

# codex alimentarius commission



FOOD AND AGRICULTURE  
ORGANIZATION  
OF THE UNITED NATIONS

WORLD  
HEALTH  
ORGANIZATION



JOINT OFFICE: Viale delle Terme di Caracalla 00100 ROME Tel: 39 06 57051 www.codexalimentarius.net Email: codex@fao.org Facsimile: 39 06 5705 4593

Agenda Item 5 d)

CX/FH 03/5-Add .4  
September 2002

## JOINT FAO/WHO FOOD STANDARDS PROGRAMME

### CODEX COMMITTEE ON FOOD HYGIENE

Thirty-fifth Session

Orlando, U.S.A., 27 January – 1 February 2003

#### **RISK PROFILE FOR ENTEROHEMORRAGIC *E. COLI* INCLUDING THE IDENTIFICATION OF THE COMMODITIES OF CONCERN, INCLUDING SPROUTS, GROUND BEEF AND PORK**

*(Prepared by the United States, with the assistance of Australia, Austria, Canada, China, France, Germany, Japan, Netherlands and the European Union)*

#### **BACKGROUND**

At its 34th session, the Committee confirmed that enterohemorrhagic *Escherichia coli* remained as a priority item of work for the Codex Committee on Food Hygiene (CCFH). The CCFH therefore agreed to have the United States prepare a risk profile with the assistance of Austria, Australia, Canada, China, France, Germany, Japan and the European Commission for enterohemorrhagic *Escherichia coli* that would include identification of the commodities of concern, including sprouts, ground beef and pork (ALINORM 03/13, para.86).

#### **SCOPE**

This Discussion Paper will provide an overview of (1) the completed risk profile which can be found in its entirety in Appendix A, (2) existing international guidance documents and codes of practice that are likely to mitigate the occurrence of human enterohemorrhagic *Escherichia coli* (EHEC) infection and (3) suggested risk management activities for consideration by CCFH. Note that this discussion paper was crafted after the risk profile in the appendix was prepared and borrows text extensively from the appendix.

## **RISK PROFILE FOR RISK MANAGEMENT OF ENTEROHEMORRHAGIC *ESCHERICHIA COLI* IN VARIOUS COMMODITIES OF CONCERN**

The fundamental risk management issue of concern, as determined in this risk profile, is that of managing the colonization of cattle herds by *E. coli* O157:H7 and, consequently, of managing the manure that can ultimately contaminate food products. This singular but broad issue greatly impacts the likelihood of human foodborne illness from EHEC. In the case of produce, good agricultural practices (GAPs), good manufacturing practices (GMPs) and appropriate retail and consumer behaviour in handling food can reduce the impact of EHEC on public health. Foods of bovine origin, also commonly implicated in cases of human infection from EHEC, can become contaminated with animal manure at slaughter or, in the case of dairy products, during milk collection. The following is an overview of the information discussed in greater detail in the risk profile (Appendix I).

### **1. Pathogen-food commodity combination(s) of concern**

#### **1.1 Pathogen of concern**

Enterohemorrhagic *Escherichia coli* (EHEC) were first identified as human pathogens in 1982, when *E. coli* strains of a previously uncommon serotype, O157:H7, were implicated in two outbreaks of hemorrhagic colitis (bloody diarrhea) in the United States (U.S.). Since then, outbreaks of this new pathogen have become a serious public health problem throughout many regions of the world (Schlundt 2001; Clarke et al. 2002). Also in the 1990s, EHEC strains of other serogroups such as O26, O103, and O111 were increasingly linked to human illness as illustrated by surveillance data from Japan (Table 1) and as stated in a WHO report (WHO 1998) (along with serotype O145); however, most clinical laboratories do not routinely screen for non-O157 EHEC, because of the lack of a biochemical marker (Mead 1998) and consequently there is little surveillance conducted for these EHEC infections. While *E. coli* O157:H7 are easily differentiated biochemically from other enteric *E. coli* because they ferment sorbitol slowly, diagnostic methods for identifying non-O157 EHEC are not widely available in most laboratories; consequently infections caused by these pathogens are often not confirmed. Recently, new methods for the detection of O103, O111, O26 and O145 serogroups have been developed; these advances may facilitate the collection of more data regarding the prevalence and significance of these serotypes as it pertains to human foodborne illness (Cudjoe 2001). Mead (1999) has estimated that the incidence of non-O157 EHEC is between 20% and 50% that of *E. coli* O157:H7 infection. Because *E. coli* O157:H7 is currently the single most important EHEC serotype in relation to public health and because of the current paucity of epidemiologic data for non-O157 EHEC, this risk profile will emphasize *E. coli* O157:H7.

##### **1.1.1 Key attributes of the pathogen including thermal stability, acid resistance and virulence characteristics.**

A number of factors have a significant influence on the survival and growth of *E. coli* O157:H7 in food, including temperature, pH, salt, and water activity (Meng and Doyle 1998). Studies on the thermal sensitivity of *E. coli* O157:H7 in ground beef have revealed that the pathogen has no unusual resistance to heat and that heating ground beef sufficiently to kill typical strains of *Salmonella* spp. will also kill *E. coli* O157:H7. The optimal temperature for growth of *E. coli* O157:H7 is approximately 37°C (98.6°F), and the organism will not grow at temperatures below 8°C to 10°C (46°F to 50°F) or above 44°C to 45°C (Doyle and Schoeni 1984; Buchanan and Doyle 1997). *E. coli* O157:H7 survives freezing, with some decline in concentration (Ansary et al. 1999).

*E. coli* O157:H7 has been reported to be more acid resistant than other *E. coli*. Acid resistance enhances the survival of *E. coli* O157:H7 in mildly acidic foods and may explain its ability to survive passage through the stomach and cause infection at low doses.

Table 1: Serotypes of human EHEC isolates from 1999-2000 in Japan\*

Serotype	1999 Cases (% of total)	2000 Cases (% of total)
O157	1394 (72.1)	1158 (69.9)
O26	346 (17.9)	377 (22.8)
O111	81 (4.2)	42 (2.5)
All other	112 (5.8)	79 (4.8)

\* <http://idsc.nih.go.jp/iasr/22/256/graph/t2563.gif>

Please refer to appendix A for a discussion of virulence characteristics associated with EHEC.

## 1.2 Description of the food or food product and/or condition of its use with which foodborne illness due to this pathogen has been associated.

In order to choose the most appropriate product to consider in this risk profile, the frequency with which various products were implicated in causing *E. coli* O157:H7 infection was considered. To accomplish this, available studies of sporadic cases of *E. coli* O157:H7 infection and outbreak investigation reports were evaluated. Food vehicles implicated most frequently are raw or inadequately cooked foods of bovine origin, especially undercooked ground or minced beef and unpasteurized milk; however, an increasing number of outbreaks are associated with the consumption of raw or minimally processed fruits and vegetables.

Due to their relevance to human cases of *E. coli* O157:H7 infection, ground beef and green leafy vegetables contaminated by *E. coli* O157:H7 from bovine faeces are the focus of this risk profile. Commodities worthy of future consideration include raw milk products, unpasteurized cider and sprouted seeds.

### 1.2.1 Foods of bovine origin

Beef was cited as the source of 46% of the foodborne outbreaks with a known vehicle of transmission in the U.S. between 1993-1999. Other products of bovine origin that have been implicated in a number of outbreaks of *E. coli* O157:H7 infection include raw and improperly pasteurised cow's milk as demonstrated by a O104:H21 outbreak from contaminated milk (Feng et al. 2001). Effective pasteurisation eliminates pathogens from milk, including *E. coli* O157:H7.

### 1.2.2 Foods of non-bovine origin

Fruits and vegetables contaminated with *E. coli* O157:H7 have accounted for a growing number of recognised outbreaks (Table 3). Examples of vegetables, fruits, and sprouts that have been implicated in foodborne outbreaks of *E. coli* O157:H7 infection include fresh potatoes (Morgan 1988), lettuce (Ackers et al. 1998, Mermin et al. 1997, Hilborn et al. 1999), radish (Michino et al. 1998), alfalfa

sprouts (Breuer et al. 2001, MMWR 1997a) and cantaloupe (Del Rosario and Beuchat 1995). As a whole, leafy green vegetables were cited as the source of 26% of the foodborne outbreaks with a known vehicle of transmission in the U.S. between 1998-99. Contamination of vegetables may occur in several ways, however, the use of manure or water contaminated with fecal matter is one possible route (Solomon et al. 2002; Wachtel et al. 2002; Solomon et al. 2002b). In a number of the instances cited above, manure from nearby cattle lots was suspected to be the original source of *E. coli* O157:H7 (Ackers et al. 1998; Hilborn et al. 1999). Similarly, in an accidental release of tertiary-treated sewage that had not been treated with chlorine, cabbage plants were found to have *E. coli* strains (not containing stx1, stx2 or eae genes) associated with the plant roots when control fields did not (Wachtel et al. 2002). Another means of contamination of these products is cross-contamination in the retail, or consumer kitchen between contaminated meat products and produce.

Current data based on both outbreaks and sporadic infections indicate that consumption of ground beef is still the single most important source of foodborne *E. coli* O157:H7 illness; however, leafy green vegetables are the second most significant cause of human foodborne illness cases of *E. coli* O157:H7 as they are subject to contamination and they are eaten raw.

Table 2: Food Vehicles Implicated in Outbreaks of *E. coli* O157:H7, U.S., 1998-1999

Vehicle	1998	1999	Total
Ground beef/hamburger	10	9	19
Roast Beef	0	2	2
Combined green leafy vegetables	4	7	9
Salad	1	1	2
Coleslaw	2	1	3
Lettuce	1	3	4
Milk	2	0	2
Other (none greater than one total)	5	5	10
Total	21	21	42

Sources: CDC 1999b; CDC 2001c.

## 2. Description of the public health problem

### 2.1 Characteristics of the disease

Following ingestion of *E. coli* O157:H7, the human response ranges from asymptomatic infection to death. The incubation period from the time of ingestion to the first symptoms ranges from one to eight days. Typically the illness begins with abdominal cramps and nonbloody diarrhea that can, but does not necessarily, progress to bloody diarrhea within two to three days (Griffin 1995, Mead 1998). Usually 70% or more of symptomatic patients will develop bloody diarrhea; however, as many as 95% have been observed in other studies (Ostroff 1989; Bell 1994). More severe manifestations of *E. coli* O157:H7 infection include hemorrhagic colitis (grossly bloody diarrhea), hemolytic uremic syndrome (HUS)<sup>1</sup> and occasionally thrombotic thrombocytopenic purpura (TTP).

<sup>1</sup> a combination of renal failure, low platelet counts and hemolytic anemia

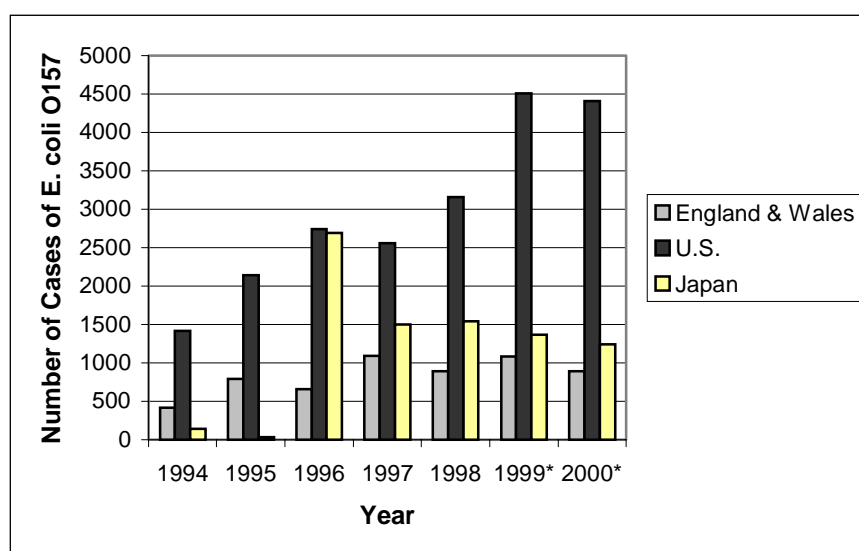
### 2.1.1 Susceptible populations

The incidence of *E. coli* O157:H7 infection varies by age group, with the highest incidence of reported cases occurring in children. In addition to children, elderly are known to be susceptible to *E. coli* O157:H7 infection. While these populations are more susceptible to illness, people of all ages can suffer infection from *E. coli* O157:H7.

