy, but most listeriosis cases 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 of infected women (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). This form of listeriosis often presents with sepsis rather than meningitis 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 is more common in late-onset neonates (Farber, 1991a). The mothers of late-onset neonates usually have an uneventful pregnancy without illness. *L. 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 *L. monocytogenes* has only recently been recognized as a distinct entity (Dalton *et al.*, 1997). Typical signs and symptoms associated with the mild form of *L. 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 (unlike listeriosis), thus existing CDC surveillance programs would miss these mild illnesses. 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 *L. 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 *L. monocytogenes.* It is possible that this manifestation of *L. monocytogenes* infection is a different disease from 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.

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
Illinois	1994	45	Chocolate Milk	Dalton *et al.*, 1997
Northern Italy	1993	18	Rice Salad	Salamina *et al.*, 1996
New York City	1989	10	Shrimp	Riedo *et al.*, 1994

Asymptomatic Carriage

The large intestine may be a reservoir for *L. 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).

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 *L. 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 *L. 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 *L. 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 *L. 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 with 7% of 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 *L. monocytogenes* is more common in persons that have been in contact with listeriosis patients and that it is 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 U.S. has been estimated to be 4.4 per million (Tappero *et al.*, 1995). The incidence of listeriosis in other countries has been reported as 3.5 per million persons, Bristol, England (hospital-based surveillance); 1.8 per million persons, England, Wales and Northern Ireland (passive surveillance); 6-7 per million persons, Denmark (laboratory-based surveillance) (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 *L. 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 sproadic clinical listeriosis in the U.S. Food isolates of *L. 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 found to be 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 *L. monocytogenes*. The organism was isolated from at least 1 food item in 64% of refrigerators. *L. 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.

Table II-3. Isolation Of *Listeria Monocytogenes* In Food Specimens Collected From The Refrigerators Of Patients With Listeriosis (From Pinner *et al.*, 1992)

Food Category	Number of positive foods (%)	Number of foods tested
Beef	50 (36)	140
Poultry	33 (31)	108
Pork	26 (27)	95
Lunch meat	18 (18)	98
Seafood	7 (12)	57
Vegetables	72 (11)	683
Fruit	5 (3)	155
Dairy	9 (2)	533
Other[a]	6 (4)	144
Total	226 (11)	2,013

[a]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 U.S. (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. For the period 1970 through 2000, 50 published outbreak investigation reports and two unpublished investigation reports were reviewed. Fifteen (28.9%) of the outbreaks occurred in the United States, with the remaining 37 outbreaks occurring outside the U.S. Of the 15 domestic outbreaks, one or more contaminated food vehicles were identified in 11 (73.3%) 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. As the focus of this risk assessment is severe listeriosis, outbreaks of listerial gastroenteritis will not be further discussed.

Outbreaks in the United States. A total of 362 cases of listeriosis occurred during 9 severe listeriosis outbreaks in the U.S. between 1970 and 2000 (Table II-4). The mean number of cases per outbreak was 40 (median, 20; range 2-142 cases). Only two outbreaks had more than 100 associated cases, and these occurred over an extended time period. Eight of the outbreaks involved RTE products and

an outbreak of 2 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 (33.8%) 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 investigation the plant was noted to have widespread environmental disruption, a known risk factor for post-kill-step recontamination of RTE products (Mead, 1999; unpublished data).

Among the six outbreaks for which mortality data were available, there were 105 deaths among 342 cases (30.7 %) and ranged within the outbreaks from 15.0 to 44.4 %. A total of 109 (44.0%) of 248 cases occurred in a fetus or neonate (perinatal listeriosis), in six 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 single food vehicle was implicated in six outbreaks involving 205 cases. Four food groups were implicated in these outbreaks. A dairy product was implicated in three outbreaks and one outbreak each was attributed to meat, eggs and vegetables. The specific food vehicles included pasteurized milk, cheese, butter, frankfurters, pâté, raw eggs, and vegetables. Considering only those outbreaks in which a single vehicle was identified, the number of cases by food vehicle were dairy, 185 (90.2%); meat, 11 (5.4%); vegetables, 7 (3.4%); eggs, 2 (0.9%). In the three outbreaks, involving a total of 157 cases, more than 1 vehicle was implicated. The largest outbreak involved RTE meats produced in the same processing establishment.