### 2.1.2 Annual incidence rate in humans including regional or seasonal variations in incidence or severity

During 1994-2000, the number of reported cases of *E. coli* O157:H7 in the U.S. increased more than two-fold from 1,420 (0.8/100,000 people) in 1994 to 4410 (approximately 1.6/100,000 people) in 2000 (CDC 1999, CDC 2001) (Figure 1).

**Figure 1.** Number of reported cases of *E. coli* O157:H7 infection, U.S. (1994-2000),<sup>a</sup> England and Wales (1994-2000),<sup>b</sup> and Japan (1996-2000);<sup>c</sup> \*provisional data are presented from 1999 and 2000 for the US.



- CDC, NNDSS; Cases include suspect and confirmed human isolations.
- PHLS Laboratory of Enteric Pathogens; Cases include only isolates (obtained from stool samples) that are submitted to PHLS from laboratories in England and Wales. They are confirmed, serotyped, phage typed and VT typed at PHLS.
- Ministry of Health and Welfare, National Epidemiological Surveillance of Infectious Diseases; Cases are restricted to those with stool samples that have been culture confirmed and include all O157 serotypes.

In Belgium 97% of HUS cases in 2000 were associated with *E. coli* O157:H7 infection (Pierard 1997). Siegler (1994) found that HUS causes chronic renal sequelae, usually mild, in 51% of survivors (48% of all cases) however, Elliot (2001) has observed significantly lower renal failure statistics in Australia.

Between 1997 and 1999 at FoodNet sites located within the U.S., the overall incidence of HUS among children younger than 15 years of age was 0.7 per 100,000; this is similar to the frequency observed in other nations such as Austria (0.65 per 100,000) and Australia (0.64 per 100,000) (Elliot 2001). For children younger than 5, the incidence was 1.4 and 1.35 per 100,000 in the U.S.

and Australia respectively (CDC 2000b). In a nationwide study of 83 patients with HUS in the U.S., 46 (55.4%) were younger than 5 years old and an additional 27 (32.5%) were 5 to 17 years old (Banatvala et al. 2001). Similarly, analyses of HUS incidence in Belgium found the majority (35/46) of HUS cases were in children (Pierard 1997).

The overall findings of this study demonstrated that the burden of illness from HUS is comparable between Australia, North America and Europe. Similarly, examples cited above suggest the strength of the association between HUS cases and *E. coli* infection is similar in various parts of the world. The correlation may be less strong between O157 infection and HUS in Australia since the O157 incidence is very low, yet the incidence of HUS appears similar to that of other countries. These facts imply that there may not be any variance in the severity of illness experienced upon infection among the countries reviewed.

It is worth noting that the severity of illness has been shown to vary between sporadic cases and those associated with outbreaks. Between 3 and 7% of sporadic cases of *E. coli* O157:H7 infection will progress to HUS whereas, 20% or more of outbreak associated cases do (Mead 1998).

### **3. Food production, processing, distribution and consumption**

#### **3.1 Source of contamination**

EHEC strains including *E. coli* O157:H7, have been isolated from the faeces or gastrointestinal tract of cattle, sheep, horses, pigs, turkeys, dogs, and a variety of wild animal species (Kudva 1996; Rice and Rice and Hancock 1995; Hancock et al. 1998b; Heuvelink 1999); Consequently, foods associated either directly or indirectly with animals (meat or dairy products) or animal waste products (for instance as fertilizer) are frequently implicated as vehicles of transmission for human illness. Epidemiological studies have found that cattle manure is the primary source of most human *E. coli* O157:H7 infections. In fact, *E. coli* O157:H7 has been described as “ubiquitous” in dairy and beef cattle and is present at least occasionally on most farms or feedlots (Hancock et al. 1998a; Hancock et al. 2001).

Many of the risk factors that are thought to influence *E. coli* O157:H7 prevalence and their levels in cattle apply to whole herds rather than to individual cattle. Therefore, mitigation strategies for reduction of *E. coli* O157:H7 in agricultural settings typically target herd-level risk factors for *E. coli* O157:H7 control. The type of herd does appear to have an affect on the prevalence of *E. coli*: herds of feedlot cattle such as steers and heifers are more likely to have colonized animals than breeding herds, which are comprised of cows and bulls. Additionally, when a feedlot herd is positive it is likely to have significantly more colonized animals than breeding cattle herds (USDA, 2001). Limited evidence suggests that dairy and cow-calf herds are similar to each other with respect to *E. coli* O157:H7 prevalence (Lag Reid et al. 1999; Sargeant et al. 2000). An increased seasonal incidence of *E. coli* O157:H7 infections in cattle and human populations has been demonstrated in the warm months (Hancock et al. 1997a, 1997b; Griffin 1998; Van Donkersgoed et al. 1997, Heuvelink 1998). The roles that water, including treated or untreated sewage used to irrigate animal feed, and feed itself play in colonizing herds may prove to be critical to on farm management strategies and should be considered (Anderson et al. 2001, Hancock et al. 2001, LeJeune et al. 2001).

### 3.2.1 Characteristics of the commodities

#### 3.2.1 Leafy Green Vegetables

Leafy green vegetables grown low to the ground are a recognized cause of *E. coli* O157:H7 outbreaks. Contamination of vegetables may occur in several ways, however, the use of manure or water contaminated with fecal matter is one possible route (Solomon et al. 2002; Wachtel et al. 2002; Solomon et al. 2002b). When contaminated, the fact that this produce is minimally processed and consumed raw increases the likelihood of *E. coli* O157:H7 infection. The source of *E. coli* O157:H7 contaminated manure can be, and frequently is, of bovine origin. Mitigation strategies that control *E. coli* O157:H7 on farm will likely lower the level of contamination of produce.

#### 3.2.2 Beef

Meat becomes contaminated with *E. coli* O157:H7 when beef carcasses come into contact with faeces and/or contaminated hides during the slaughter process (Elder et al. 2000). A determination of the quantitative association between the incoming status of cattle and the outgoing status of harvested meat is critical in an exposure assessment. This quantitative correlation between pre-harvest and post-harvest contamination is best predicted using fecal *E. coli* O157:H7 prevalence data (Elder et al. 2000).

### 3.3 Retail and Consumer Behaviour

The food preparation industry as well as consumer choices and behaviours have a large influence on the probability of contracting an *E. coli* O157:H7 infection. Specifically, inadequately cooked beef (in particular ground or minced products) is correlated to infection as previously discussed. Cooking these products to an internal temperature of  $\geq 68$  °C has been shown to be an adequate precaution; however, consumers continue to choose undercooked beef products.<sup>2</sup> Similarly, awareness of and precautions against cross-contamination between raw meat products and either cooked foods or raw vegetables would limit the likelihood of infection.<sup>3</sup> Consumer behavior that can limit illness from vegetables contaminated at the farm is likely limited to thoroughly cleaning produce, in particular commodities to be consumed raw. In the case of sprouted seeds and some fruits and vegetables (Solomon et al. 2002), which have been shown to integrate the bacteria, washing may not be a sufficient intervention.

### 3.4 Interventions

A Canadian risk assessment was published that predicted the reduction in illnesses expected from various mitigation scenarios for ground beef (Table 4) (Cassin et al. 1998). These mitigations included achievement of maximum temperature control during storage, preslaughter screening of cattle faeces and cooking at appropriate temperatures. Based on the Cassin approach, an Australian risk assessment also modeled risk mitigation scenarios including hot water decontamination of carcasses, irradiation of frozen boxed beef, preslaughter reduction in faecal concentrations, retail temperature control and consumer education about good cooking practices (Lammerding et al. 1999; P Vanderlinde, personal communication).

Due to the impact on-farm cattle colonization can have on other commodities such as leafy green vegetables, interventions that control *E. coli* O157:H7 in live animals are also of great interest.

---

<sup>2</sup> <http://www.fsis.usda.gov/oa/news/1998/colorpr.htm>

<sup>3</sup> [http://www.fsis.usda.gov/oa/pubs/keep\\_apart.htm](http://www.fsis.usda.gov/oa/pubs/keep_apart.htm)

These include the impact of employing probiotic (Zhao et al. 1998) bacterial flora in cattle, the impact of various feeding regimens (Cray et al. 1998), the result of different composting protocols (Lung et al. 2001) and the impact of various irrigation methods.

### **EXISTING CODEX DOCUMENTS RELEVANT TO THE CONTROL OF ENTEROHEMORRHAGIC *ESCHERICHIA COLI* IN VARIOUS COMMODITIES OF CONCERN**

The Risk Management strategies for reducing human illness from enterohemorrhagic *Escherichia coli* associated with the consumption of leafy green vegetables and beef are described individually below.

#### **1. Leafy Green Vegetables**

Contamination of commodities derived from fresh produce (e.g., sprouted seeds and prepared lettuce) is usually a consequence of (1) irrigation practices, (2) inadequate cleaning (3) cleaning with contaminated water, (4) non-hygienic farm workers or (5) cross contamination from other products. We suggest existing international guidance directed toward the production of these products (Draft Code of Hygienic Practice for Fresh Fruits and Vegetables, ALINORM 03/30, Appendix II), is sufficient for addressing the majority of the problems cited above when appropriately implemented. However, this document does not effectively address methods specifically targeting the reduction of human illness from EHEC associated with cross contamination including from agricultural environments. Additionally, educational efforts may be most effective for reducing human illness from EHEC associated with cross contamination during food preparation.

#### **2. Beef**

Contamination of ground beef is usually a consequence of faecal contamination that occurs at or is not adequately removed during slaughter. Current international guidance directed toward the production of hygienic meat includes the Proposed General Principles of Meat Hygiene<sup>4</sup> (under development) and Proposed Draft Code of Hygienic Practice for Fresh Meat<sup>5</sup> (under development). These documents include useful approaches for minimizing contamination of beef such as implementation of HACCP and good plant sanitation. Additionally, they provide some guidance on the importance of:

- Feedstuffs in minimizing cattle colonization and potential impact of sub-therapeutic antibiotic use. (Footnote 2, Paragraphs 24, 25 and 27)
- Maintenance of animal hygiene throughout transport. (Footnote 2, Paragraphs 17, 30 and 40)
- Development of rigorous record keeping systems both on-farm and in-plant to facilitate animal identification and traceback. (Footnote 2, Paragraphs 16, 38 and 46)
- Ensuring only clean and healthy animals are presented for slaughter through ante-mortem inspections and other means determined useful to the establishment. (Footnote 2, Paragraphs 34, 38 and 40)

Based on the review of existing Codex risk management guidance information pertinent to the control of EHEC in foods, it appears appropriate for the Committee to consider developing a

---

<sup>4</sup> Alinorm 03/16: Appendix II

<sup>5</sup> Alinorm 03/16: Appendix III

separate guidance document on methods for minimizing EHEC infection associated with the consumption of foods contaminated with *E. coli* O157:H7 from bovine faecal material. This can best be accomplished after the Committee is further informed by a complete risk assessment. We therefore recommend that a risk assessment be conducted to consider EHEC illnesses associated with the consumption of ground beef and leafy green vegetables.

### **RISK ASSESSMENT NEEDS AND QUESTIONS FOR THE RISK ASSESSORS**

We propose the development of a farm-to-table risk assessment for ground beef and leafy green vegetables. Development of an on-farm module that could be used in combination with other modules for risk assessments of *E. coli* O157:H7 infection associated with either ground beef or leafy green vegetables should be considered.

#### **1. On-farm mitigation strategies that should be investigated by risk assessors for their possible impact on human illness include:**

- The effect of probiotics [<http://www.amif.org/ProbioticsReport042302.pdf>]
- The effect of antimicrobials including bacteriophage
- The effect of specific feeding regimens (Cray et al. 1998)
- The effect of specific composting regimens (Lung et al. 2001)
- The effect of distance and water management practices on contamination of downstream and downwind crops by bovine faeces.
- Strategies investigated in Jordan, et al. 1999 A simulation model for studying the role of pre-slaughter effects on the exposure of beef carcasses to human microbial hazards. *Prev. Vet. Med.*, 41: 37-54 and Jordan et al. 1999. Pre-slaughter control of *Escherichia coli* O157 in beef cattle: a simulation study. *Prev. Vet. Med.*, 41: 55-74.

#### **2. Other mitigations (discussed in further detail in the appended risk profile) that should be evaluated in the risk assessment include:**

- Temperature control for preventing the growth in foods of pathogenic microorganisms, specifically *E. coli* O157:H7, while in transit and during storage.
- Measures to minimize fecal shedding of *E. coli* O157:H7 in animals presented for slaughter.
- Measures to minimize contamination of carcasses at slaughter.
- Measures to minimize consumer exposure to contaminated products.
- Retail Codes / Consumer education.
- Measures to minimize contamination of food products in international trade.

### **AVAILABLE INFORMATION**

A number of countries have evaluated the risk associated with foodborne *E. coli* O157. These assessments are listed in Table 3. Specifically, Canada has analyzed the risk associated with *E. coli* O157:H7 infection from consuming ground beef hamburgers (Cassin 1998), sprouts (personal communication with Health Canada, January 2002) and juices (personal communication with Health Canada, January 2002) since each of these commodities have contributed to outbreaks or

sporadic incidents of illness in that nation. An academic group in Canada has also assessed risk factors associated with on-farm *E. coli* O157 prevalence in cattle (Jordan 1999a, 1999b). The Netherlands chose to investigate steak tartare as the vehicle of transmission in their risk assessment because: (1) a steak tartare is thicker than a hamburger, therefore the risk of insufficient heating of the center is larger, (2) people tend to accept a partially raw tartare but do not accept a partially raw hamburger, (3) tartare is sometimes consumed raw (e.g., a tartare roll in snack bars). Steak tartare was chosen after also considering consumption levels. The U.S. has developed a farm-to-table risk assessment for *E. coli* O157:H7 in ground beef in addition to a comparative risk assessment for *E. coli* O157:H7 in tenderized and non-tenderized steaks. Due to the smaller contribution O157 serotypes make to human illness in Australia, that country has developed one risk assessment for O157:STEC and another for all STEC in ground beef production and in fermented meat. FAO/WHO may find many of these risk assessments useful in the development of a risk assessment for Codex. Further evaluation of each is necessary.

Table 3: Risk assessments for *E. coli* O157:H7

Nation	Topic	Reference
Australia	Ground Beef <sup>1</sup>	Lammerding 1999
Australia	STEC in Ground Beef <sup>1</sup>	Lammerding 1999
Canada	Ground Beef Hamburgers	Cassin 1998
Canada	Seeds/Beans and Sprouted Seeds/Beans <sup>2,3</sup>	Personal Communication with Health Canada
Canada	Unpasteurized Fruit Juice/Cider <sup>4</sup>	Personal Communication with Health Canada
Canada	Pre-harvest Husbandry Practices	Jordan 1999a,b
Ireland	Beef/Beef Products	<a href="http://www.science.ulst.ac.uk/food/E_coli_Risk_Assess..htm">www.science.ulst.ac.uk/food/E_coli_Risk_Assess..htm</a>
Netherlands	Raw Fermented Products	<a href="http://www.research.teagasc.ie/vteceurope/S+Gprog/hoornstrasg.html">www.research.teagasc.ie/vteceurope/S+Gprog/hoornstrasg.html</a>
Netherlands	Steak Tartare	RIVM report 257851003/2001
U.S.	Ground Beef <sup>5</sup>	<a href="http://www.fsis.usda.gov/OPPDE/rdad/FRPubs/00-023NReport.pdf">www.fsis.usda.gov/OPPDE/rdad/FRPubs/00-023NReport.pdf</a>
U.S.	Tenderized vs. Non-tenderized Beef Steaks	Personal Communication with USDA

<sup>1</sup>ANZFA Food Standard Code 1.6.1 sets Microbiological limits for total generic *E. coli* in a variety of foods. <http://www.anzfa.gov.au/foodstandardscodecontents/standard16/index.cfm>. Additionally, dairy products must be produced from pasteurized milk.

<sup>2</sup>Subsequent policy and management documents include “Consultation/Policy Document: A Dialogue on Developing a Risk Management Strategy for Sprouted Seeds and Beans”.

<sup>3</sup>Subsequent policy and management documents include “Code of Practice for the Hygienic Production of Sprouted Seeds”

<sup>4</sup>Subsequent policy and management documents include “Code of Practice for the Production and Distribution of Unpasteurized Apple and Other Fruit Juice/Cider in Canada”

<sup>5</sup>The U.S. has a microbiological criteria equivalent to a zero-tolerance for *E. coli* O157:H7 in raw ground beef

## DATA GAPS

Several data gaps have been identified based on currently available risk assessments for *E. coli* O157:H7, including:

- Information describing the human health impact of *E. coli* O157 in less developed nations.
- Commodities likely to be associated with *E. coli* O157 foodborne illness in less developed nations.
- Data regarding the exposure dose of *E. coli* O157:H7 likely to cause illness in susceptible populations.
- Frequency and severity of illness among children ages 0 to 5 from *E. coli* O157:H7 that become ill from consuming ground beef d in raw produce.
- Industry and consumer practices for various methods of cooking ground beef (e.g., grill vs. fry).
- Survival of *E. coli* O157:H7 on produce as a result of contamination by water or organic fertilizer.
- Information describing the critical contamination levels of meat products that may lead to cross contamination of uncooked produce.
- Information on the percentage of fresh leafy vegetables contaminated by bovine faeces containing *E. coli* O157:H7 as opposed to feral animal faeces, or human faeces
- Quantify the heat resistance (e.g., D and z values) of the individual strains of *E. coli* O157:H7 used in the Sporing (1999) study. Individual strains should be identified and characterized.
- Information on the maximum density of *E. coli* O157:H7 organisms in ground beef servings as a result of matrix effects, competitive microflora in ground beef, and environmental conditions (e.g., pH, water activity).
- Predictive microbiological data on the increase and decrease in the number of *E. coli* O157:H7 organisms in ground beef under various storage and preparation conditions along with frequencies of occurrence of these storage and preparation conditions.
- Data on cross-contamination of *E. coli* O157:H7 between carcasses during carcass splitting.
- Time-temperature data (quantitative) for chillers in slaughter establishments.
- Marketing data on the proportion of beef ground at slaughter versus at retail.
- Data on retail and consumer storage, cooking, and consumption (frequency and serving size) patterns by type of ground beef meal (e.g., grilled hamburger in July and baked meat loaf in October).
- Descriptive epidemiologic information about sporadic cases of *E. coli* O157:H7 illness, including the month of disease onset, age, sex, hospitalizations, summary of clinical manifestations including severe disease manifestations, and food vehicles involved (if known).
- Additional case-control studies of sporadic *E. coli* O157:H7 cases to calculate etiologic fraction attributable to ground beef.

## RECOMMENDATIONS

1. Commission a farm-to-table risk assessment for ground beef and leafy green vegetables with an on-farm module that could be used to clearly answer questions related to the impact various manure control strategies would have on cases of human illness from *E. coli* O157:H7 associated with the consumption of either ground beef or leafy green vegetables.

2. After evaluating the outputs from the above risk assessment, the Committee reevaluate existing Codex food codes and guidance documents to consider whether any existing food codes or guidance documents should be amended or if annexes should be developed for them specific to the control of *E. coli* 0157:H7. This would require a through review of these documents and of the risk assessment. These documents may include:

- The Draft Code of Hygienic Practice for Fresh Fruits and Vegetables, ALINORM 03/13, Appendix II;
- The Proposed General Principles of Meat Hygiene<sup>6</sup> (under development), and;
- The Proposed Draft Code of Hygienic Practice for Fresh Meat<sup>7</sup> (under development).

3. Consider, after evaluating the outputs of the above risk assessment and the findings resulting from recommendation 2, the need to develop a separate guidance document on measures for minimizing EHEC infection associated with the consumption of foods contaminated with *E. coli* 0157:H7 from bovine faecal material.

4. Encourage research efforts be undertaken to address the data gaps listed previously in the paper in order to develop more informed and appropriate risk management guidance.

---

<sup>6</sup> ALINORM 03/16: Appendix II

<sup>7</sup> ALINORM 03/16: Appendix III

Appendix A

**ENTEROHEMORRHAGIC *ESCHERICHIA COLI*  
INFECTION (EHEC)**

**A RISK PROFILE**

**AUGUST 2002**

## 1. PATHOGEN-FOOD COMMODITY COMBINATION(S) OF CONCERN

### *Escherichia coli*

*E. coli* strains that are pathogenic for humans and cause diarrheal illness may be categorized into specific groups based on virulence properties, mechanisms of pathogenicity, and clinical syndromes. These categories include enteropathogenic *E. coli* (EPEC), enterotoxigenic *E. coli* (ETEC), enteroinvasive *E. coli* (EIEC), diffusely-adherent *E. coli* (DAEC), enteroaggregative *E. coli* (EaggEC), and enterohemorrhagic *E. coli* (EHEC). The EHEC group comprises a subset of Shiga toxin-producing *E. coli* (STEC),<sup>8</sup> which include strains of *E. coli* that cause bloody diarrhea in many infected patients. Shiga toxin-producing *E. coli* strains produce either or both of two phage-encoded toxins, Shiga toxin 1 (Stx1) and Shiga toxin 2 (Stx2). However, Stx production alone may not be enough to cause illness. Some EHEC strains also contain genes that encode for the ability to attach to and damage intestinal tract cells, causing what is commonly referred to as attaching-and-effacing lesions. *E. coli* O157:H7 is the single most important EHEC serotype in relation to public health. For a detailed review of the pathogenesis of EHEC and other STEC, interested readers are referred to recent publications by Paton and Paton (1998) and Nataro and Kaper (1998).

#### 1.1 Pathogen of concern

Enterohemorrhagic *Escherichia coli* (EHEC) were first identified as human pathogens in 1982, when *E. coli* strains of a previously uncommon serotype, O157:H7, were implicated in two outbreaks of hemorrhagic colitis (bloody diarrhea) in the United States (U.S.). Since then, outbreaks of this new pathogen have become a serious public health problem throughout many regions of the world (Schlundt 2001; Clarke et al. 2002). The continued occurrence of large outbreaks and an increase in the incidence of reported cases suggests *E. coli* O157:H7 is an emerging pathogen (Tauxe 1997; Altekruze et al. 1997). Also in the 1990s, EHEC strains of other serogroups such as O26, O103, O111, and O145 were increasingly linked to human illness as illustrated by surveillance data from Japan (Table 1). This is also suggested by the WHO, which reported that O26, O103, O111 and O145 are the most important non-O157 serogroups (WHO 1998). Three outbreaks in the U.S. have been ascribed to non-O157 EHEC: a family outbreak of *E. coli* O111 with a case of HUS, a milk-associated episode of *E. coli* O104:H21 affecting 18 individuals and an outbreak of gastrointestinal illness, including bloody diarrhea, associated with *E. coli* O111:H8 in 56 persons (CDC 2000). Non-O157 serotypes of *E. coli* including O26:H11, O111:H8, O103:H2, O113:H21, and O104:H21 have been responsible for a small number of outbreaks in other parts of the world (CDC 1995b; Goldwater and Bettelheim 1995; Paton et al. 1996; Robins-Browne et al. 1998). In a cluster of three cases of HUS caused by O113:H21 in Australia, this organism was found not to have the attaching-and-effacing gene (Paton et al. 1999).