Table II-4. Outbreaks Of Listeriosis, Known Vehicle, United States, 1970-2000

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 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, 1989
1986-1987	Raw eggs	CA	2	Unknown	Unknown	4b	Schwartz, 1988
1987	Butter	CA	11	Unknown	Unknown	Unknown	Ryser, 1999a
?	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)	3 (27.2)	1/2a	Carter, 2000
Total			362				

Outbreaks outside the United States. A total of 1,058 listeriosis cases occurred during 18 listeriosis outbreaks outside the U.S. 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 U.S. 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 17 outbreaks. A total of 253 (24.6%) of 1,030 persons who were ill died. The number of hospitalized cases was available for five outbreaks; 91 (42.9%) of 212 cases were hospitalized. Eleven reports contained information about the number of perinatal cases; 388 (44.9%) of 864 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 16 outbreaks involving 1,030 cases. Dairy products were implicated in six (35.3%) outbreaks, meat products in five (29.4%) outbreaks, fish 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. In one outbreak in Austria in 1978, multiple food vehicles were identified during the epidemiologic investigation (unpasteurized milk, vegetables).

Table II-5. Outbreaks Of Listeriosis Outside The United States, Known Vehicle, 1970-2000

Year	Food Vehicle	Country	Cases	Perinatal cases (% of total)	Deaths (% of total)	Serotype	Reference
1978-1979	Raw vegetables	Australia	12	Unknown	0 (0)	Unknown	Le Souef and Walters, 1981
1980	Shellfish or raw fish	New Zealand	22	22 (100.0)	6 (27.3)	1b	Lennon, 1984
1981	Cream	England	11	Unknown	5 (45.5)	1/2a	Ryser, 1999a
1981	Cabbage	Canada	41	34 (82.9)	17 (41.5)	4b	Schlech, 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	England	355	185 (52.1)	94 (26.5)	4bX	McLaughlin *et al.*, 1991
1989 - 1990	Blue-mould cheese	Denmark	23	Unknown	0 (0)	4b	Jensen, 1994
1990	Pâté	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, 1991
1992	Smoked mussels	New Zealand	4	0 (0)	0 (0)	1/2	Brett, 1998
1992	Pork tongue in jelly	France	280	93 (33.2)	63 (22.5)	4b	Jacquet, 1995
1993	Rillettes	France	38	31 (81.6)	11 (28.9)	4b	Goulet, 1998
1994-1995	Cold-smoked rainbow trout	Sweden	9	3 (33.3)	2 (22.2)	4b	Ericsson, 1997
1995	Raw milk soft cheese (Briede Meaux)	France	33	9 (45.0)	4 (20.0)	4b	Goulet, 1995; Jacquet, 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, 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 U.S. 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 number one, followed by meat products, then fish products and finally, vegetables. Together, dairy and meat products were responsible for 70.8% of the outbreaks for which a food vehicle was identified. 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 92.4% 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).

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 were involved in outbreaks, but all were RTE meats and included frankfurters, 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 *L. monocytogenes*, and foods from which serotype 4b was isolated. In this analysis of outbreaks, serotype 4b was found in almost 70% of the outbreaks.

Approximately 25% of cases associated with outbreaks were fatal. This proportion of fatal cases was similar for domestic and foreign 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 + neonatal) cases was approximately 45%, and was similar between outbreaks in the U.S. and outside the U.S**.** 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. 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%); fish, 39 (3.8%).

The epidemiology of listeriosis outbreaks occurring within the U.S. appears to be similar to outbreaks occurring outside the U.S. Outbreaks appear to be similar with regard to the frequency of serotype 4b, the number of cases per outbreak, proportion of fatal cases, and the food groups implicated in causing outbreaks. Therefore, it appears valid to generalize the results from international listeriosis outbreaks to the U.S. Overall, the incidence reported in these other countries is similar to the incidence reported in the U.S, further supporting the idea that the epidemiology of listeriosis is similar among developed countries.

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 *L. monocytogenes* can survive the pasteurization process (Fleming *et al.*, 1985); however, Ryser (1999c) has raised doubts about this conclusion, citing studies that have shown *L. monocytogenes* is unlikely to survive pasteurization. Schuchat (1992) proposed post-pasteurization contamination of the implicated milk. 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).

Table II-6. Ranking Of Types Of Food Group Vehicles By Number Of Outbreaks And Number Of Cases, United States And International Outbreaks Combined

Type of Food Vehicle	Ranking by Number	
	Outbreaks	Cases
Dairy	1	2
Meat	2	1
Fish	4	4
Vegetables	3	3