Table 1: Serotypes of human EHEC isolates from 1999-2000 in Japan\*

Serotype	1999 Cases (% of total)	2000 Cases (% of total)
O157	1394 (72.1)	1158 (69.9)
O26	346 (17.9)	377 (22.8)

<sup>8</sup> STEC are also referred to as VTEC (verotoxigenic *Escherichia coli*) in some member states. Both names are frequently employed in the scientific literature.

O111	81 (4.2)	42 (2.5)
All other	112 (5.8)	79 (4.8)

\* <http://idsc.nih.gov/iasr/22/256/graph/t2563.gif>

Most clinical laboratories do not routinely screen for non-O157 EHEC, because of the lack of a biochemical marker (Mead et al. 1998) and consequently there is little surveillance conducted for these EHEC infections. While *E. coli* O157:H7 are easily differentiated biochemically from other enteric *E. coli* because they ferment sorbitol slowly, diagnostic methods for identifying non-O157 EHEC are not widely available in most laboratories; consequently infections caused by these pathogens are often not confirmed. Recently, new methods for the detection of O103, O111, O26 and O145 serogroups have been developed; these advances may facilitate the collection of more data regarding the prevalence and significance of these serotypes as it pertains to human foodborne illness (Cudjoe 2001). Mead et al. (1999) has estimated that the incidence of non-O157 EHEC is between 20% and 50% that of *E. coli* O157:H7 infection. Because *E. coli* O157:H7 is the single most important EHEC serotype in relation to public health and because of the current paucity of epidemiologic data for non-O157 EHEC, this risk profile will emphasize *E. coli* O157:H7.

## 1.2 Commodities of Concern

In order to choose the most appropriate product to consider in this risk profile, the frequency with which various products were implicated in causing *E. coli* O157:H7 infection was considered. To accomplish this, we evaluated available studies of sporadic cases of *E. coli* O157:H7 infection and outbreak investigation reports. Sporadic cases account for the majority of reported cases in a given year and therefore may be more representative of persons with *E. coli* O157:H7 infection. For example, 75% of reported cases in one region of the U.S. during 1991-97, and 83% of reported cases in another region during 1992-1999, were sporadic (OCD 1998, Proctor and Davis 2000). Food vehicles implicated most frequently are raw or inadequately cooked foods of bovine origin, especially undercooked hamburgers and unpasteurized milk; however, an increasing number of outbreaks are associated with the consumption of raw or minimally processed fruits and vegetables.

- Enterohemorrhagic *Escherichia coli* (EHEC) were first identified as human pathogens in 1982, when *E. coli* strains of a previously uncommon serotype, O157:H7, were implicated in two outbreaks of hemorrhagic colitis (bloody diarrhea) in the United States.
- Since then, outbreaks of this new pathogen have become a serious public health problem throughout the industrialized world and have led to the designation of *E. coli* O157:H7 as an emerging pathogen.
- EHEC strains of other serogroups such as O26, O103, O111, and O145 have been increasingly linked to human illness.
- At present, *E. coli* O157:H7 is the single most virulent and important EHEC serotype in relation to public health and since epidemiologic data for non-O157 EHEC is lacking, CCFH should limit its immediate efforts to *E. coli* O157:H7.

### **Foods of bovine origin**

Case control studies of sporadic illness have described the association between ground beef consumption (in most cases, undercooked product) and *E. coli* O157:H7 infection (Table 2). Grinding meat introduces the pathogen into the interior of the

meat. When ground beef does not achieve the required internal temperature (e.g., > 68°C)<sup>9</sup> or when the product is cooked unevenly, *E. coli* O157:H7 may survive. In most countries, many thousands of pounds of meat trim from many carcasses are ground together; therefore, a small number of carcasses with *E. coli* O157:H7 can contaminate a large supply of ground beef. Additionally, contaminated beef may transfer *E. coli* O157:H7 to meat grinding equipment, which may later contaminate other lots of raw meat. Ground-beef products, therefore, pose a greater hazard than intact cuts of meat. Dry fermented meats have also been implicated in reported outbreaks of EHEC infection (Tilden et al. 1996). A case-control study showed a relation between consumption of two sausages, mortadella (cooked) and teewurst (fermented, containing beef), and illness (Ammon et al. 1999).

Table 2: Case-control studies implicating ground beef in *E. coli* O157:H7 infection

Study Reference	Study Type	Finding
Slutsker 1998	Case-control, sporadic illness	Consumption of round beef with “pink center” had 34% population attributable risk.
Mead 1997	Case-control, sporadic illness	45% of ill persons consumed ground beef with “pink center” in the preceding week while only 33% of controls did the same.
Kassenborg 2001	Case-control, sporadic illness	Ground beef with “pink center” was a statistically significant risk factor while consumption of just ground beef was not.
MacDonald 1988	Prospective study	Rare ground beef was consumed more often by ill persons than healthy persons.
Le Saux 1993	Case-control, sporadic illness	Consumption of undercooked ground beef had an attributable risk factor of 17%.

Outbreak investigations have also contributed significantly to our understanding of how *E. coli* O157:H7 is transmitted. Ground beef was identified as the transmission source in seven out of 13 (53.9%) outbreaks that occurred between 1982 and 1993 in the U.S. (Griffin 1995); however, outbreaks have been attributed to foodborne, waterborne and person-to-person means of transmission.

Beef was cited as the source of 46% of the foodborne outbreaks with a known vehicle of transmission in the U.S. between 1993-1999. Of the 21 beef-associated outbreaks that occurred during 1998-1999, ground beef was identified as the vehicle in 19 (Table 3). Five (26.3%) of the 19 ground beef/hamburger-associated outbreaks occurred in multiple states. Two outbreaks in 1999 were attributed to roast beef and one of these was a result of environmental contamination from manure in a pasture where a picnic was held.

<sup>9</sup> Recommendations ranging between 68.3 and 71 °C have been made. In some cases these are associated with holding times at the specified temperature such as 15 seconds.

Table 3: Food Vehicles Implicated in Outbreaks of *E. coli* O157:H7, U.S., 1998–1999

Vehicle	1998	1999	Total
Ground beef/hamburger	10	9	19
Roast beef	0	2	2
Combined green leafy vegetables	4	7	9
Lettuce	1	3	4
Coleslaw	2	1	3
Salad	1	1	2
Milk	2	0	2
Other (none with greater than 1 total)	5	5	10
<b>Total</b>	<b>21</b>	<b>21</b>	<b>42</b>

Sources: CDC 1999b; CDC 2001c.

Other products of bovine origin that have been implicated in a number of outbreaks of *E. coli* O157:H7 infection include raw and improperly pasteurised cow's milk as demonstrated by a O104:H21 outbreak from contaminated milk (Feng et al. 2001). Milk borne outbreaks mostly have been associated with the consumption of raw milk or milk products from local farms. Raw milk is often contaminated with enteric organisms during its collection and may result in a direct risk for consumers choosing to drink raw milk. Effective pasteurisation eliminates pathogens from milk, including *E. coli* O157:H7.

### **Foods of non-bovine origin**

A variety of foods may occasionally become contaminated with *E. coli* O157:H7 by cross-contamination with beef or other meats and contaminated kitchen surfaces during food preparation. Mayonnaise and mayonnaise-based dressings and sauces were identified as the most likely foods to have been contaminated in a series of outbreaks of *E. coli* O157:H7 infections in the U.S. (Jackson et al. 2000). Survival studies indicated that mayonnaise could serve as a vehicle for EHEC infections when stored at refrigeration temperatures, despite the low pH of mayonnaise. Sandwiches were cited as the probable source in an outbreak of *E. coli* O157:H7 at a nursing home (Carter et al. 1987). Additionally, several outbreaks associated with wild game meat have been reported (Asakura et al. 1998, Keene et al. 1997).

Fruits and vegetables contaminated with *E. coli* O157:H7 have accounted for a growing number of recognised outbreaks (Table 3). Examples of vegetables, fruits, and sprouts that have been implicated in foodborne outbreaks of *E. coli* O157:H7 infection include fresh potatoes (Morgan 1988), lettuce (Ackers et al. 1998, Mermin et al. 1997, Hilborn et al. 1999), radish (Michino et al. 1998), alfalfa sprouts (Breuer et al. 2001, MMWR 1997a) and cantaloupe (Del Rosario and Beuchat 1995). As a whole, leafy green vegetables were cited as the source of 26% of the foodborne outbreaks with a known vehicle of transmission in the U.S. between 1998-99. Contamination of vegetables may occur in several ways, however, the use of manure or water contaminated with fecal matter is one possible route (Solomon et al. 2002; Wachtel et al. 2002; Solomon et al. 2002b). In a number of the instances cited above, manure from nearby cattle lots was suspected to be the original source of *E. coli* O157:H7 (Ackers et al. 1998; Hilborn et al. 1999). Similarly, in an accidental release of tertiary-treated sewage that had not been treated with chlorine, cabbage plants were found to have *E. coli* strains (not containing stx1, stx2 or eae genes) associated with the plant roots when control fields did not (Wachtel et al. 2002). Another means of contamination of these products is cross-contamination in the retail, or consumer kitchen between contaminated meat products and produce.

Fruit juices have also been implicated in outbreaks of *E. coli* O157:H7 infection (Besser 1993, CDC 1996, CDC 1997, Cody 1999, MMWR 1997b, Steele 1982). Although the low pH of fruit juices will generally not allow the survival and outgrowth of many of the Enterobacteriaceae, these products may allow survival of *E. coli* O157:H7 when they become contaminated because of the microorganism's high acid-tolerance. Although the exact mechanisms of contamination for these outbreaks were not clearly determined, animal manure was suspected to have contaminated the fruit.

In summary, there are many foodborne pathways by which individuals can be exposed to *E. coli* O157:H7. Other significant risk factors reported in literature are exposure to farm animals or the farm environment, eating at a table service restaurant, using immune suppressive medication (for adults only) and obtaining beef through a private slaughter arrangement (Kassenborg et al. 2001; OCD 1998). Current data based on both outbreaks and sporadic infections indicate that consumption of ground beef is still the single most important source of foodborne *E. coli* O157:H7 illness. Leafy green vegetables are the second most significant cause of human foodborne illness cases of *E. coli* O157:H7 as they are subject to contamination and they are eaten raw. Table 5 in the final section of this document describes the national and academic risk assessments that have been conducted to date for *E. coli* O157:H7 infection.

Due to their relevance to human cases of *E. coli* O157:H7 infection, ground beef and green leafy vegetables contaminated by *E. coli* O157:H7 from bovine faeces are the focus of this risk profile. Commodities worthy of future consideration include raw milk products, unpasteurized cider and sprouted seeds.

- Foods associated either directly or indirectly with animals (meat or dairy products) or foods subject to contamination by animal waste products such as fertilizer or agricultural runoff are frequently implicated as vehicles of transmission for human illness.
- Beef was cited as the source of 46% of the foodborne outbreaks with a known vehicle of transmission in the U.S. between 1993-1999.
- Leafy green vegetables were cited as the source of 26% of the foodborne outbreaks with a known vehicle of transmission in the U.S. between 1998-99.
- Ground-beef products pose a greater hazard than intact cuts of meat.
- For these reasons, this working group will only address the threat associated with ground beef and leafy green vegetables that have been contaminated with bovine faeces as vehicles of transmission.

## **2. Description of the public health problem**

### **Epidemiology**

Following ingestion of *E. coli* O157:H7, the human response ranges from asymptomatic infection to death. To cause disease after ingestion, the *E. coli* O157:H7 must survive acidic conditions within the stomach prior to moving to distal portions of the gastrointestinal tract. Disease due to *E. coli* O157:H7 occurs primarily in the colon. The incubation period from the time of ingestion to the first symptoms ranges from one to eight days. Asymptomatic shedding of *E. coli* O157:H7 has been documented (Swerdlow 1997); however, the proportion of exposed individuals who shed *E. coli* O157:H7 but do not

develop symptoms is unknown. Typically the illness begins with abdominal cramps and nonbloody diarrhea that can, but does not necessarily, progress to bloody diarrhea within two to three days (Griffin 1995, Mead et al. 1998). Usually 70% or more of symptomatic patients will develop bloody diarrhea; however, as many as 95% have been observed in other studies (Ostroff et al. 1989; Bell et al. 1994). More severe manifestations of *E. coli* O157:H7 infection include hemorrhagic colitis (grossly bloody diarrhea), hemolytic uremic syndrome (HUS)<sup>10</sup> and occasionally thrombotic thrombocytopenic purpura (TTP).

Symptoms of hemorrhagic colitis include severe abdominal cramps followed by grossly bloody diarrhea and edema (swelling), erosion, or hemorrhage of the mucosal lining of the colon (Su and Brandt 1995). Hemorrhagic colitis may be the only manifestation of *E. coli* O157:H7 infection, or it may precede development of HUS. Complications from hemorrhagic colitis associated with *E. coli* O157:H7 include upper-gastrointestinal bleeding and stroke (Su and Brandt 1995). Roberts et al. (1998, citing Boyce et al. 1995a, Ryan et al. 1986) estimates the mortality rate of those suffering hemorrhagic colitis without progression to HUS to be 1%, although Griffin (personal communication) believes this rate is too high. Approximately 30% to 45% of patients are hospitalized (Ostroff et al. 1989, Le Saux et al. 1993, Bell et al. 1994, Slutsker et al. 1998). Of the 631 cases reported to FoodNet sites in 1999, 39% were hospitalized (CDC 2000b). Treatment for the more serious manifestations of *E. coli* O157:H7 infection is supportive and the use of antimicrobial agents has been debated (Mead 1998).

The incidence of *E. coli* O157:H7 infection varies by age group, with the highest incidence of reported cases occurring in children. In addition to children, elderly are known to be susceptible to *E. coli* O157:H7 infection. A report detailing a Scottish outbreak resulting from contaminated beef involving at least 292 confirmed cases of *E. coli* O157:H7 infection resulted in 151 hospitalizations and 18 deaths; all fatalities were elderly patients (Ahiied 1997).

The number of reported *E. coli* O157:H7 cases derived from surveillance is known to underreport the true disease burden. Underestimation of the actual incidence of infection occurs for a variety of reasons, including:

- some infected persons do not seek medical care;
- physicians do not perform diagnostic testing on all patients with symptoms of infection;
- some persons who obtain medical care do not provide a stool specimen;
- laboratories do not culture all stool samples for *E. coli* O157:H7. In a 1994 national survey in the U.S., 70 (54.3%) of 129 randomly selected clinical laboratories reported that they did not routinely test all stools or all bloody stools for *E. coli* O157:H7 (Boyce 1995b).
- some proportion of laboratory results are false negatives; and
- not all culture-confirmed infections are reported by health care providers and laboratories to public health authorities.

Using surveillance data, and accounting for the factors that contribute to underreporting, Mead (1999) estimated that 73,480 cases of *E. coli* O157:H7 infection occur annually in the U.S. and that 85% (62,456 cases) are a result of foodborne exposure.

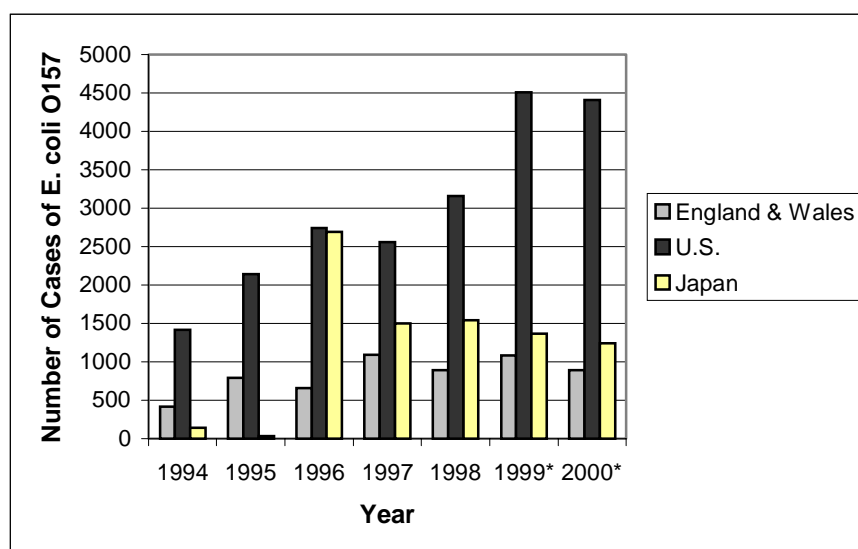
*E. coli* O157:H7 was designated by the Council of State and Territorial Epidemiologists as a nationally notifiable disease in the U.S. beginning in 1994. During 1994-2000, the number of reported cases of *E.*

---

<sup>10</sup> a combination of renal failure, low platelet counts and hemolytic anemia

*E. coli* O157:H7 in the U.S. increased more than two-fold from 1,420 (0.8/100,000 people) in 1994 to 4410 (approximately 1.6/100,000 people) in 2000 (CDC 1999, CDC 2001) (Figure 1). Cases in the U.S. are reported by passive surveillance through the National Notifiable Diseases Surveillance System (NNDSS).<sup>11</sup> This is a passive surveillance system in which health care providers report notifiable disease cases to local or state health departments. Other national or regional surveillance systems include (1) Enter-net<sup>12</sup> which includes a catchment area of 15 European Union (EU) member states as well as Switzerland and Norway, (2) The Communicable Disease Network Australia – National Notifiable Surveillance System,<sup>13</sup> (3) Japan’s Statistics on Communicable Diseases in Japan (former Ministry of Health and Welfare) and the National Epidemiological Surveillance of Infectious Diseases (NESID) which are reported in Infectious Agents Surveillance Reports<sup>14</sup> and (4) the EU’s Zoonoses Reporting System.<sup>15</sup> In addition to these surveillance systems, the EU, Japan and U.S. have each developed a pulsed-field gel electrophoresis (PFGE) database to assist in epidemiological investigations of disease from this and other bacteria. The increase in reported cases of *E. coli* O157:H7 over time is probably due to a combination of factors, including (1) improvement in the effectiveness of the surveillance system over time, (2) increased awareness of *E. coli* O157:H7 infection among health care providers and the public leading to improved detection and reporting, (3) enhanced ability to detect disease through better diagnostic tests, and (4) a true increase in the incidence of disease. Figure 1 illustrates the rising incidence of *E. coli* O157:H7 infection in three different regions of the world. For more information on the global impact of EHEC see the WHO Consultation report (WHO 1997).

**Figure 1.** Number of reported cases of *E. coli* O157:H7 infection, U.S. (1994-2000),<sup>a</sup> England and Wales (1994-2000),<sup>b</sup> and Japan (1996-2000);<sup>c</sup> \*provisional data are presented from 1999 and 2000 for the US.



<sup>11</sup> <http://www.cste.org/nndss/reportingrequirements.htm>

<sup>12</sup> [http://www.phls.org.uk/topics\\_az/ecoli/data.htm](http://www.phls.org.uk/topics_az/ecoli/data.htm)

<sup>13</sup> <http://www.health.gov.au/pubhlth/cdi/nndss/year054.htm>

<sup>14</sup> <http://idsc.nih.gov/jp/iasr/22/256/tpc256.html>; <http://idsc.nih.gov/jp/index.html>; Note that in the former system, known as the Ministry of Health and Welfare, communicable diseases in Japan were reported in “Statistics on Communicable Diseases in Japan” and, during a transitional period, in the “Annual Report on National Epidemiological Surveillance of Infectious Diseases”. The new system, known as the National Epidemiological Surveillance of Infectious Diseases (NESID), publishes “Infectious Agents Surveillance Reports” monthly describing pathogen isolates and related information and “Infectious Disease Surveillance Data” annually describing notified human cases (IDSD is currently only available by CD-ROM format).

<sup>15</sup> EU Council Directive 92/117/EEC; [http://europa.eu.int/eur-lex/en/com/pdf/2001/en\\_501PC0452\\_01.pdf](http://europa.eu.int/eur-lex/en/com/pdf/2001/en_501PC0452_01.pdf)

- a) CDC, NNDSS; Cases include suspect and confirmed human isolations.
- b) PHLS Laboratory of Enteric Pathogens; Cases include only isolates, obtained from stool samples, that are submitted to PHLS from laboratories in England and Wales. They are confirmed, serotyped, phage typed and VT typed at PHLS.
- c) Ministry of Health and Welfare, National Epidemiological Surveillance of Infectious Diseases; Cases are restricted to those with stool samples that have been culture confirmed and include all O157 serotypes.

In 1996, the Emerging Infection Program Foodborne Diseases Active Surveillance Network (FoodNet) began a program of active surveillance of clinical laboratories for specific foodborne diseases, including *E. coli* O157:H7. Five states in the U.S. participated initially (Minnesota, Oregon, selected counties of California, Connecticut and Georgia) (CDC 2001a). As of 2000, the areas under active surveillance included 8 states representing 29.5 million persons (10.8% of the 1999 U.S. population). The number of cases of *E. coli* O157:H7 infection reported annually to FoodNet ranged from 388 in 1996 to 631 in 2000 (Bender et al. 2000, CDC 2000b, CDC 2001a). Because the population under surveillance has increased, it is more appropriate to compare the number of reported cases per 100,000 persons in a population.

Data on the prevalence of symptomatic *E. coli* O157:H7 infection prior to the inception of FoodNet are scarce and include studies which estimate between two and 10 cases for every 100,000 persons (Ostroff et al. 1989, MacDonald et al. 1988). The higher estimates obtained in some of these studies is likely a consequence of the active method for data collection and may provide a more accurate estimate of the incidence of *E. coli* O157:H7 infection thereby suggesting that statewide passive surveillance programs are hindered by underreporting.

HUS is the most common cause of acute renal failure in young children, yet it also has long-term complications. In Belgium 97% of HUS cases in 2000 were associated with *E. coli* O157:H7 infection (Pierard et al. 1997). Siegler (1994) found that HUS causes chronic renal sequelae, usually mild, in 51% of survivors (48% of all cases) however, Elliot et al. (2001) has observed significantly lower renal failure statistics in Australia. Neurologic complications occur in about 25% of HUS patients (Mead et al. 1998). Generally neurologic symptoms are mild, but serious complications, such as seizure, stroke and coma, can occur (Su and Brandt 1995). Similar to treatment for *E. coli* O157:H7 infection, only symptomatic treatment for neurologic complications is available, making this manifestation of HUS especially dangerous and an important cause of death in HUS patients. Other complications of HUS include pancreatitis, diabetes mellitus and pleural and pericardial effusions (Mead et al. 1998). In a nationwide study of HUS patients, 46 (55%) of 83 patients required either peritoneal dialysis or hemodialysis during the acute phase of their illness (Banatvala et al. 2001). Siegler et al. (1994) found that severe kidney or neurological impairments (end stage renal disease or stroke) occurred in 9 (5.7%) of 157 HUS cases over a 20-year period in Utah. A number of studies have suggested the mortality rate associated with HUS is between 3 and 7% (Martin 1990; Tarr 1987; Rowe 1991; Mahon 1997; Banatvala 2001; Siegler 1994).

The percent of *E. coli* O157:H7 infections which progress to HUS varies between sporadic cases and those associated with outbreaks. Between 3% to 7% of sporadic, and 20% or more of outbreak associated cases of *E. coli* O157:H7 infection will progress to HUS (Mead 1998). The proportion of patients who develop HUS following *E. coli* O157:H7 infection is influenced by a variety of factors including age, bloody diarrhea, fever, elevated leukocyte count, and toxin type (Griffin et al. 1995). Wong (2000) found that 10 (14.1%) of 71 children with *E. coli* O157:H7 infection developed HUS. Similarly, the severity of HUS illness may differ between sporadic cases and those associated with outbreaks; outbreaks often resulted in a shorter diarrheal prodrome, a higher rate of bloody diarrhea and severe hemorrhagic colitis (Elliot et al. 2001).

Between 1997 and 1999 at FoodNet sites located within the U.S., the overall incidence of HUS among children younger than 15 years of age was 0.7 per 100,000; this is similar to the frequency observed in other nations such as Austria (0.65 per 100,000) and Australia (0.64 per 100,000) (Elliot et al. 2001). For children younger than 5, the incidence was 1.4 and 1.35 per 100,000 in the U.S. and Australia respectively (CDC 2000b). In a nationwide study of 83 patients with HUS in the U.S., 46 (55.4%) were younger than 5 years old and an additional 27 (32.5%) were 5 to 17 years old (Banatvala et al. 2001). In 1999, 35.3% of reported HUS cases in the U.S. occurred in 1- to 10-year-olds, 17.6% of cases occurred in 10- to 20-year-olds, and 14.1% of cases occurred in persons older than 60 (CDC 2000b). Similarly, analyses of HUS incidence in Belgium found the majority (35/46) of HUS cases were in children (Pierard et al. 1997). The overall findings of this study demonstrated that the burden of illness from HUS is comparable between Australia, North America and Europe. A national study of postdiarrheal HUS in the U.S. estimated that  $\leq 20\%$  of HUS cases were due to non-O157 EHEC; however, the authors qualified that estimate, commenting that it was difficult to determine the proportion of EHEC-associated HUS due to non-O157 EHEC (Banatvala et al. 2001). In Australia, between July 1994 and June 1998, only 8% of the EHEC associated cases of HUS were the result of *E. coli* O157 infection (Elliot et al. 2001). This suggests that while illness from HUS is similar on different continents, the predominant EHEC serotype responsible may vary.

Occasionally, patients with *E. coli* O157:H7 are diagnosed as having thrombotic thrombocytopenic purpura (TTP), a condition similar to HUS but more likely to occur in adults and with more prominent neurological findings and less renal involvement. In the study by Banatvala et al. (2001), of 73 children and 10 adults that met the case definition of HUS, 8 (11.0%) children and 8 (80.0%) adults also met the case definition for TTP. None of the 8 children, but 2 (25.0%) adults died. There are many causes of TTP other than the association with *E. coli* O157:H7 and prior to the 1980s, gastrointestinal infections had not been strongly implicated in the pathogenesis of TTP (CDC 1986). When associated with *E. coli* O157:H7 infection, TTP is probably the same disorder as HUS (Mead et al. 1998).

- Between 70 and 95% of symptomatic patients develop bloody diarrhea.
- More severe manifestations of *E. coli* O157:H7 infection include hemorrhagic colitis (grossly bloody diarrhea), HUS and occasionally TTP.
- The incidence of *E. coli* O157:H7 infection varies by age group, with the highest incidence of reported cases occurring in children.
- In addition to children, elderly are known to be susceptible to *E. coli* O157:H7 infection.
- A number of national and regional disease surveillance systems exist that record *E. coli* O157 infection.
- While the incidence of hemolytic uremic syndrome is similar on different continents, the predominant EHEC serotype responsible may vary.

### **3. Food production, processing, distribution and consumption**

#### 1. The farm to table continuum

As was previously mentioned, EHEC strains including *E. coli* O157:H7, have been isolated from the faeces or gastrointestinal tract of cattle, sheep, horses, pigs, turkeys, dogs, and a variety of wild animal species (Kudva 1996; Rice and Hancock 1995; Hancock et al. 1998b; Heuvelink et al. 1999); consequently, foods associated either directly or indirectly with animals (meat or dairy products) or foods subject to contamination by animal waste products (for instance as manure fertilizers) are frequently implicated as vehicles of transmission for human illness. Epidemiological studies have found that cattle manure is the primary source of most human *E. coli* O157:H7 infections. In fact, *E. coli* O157:H7 has been described as

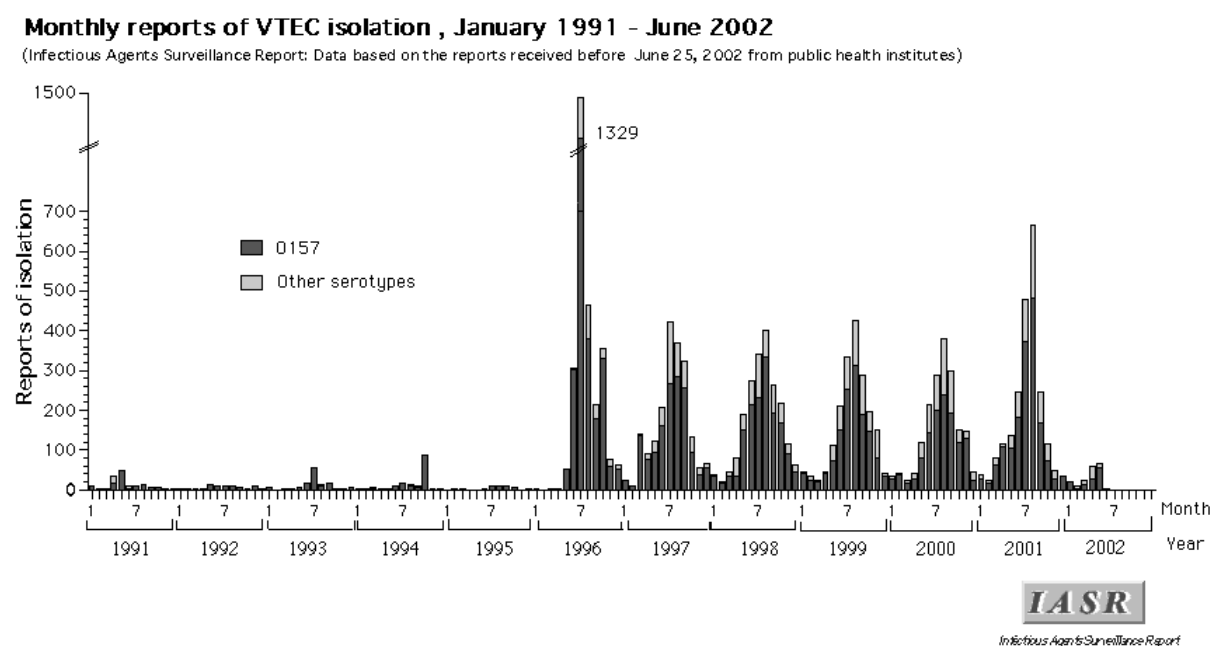
“ubiquitous” in dairy and beef cattle and is present at least occasionally on most farms or feedlots (Hancock et al. 1998a; Hancock et al. 2001). Factors contributing to the presence of *E. coli* O157:H7 include:

- the pathogen’s ability to survive for at least 4 months in water trough sediments (Hancock et al. 1998a); and
- the pathogen’s presence in some animal feeds (Hancock et al. 2001).

Many of the risk factors that are thought to influence *E. coli* O157:H7 prevalence and their levels in cattle apply to whole herds rather than to individual cattle. Therefore, mitigation strategies typically target herd-level risk factors for *E. coli* O157:H7 control. The roles that water, including treated or untreated sewage used to irrigate animal feed, and feed itself play in colonizing herds may prove to be critical to on farm management strategies and should be considered (Anderson et al. 2001, Hancock et al. 2001, LeJeune et al. 2001). The type of herd does appear to have an affect on the prevalence of *E. coli*. Herds of feedlot cattle such as steers and heifers are more likely to have colonized animals than breeding herds, which are comprised of cows and bulls. Additionally, when a feedlot herd is positive it is likely to have significantly more colonized animals than breeding cattle herds (USDA, 2001). Limited evidence suggests that dairy and cow-calf herds are similar with respect to *E. coli* O157:H7 (Lagreid et al. 1999; Sargeant et al. 2000).

An increased seasonal incidence of *E. coli* O157:H7 infections in cattle and human populations has been demonstrated in the warmer months of the year (Hancock et al. 1997a, 1997b; Griffin 1998; Van Donkersgoed et al. 1997, Heuvelink et al. 1998); this is evidenced in data from Japan (Figure 2). It is therefore not surprising that the incidence of HUS is also more common in the summer months ([www.hcsc.gc.ca/hpb/lcdc/bmb/epiic95/95\\_ii\\_e.html](http://www.hcsc.gc.ca/hpb/lcdc/bmb/epiic95/95_ii_e.html); Mead and Griffin 1998; CDC 1999a; CDC 2000b, Van de Kar 1996; Van Duynhoven accepted for publication). Of the sporadic cases of human *E. coli* O157 infection reported by FoodNet sites, 70% occurred during June through September for the years 1996 to 1998 (Bender et al. 2000; CDC 1999a). Similarly, *E. coli* O157 outbreaks also occur more frequently in the summer (CDC 1999a; CDC 2000c; CDC 2001c).

Figure 2: From IASR Infectious Agents Surveillance Report at <http://idsc.nih.gov/jp/prompt/graph/vt9.gif>



*E. coli* O157:H7 has also been isolated from other water sources such as ponds, streams and wells (Wang and Doyle 1998 Hancock et al. 1998a Kudva et al. 1998; Sargeant 2000). Tainted water used to

clean food or as an ingredient in a food commodity (e.g. juice) can also contribute to the contamination of foodstuffs.

### Characteristics of the commodities

Leafy green vegetables grown low to the ground are a recognized cause of *E. coli* O157:H7 outbreaks. Contamination of vegetables may occur in several ways, however, the use of manure or water contaminated with fecal matter is one possible route (Solomon et al. 2002; Wachtel et al. 2002; Solomon et al. 2002b; Wachtel et al. 2002b). When contaminated, the fact that fresh produce is minimally processed and consumed raw increases the likelihood of *E. coli* O157:H7 infection. The source of *E. coli* O157:H7 contaminated manure can be, and frequently is, of bovine origin. Mitigation strategies that control *E. coli* O157:H7 on farm will likely impact the level of contamination of produce.

Meat becomes contaminated with *E. coli* O157:H7 when beef carcasses come into contact with contaminated hides and faeces during the slaughter process (Elder et al. 2000). A determination of the quantitative association between the incoming status of cattle and the outgoing status of harvested meat is critical in an exposure assessment. This quantitative correlation between pre-harvest and post-harvest contamination is best predicted using fecal *E. coli* O157:H7 prevalence data (Elder et al. 2000).

A number of factors have a significant influence on the survival and growth of *E. coli* O157:H7 in food, including temperature, pH, salt, and water activity (Meng and Doyle 1998). Studies on the thermal sensitivity of *E. coli* O157:H7 in ground beef have revealed that the pathogen has no unusual resistance to heat and that heating ground beef sufficiently to kill typical strains of *Salmonella* will also kill *E. coli* O157:H7. The optimal temperature for growth of *E. coli* O157:H7 is approximately 37°C (98.6°F), and the organism will not grow at temperatures below 8°C to 10°C (46°F to 50°F) or above 44°C to 45°C (Doyle and Schoeni 1984; Buchanan and Doyle 1997). *E. coli* O157:H7 survives freezing, with some decline in the concentration of *E. coli* O157:H7 (Ansary et al. 1999).

*E. coli* O157:H7 has been reported to be more acid resistant than other *E. coli*. Acid resistance enhances the survival of *E. coli* O157:H7 in mildly acidic foods and may explain its ability to survive passage through the stomach and cause infection at low doses. The ability to be acid resistant varies among strains and is influenced by growth phase and other environmental factors. Once induced, acid resistance is maintained for long periods of time during cold storage (Meng and Doyle 1998). Stationary-phase *E. coli* O157:H7 are more resistant than growing cells to acid (Meng and Doyle 1998). The presence of other environmental stresses, such as temperature or water activity stress will raise the minimum pH for growth (Buchanan and Doyle 1997). *E. coli* O157:H7 survives in such foods as dry salami, apple cider, and mayonnaise, which were previously considered too acidic to support the survival of foodborne pathogens. Published literature contains conflicting reports about the efficacy of acid spray washing of beef carcasses. A study by Brachett et al. (1994) found that warm and hot acid sprays did not significantly reduce the concentration of *E. coli* O157:H7 on beef carcasses; however, two recent studies have found organic acids to be effective in reducing the presence of *E. coli* O157:H7 on beef carcasses (Berry and Cutter 2000; Castillo et al. 2001). These apparently contradictory results may reflect differences in acid resistance among strains of *E. coli* O157:H7 (Berry and Cutter 2000).

*E. coli* O157:H7 can survive for extended periods under conditions of reduced water activity while refrigerated; however, the organism does not tolerate high salt conditions (Buchanan and Doyle 1997).

### Retail and Consumer Behavior

The food preparation industry and consumer choices and behaviors have a large influence on the probability of contracting an *E. coli* O157:H7 infection. Specifically, inadequately cooked beef (in particular ground or minced products) is correlated to infection as previously discussed. Cooking these products to an internal temperature of  $\geq 68$  °C has been shown to be an adequate precaution; however, consumers continue to choose undercooked beef products.<sup>16</sup> It has also to be borne in mind that in

---

<sup>16</sup> <http://www.fsis.usda.gov/oa/news/1998/colorpr.htm>

certain countries consumption of products made from raw minced beef (such as “tartare” steak, beef “americaine”) is common. Similarly, awareness of and precautions against cross-contamination between raw meat products and either cooked foods or raw vegetables would limit the likelihood of infection.<sup>17</sup> Consumer behavior that can limit illness from vegetables contaminated at the farm is likely limited to thoroughly cleaning produce, in particular commodities to be consumed raw. In the case of sprouted seeds and some fruits and vegetables (Solomon et al. 2002), which have been shown to integrate the bacteria, washing may not be a sufficient intervention.

2.

### 3. Interventions

A Canadian risk assessment was published that predicted the reduction in illnesses to be expected from various mitigation scenarios for ground beef (Table 4) (Cassin et al. 1998). These mitigations included achievement of maximum temperature control during storage, preslaughter screening of cattle faeces and cooking at appropriate temperatures. Based on the Cassin approach, an Australian risk assessment also modeled risk mitigation scenarios including hot water decontamination of carcasses, irradiation of frozen boxed beef, preslaughter reduction in faecal concentrations, retail temperature control and consumer education about good cooking practices (Lammerding et al. 1999; P Vanderlinde, personal communication).

- Meat becomes contaminated with *E. coli* O157:H7 when beef carcasses come into contact with contaminated hides and faeces during the slaughter process.
- An increased seasonal incidence of *E. coli* O157:H7 infections in cattle and human populations has been demonstrated in the warmer months of the year.
- *E. coli* O157:H7 has no unusual resistance to heat and heating ground beef sufficiently to kill typical strains of *Salmonella* will also kill *E. coli* O157:H7.
- Consumer choices and actions such as undercooking beef have a large influence on the probability of contracting an *E. coli* O157:H7 infection.

Due to the impact on-farm cattle colonization can have on other commodities such as leafy green vegetables, interventions that control *E. coli* O157:H7 in live animals are also of great interest. These include the impact of employing probiotic (Zhao 1998) bacterial flora in cattle, the impact of various feeding regimens (Lung et al. 2001), the result of different composting protocols (Cray et al. 1998) and the impact of various irrigation methods.

## **4. Risk Assessment Needs and Questions for the Risk Assessors**

### **Is a microbiological risk assessment appropriate to fulfill the desired CCFH output(s)?**

As both leafy green vegetables grown low to the ground contaminated by bovine faeces and ground beef are commonly associated with these illnesses they should each be considered, either together or separately, in a risk assessment. It would be useful for CCFH to request a risk assessment be conducted to specifically assess the impact of any proposed guidance. These same documents also suggest useful questions to be directed to the risk assessors to evaluate methods for minimizing (1) the colonization of cattle with *E. coli* O157:H7, (2) the contamination of

---

<sup>17</sup> [http://www.fsis.usda.gov/oa/pubs/keep\\_apart.htm](http://www.fsis.usda.gov/oa/pubs/keep_apart.htm)

ground beef with faeces and (3) the contamination of produce with bovine faeces. It is possible that the benefits achievable through downstream interventions are less important than those obtained via interventions at the farm due to the multiple infection pathways (and commodities) that can be minimized through effective manure management.

Any risk assessment undertaken by FAO/WHO should provide an estimate of the risk of illness and death from *E. coli* O157:H7 in countries where sufficient data are available. Illness must be explicitly defined by CCFH as a specified endpoint. Also, an assessment should be provided of the potential benefit (i.e. number of cases of illness and death prevented) for intervention strategies including those currently in effect or under consideration in member states [listed in brackets] such as:

**Measure effect of controlling *E. coli* O157:H7 at the farm level with respect to subsequent agricultural use of manure.**

- The impact of employing probiotic bacterial flora in cattle.
- The impact of various feeding regimens.
- Outcomes from different composting protocols
- The impact of various irrigation methods (Solomon et al. 2002).
- The impact of hygienic measures at the farm (such as cleaning and disinfection of premises between lots)
- Calf management at weaning

**Measures to minimize fecal shedding of *E. coli* O157:H7 in animals presented for slaughter [Belgium, Sweden, others]**

- Enforcing or tightening controls on animal feed quality.
- The impact of employing probiotic bacterial flora in cattle.
- The impact of various feeding regimens and fasting before transport
- Calf management at weaning
- Monitoring of human illness with mandatory testing of farms linked to an outbreak of human illness resulting from *E. coli* O157:H7. Restrictions on positive farms include controls over the sale of live animals, and restriction on the sale of animals for slaughter (slaughter hygiene and swab tests at slaughter).

**Measures to minimize contamination of carcasses at slaughter [Australia, Denmark, Germany, Portugal, Sweden, U.K., U.S.].**

- Scoring the level of fecal contamination on the hides of incoming animals with remedial action (e.g. logistic slaughter) when scores exceed a predetermined level (clean cattle policy).
- Rodding and clipping the esophagus and bagging and tying the rectum.
- Hygienic dressing and evisceration.
- Random testing of *E. coli* O157:H7 on beef carcasses in the slaughterhouse. A positive test results in testing on the farm of origin. Positive on-farm tests resulting in increased farm sanitation measures.
- Random testing of carcasses for (generic) *E. coli* contamination and measures to improve sanitation when predetermined levels are exceeded.
- Random testing of carcasses for enterobacteriaceae.
- Visual inspections of carcasses.
- The use of HACCP in slaughter and processing.

- Different decontamination procedures.

### **MEASURES TO MINIMIZE CONSUMER EXPOSURE TO CONTAMINATED PRODUCTS**

[Australia, U.K., U.S.].

- Random testing for *E. coli* O157:H7 in trim and ground meat.
- Random testing for (generic) *E. coli* or enterobacteriaceae in ground beef.
- Destruction or diversion of positive product to cooked product.
- Irradiation or pasteurization.
- Specified cooling guidance.
- Enhanced hygienic practice during cutting, boning and other steps between slaughter and retail.
- Restaurant cooking requirements.
- HACCP in the food production and service sector.

#### **Retail Codes / Consumer education.**

- Cooking ground beef to a specified internal temperature as indicated by the use of a meat thermometer [Canada, Germany, U.S.]

#### **Measures to minimize contamination of food products in international trade**

[special consideration of CCFH]

- A certification program to insure that exported products meet the acceptable level of protection of the importing country.

A WHO Consultation discussed the global impact of EHEC and the controls and prevention strategies employed by a number of nations (WHO 1997). European national guidance documents and mitigations are discussed in the European Commission Health and Consumer Protection Directorate-General's report SANCO/4320/2001.<sup>18</sup> Canada has produced (1) interim guidelines for the control of verotoxigenic (Shiga toxin producing) *Escherichia coli* including *E. coli* O157:H7 in ready-to-eat fermented sausages containing beef or a beef product as an ingredient,<sup>19</sup> (2) policies concerning raw products of animal origin,<sup>20</sup> and (3) policies for ground beef containing *E. coli* O157:H7.<sup>21</sup> Australia has developed microbiological standards and Advisory Guidelines for the Hygienic Production of Uncooked Fermented Comminuted Meat Products based on generic *E. coli* so as to include all STEC serotypes.<sup>22</sup>

These issues will need to be prioritized by the Committee and explicit questions for the risk assessors subsequently formulated.

## **5. Available Information**

A number of countries have evaluated the risk associated with foodborne *E. coli* O157. These assessments are listed in Table 5. Specifically, Canada has analyzed the risk associated with *E. coli* O157:H7 infection

<sup>18</sup> [http://europa.eu.int/comm/food/fs/inspections/special\\_reports/sr\\_rep\\_4320-2001\\_en.pdf](http://europa.eu.int/comm/food/fs/inspections/special_reports/sr_rep_4320-2001_en.pdf)

<sup>19</sup> [http://www.hc-sc.gc.ca/food-aliment/english/organization/microbial\\_hazards/guideline\\_for\\_fermented\\_sausages.html](http://www.hc-sc.gc.ca/food-aliment/english/organization/microbial_hazards/guideline_for_fermented_sausages.html)

<sup>20</sup> [http://www.hc-sc.gc.ca/food-aliment/english/organization/microbial\\_hazards/pdf/rfao\\_sept21.pdf](http://www.hc-sc.gc.ca/food-aliment/english/organization/microbial_hazards/pdf/rfao_sept21.pdf)

<sup>21</sup> [http://www.hc-sc.gc.ca/food-aliment/english/organization/microbial\\_hazards/guidelines\\_for\\_raw\\_ground\\_beef.html](http://www.hc-sc.gc.ca/food-aliment/english/organization/microbial_hazards/guidelines_for_raw_ground_beef.html)

<sup>22</sup> <http://www.anzfa.gov.au/foodstandards/oldfoodstandardscodecontents/partmeatcannedmeatandproductsthereof/c1meatgamemeatandrel686.cfm>

from consuming ground beef hamburgers (Cassin et al. 1998), sprouts (personal communication with Health Canada, January 2002) and juices (personal communication with Health Canada, January 2002) since each of these commodities have contributed to outbreaks or sporadic incidents of illness in that nation. An academic group in Canada has also assessed risk factors associated with on-farm *E. coli* O157 prevalence in cattle (Jordan et al. 1999a, 1999b). The Netherlands chose to investigate steak tartare as the vehicle of transmission in their risk assessment because: (1) a steak tartare is thicker than a hamburger, therefore the risk of insufficient heating of the center is larger, (2) people tend to accept a partially raw tartare but do not accept a partially raw hamburger, (3) tartare is sometimes consumed raw (e.g., a tartare roll in snack bars). Steak tartare was chosen after also considering consumption levels. The U.S. has developed a farm-to-table risk assessment for *E. coli* O157:H7 in ground beef in addition to a comparative risk assessment for *E. coli* O157:H7 in tenderized and non-tenderized steaks. Due to the smaller contribution O157 serotypes make to human illness in Australia, that state has developed one risk assessment for O157:STEC and another for all STEC in ground beef production and in fermented meat.

- FAO/WHO may find many of these risk assessments useful in the development of a risk assessment for Codex. Further evaluation of each is necessary.

Table 5: Risk assessments for *E. coli* O157:H7

Nation	Topic	Reference
Australia	Ground Beef <sup>1</sup>	Lammerding 1999
Australia	STEC in Ground Beef <sup>1</sup>	Lammerding 1999
Canada	Ground Beef Hamburgers	Cassin 1998
Canada	Seeds/Beans and Sprouted Seeds/Beans <sup>2,3</sup>	Personal Communication with Health Canada
Canada	Unpasteurized Fruit Juice/Cider <sup>4</sup>	Personal Communication with Health Canada
Canada	Pre-harvest Husbandry Practices	Jordan 1999a,b
Ireland	Beef/Beef Products	<a href="http://www.science.ulst.ac.uk/food/E_coli_Risk_Assess.htm">www.science.ulst.ac.uk/food/E_coli_Risk_Assess.htm</a>
Netherlands	Raw Fermented Products	<a href="http://www.research.teagasc.ie/vteceurope/S+Gprog/hoornstrag.html">www.research.teagasc.ie/vteceurope/S+Gprog/hoornstrag.html</a>
Netherlands	Steak Tartare	RIVM report 257851003/2001
U.S.	Ground Beef <sup>5</sup>	<a href="http://www.fsis.usda.gov/OPPDE/rdad/FRPubs/00-023NReport.pdf">www.fsis.usda.gov/OPPDE/rdad/FRPubs/00-023NReport.pdf</a>
U.S.	Tenderized vs Non-tenderized Beef Steaks	Personal Communication with USDA

<sup>1</sup>ANZFA Food Standard Code 1.6.1 sets Microbiological limits for total generic *E. coli* in a variety of foods. <http://www.anzfa.gov.au/foodstandardscodecontents/standard16/index.cfm>. Additionally, dairy products must be produced from pasteurized milk.

<sup>2</sup>Subsequent policy and management documents include “Consultation/Policy Document: A Dialogue on Developing a Risk Management Strategy for Sprouted Seeds and Beans”.

<sup>3</sup>Subsequent policy and management documents include “Code of Practice for the Hygienic Production of Sprouted Seeds”

<sup>4</sup>Subsequent policy and management documents include “Code of Practice for the Production and Distribution of Unpasteurized Apple and Other Fruit Juice/Cider in Canada”

<sup>5</sup>The U.S. has a microbiological criteria equivalent to a zero-tolerance for *E. coli* O157:H7 in raw ground beef

## **6. Data Gaps**

Several data gaps have been identified based on currently available risk assessments for *E. coli* O157:H7, including:

- Information describing the human health impact of *E. coli* O157 in less developed nations.
- Commodities likely to be associated with *E. coli* O157 foodborne illness in less developed nations.
- Data regarding the exposure dose of *E. coli* O157:H7 likely to cause illness in susceptible populations.
- Frequency and severity of illness among children ages 0 to 5 from *E. coli* O157:H7 that become ill from consuming ground beef d in raw produce.

- Industry and consumer practices for various methods of cooking ground beef (e.g., grill vs. fry).
- Survival of *E. coli* O157:H7 on produce as a result of contamination by water or organic fertilizer.
- Information describing the critical contamination levels of meat products that may lead to cross contamination of uncooked produce.
- Information on the percentage of fresh leafy vegetables contaminated by bovine faeces containing *E. coli* O157:H7 as opposed to feral animal faeces, or human faeces
- Quantify the heat resistance (e.g., D and z values) of the individual strains of *E. coli* O157:H7 used in the Sporing (1999) study. Individual strains should be identified and characterized.
- Information on the maximum density of *E. coli* O157:H7 organisms in ground beef servings as a result of matrix effects, competitive microflora in ground beef, and environmental conditions (e.g., pH, water activity).
- Predictive microbiological data on the increase and decrease in the number of *E. coli* O157:H7 organisms in ground beef under various storage and preparation conditions along with frequencies of occurrence of these storage and preparation conditions.
- Data on cross-contamination of *E. coli* O157:H7 between carcasses during carcass splitting.
- Time-temperature data (quantitative) for chillers in slaughter establishments.
- Marketing data on the proportion of beef ground at slaughter versus at retail.
- Data on retail and consumer storage, cooking, and consumption (frequency and serving size) patterns by type of ground beef meal (e.g., grilled hamburger in July and baked meat loaf in October).
- Descriptive epidemiologic information about sporadic cases of *E. coli* O157:H7 illness, including the month of disease onset, age, sex, hospitalizations, summary of clinical manifestations including severe disease manifestations, and food vehicles involved (if known).
- Additional case-control studies of sporadic *E. coli* O157:H7 cases to calculate etiologic fraction attributable to ground beef.

## References

- Ackers ML, Mahon BE, Leahy E, Goode B, Damrow T, Hayes PS, et al. An outbreak of *Escherichia coli* O157:H7 infections associated with leaf lettuce consumption. *J Infect Dis* 1998; 177:1588-1593.
- Adak, G.; Smith, H.; Willshaw, G.; Cheasty, T.; Wall, P.; Rowe, B. "A review of outbreaks of Verocytotoxin producing *Escherichia coli* O157 in England and Wales, 1992-1996" presented at 3<sup>rd</sup> International Symposium and Workshop on Shiga Toxin (Verocytotoxin) – Producing *Escherichia coli* (STEC) Infections June 22<sup>nd</sup>-26<sup>th</sup> 1997.
- Ahiiid S.; Cowdeii, J. "An outbreak of *E.coli* O157 in central Scotland" presented at 3<sup>rd</sup> International Symposium and Workshop on Shiga Toxin (Verocytotoxin) – Producing *Escherichia coli* (STEC) Infections June 22<sup>nd</sup>-26<sup>th</sup> 1997.
- Allerberger F.; Dierich, M. P. "Enterohemorrhagic *Escherichia coli* in Austria" presented at 3<sup>rd</sup> International Symposium and Workshop on Shiga Toxin (Verocytotoxin) – Producing *Escherichia coli* (STEC) Infections June 22<sup>nd</sup>-26<sup>th</sup> 1997.
- Altekruse S. F., Cohen M. L., Swerdlow, D. L. (1997) Emerging Foodborne Diseases. *Emerging Infect. Dis.* 3(3).
- Ammon A; Petersen LR; Karch, HA (1999) A large outbreak of hemolytic uremic syndrome caused by an unusual sorbitol-fermenting strain of *Escherichia coli* O157:H-. *J. Infect. Dis.* 179: 1274-1277.
- Anderson RJ, House JK, Smith BP, Kinde H, Walker RL, VandeSteege BJ, Breitmeyer RE (2001) Epidemiologic and biological characteristics of salmonellosis in three dairy herds. *JAVMA* 219(3):310-321.
- Ansary SE, Darling KA, Kaspar CW (1999) Survival of *Escherichia coli* O157:H7 in ground-beef patties during storage at 2, -2, 15 and then -2 degrees C, and -20 degrees C. *J Food Prot* 62(11):1243-7.
- Asakura H, Makino S, Shirahata T, Tsukamoto T, Kurazono H, Ikeda T, et al. (1998) Detection and genetical characterization of Shiga toxin-producing *Escherichia coli* from wild deer. *Microbiol Immunol.* 42:815-822.
- Banatvala N, Griffin PM, Greene KD, et al. (2001). The United States national prospective hemolytic uremic syndrome study: microbiologic, serologic, clinical, and epidemiologic findings. *J Infect Dis* 183:1063-1070.
- Bell BP, Goldoft M, Griffin PM, et al. (1994). A multistate outbreak of *Escherichia coli* O157:H7-associated bloody diarrhea and hemolytic uremic syndrome from hamburgers: the Washington experience. *JAMA* 272:1349-1353.
- Bender J, Mead P, Voetsch D, et al. (1998). Hemolytic uremic syndrome (HUS) cases identified in the 1996 FoodNet *Escherichia coli* O157:H7 surveillance. 1<sup>st</sup> International Conference on Emerging Infectious Diseases. Atlanta, GA, March.
- Bender J, Smith K, McNeese A, et al. (2000). Surveillance for *E. coli* O157:H7 infections in FoodNet sites, 1996-1998: No decline in incidence and marked regional variation. 2<sup>nd</sup> International Conference on Emerging Infectious Diseases, Atlanta, Georgia, July.
- Besser RE, Lett SM, Weber JT, Doyle MP, Barrett TJ, Wells JG, Griffin PM (1993). An outbreak of diarrhea and hemolytic uremic syndrome from *Escherichia coli* O157:H7 in fresh-pressed apple cider. *JAMA* 267(17):2217-2220.
- Bokete TM, O'Callahan CM, Clausen CR, et al. (1993). Shiga-like toxin producing *Escherichia coli* in Seattle children: a prospective study. *Gastroenterology* 105:1724-1731.
- Boyce TG, Swerdlow DL, Griffin PM (1995a). *Escherichia coli* O157:H7 and the hemolytic-uremic syndrome. *N Engl J Med* 333:364-8.

- Boyce TG, Pemberton AG, Wells JG, *et al.* (1995b). Screening for *Escherichia coli* O157:H7—a nationwide survey of clinical laboratories. *J Clin Microbiol* 33: 3275-3277.
- Breuer T, Benkel DH, Shapiro RL, Hall WN, Winnett MM, Linn MJ, Neimann J, Barrett TJ, Dietrich S, Downes FP, Toney DM, Pearson JL, Rolka H, Slutsker L, Griffin PM; Investigation Team. (2001) A multistate outbreak of *Escherichia coli* O157:H7 infections linked to alfalfa sprouts grown from contaminated seeds. *Emerg Infect Dis* 7:977-82.
- Buchanan RL, Doyle MP (1997). Foodborne disease significance of *Escherichia coli* O157:H7 and other enterohemorrhagic *E. coli*. *Food Technology* 51(10): 69-76.
- Buzby JC, Roberts T, Lin CTJ, *et al.* (1996). Bacterial foodborne disease: medical costs & productivity losses. U.S. Department of Agriculture Economic Research Service. Agricultural Economic Report No. 741.
- Carter AO, Borczyk AA, Carlson JA, Harvey B, Hockin JC, Karmali MA, *et al.* (1987) A severe outbreak of *Escherichia coli* O157:H7--associated hemorrhagic colitis in a nursing home. *N Engl J Med* 317:1496-1500.
- Cassin M. H.; Lammerding, A. M.; Todd, E. C. D.; Ross, W.; McColl, R. S. (1998) Quantitative risk assessment for *Escherichia coli* O157:H7 in ground beef hamburgers. *Int. J. Food Microb.* 21-44.
- Centers for Disease Control and Prevention (CDC) (1986). Thrombotic thrombocytopenic purpura associated with *Escherichia coli* O157: H7 – Washington. *MMWR* 35(34): 549-551.
- CDC (1995a). Outbreak of acute gastroenteritis attributable to *Escherichia coli* Serotype O104:H21 - Helena, Montana, 1994. *MMWR* 44(27):501-503.
- CDC (1995b) Community outbreak of hemolytic uremic syndrome attributable to *Escherichia coli* O111:NM - South Australia, 1995. *MMWR Morbidity and Mortality weekly Report* 44, 550-558.
- CDC (1996). Outbreak of *Escherichia coli* O157:H7 infections associated with drinking unpasteurized commercial apple juice--British Columbia, California, Colorado, and Washington, October 1996. *MMWR* 45(44):975.
- CDC (1997). Outbreaks of *Escherichia coli* O157:H7 infection and cryptosporidiosis associated with drinking unpasteurized apple cider--Connecticut and New York, October 1996. *MMWR* 46(1):4-8.
- CDC (1999). Summary of notifiable diseases, United States, 1998. *MMWR* 47(53):1-94.
- CDC (1999b). Surveillance for outbreaks of *Escherichia coli* O157:H7 infection. Summary of 1998 data. Report from the National Center for Infectious Diseases, Division of Bacterial and Mycotic Diseases to CSTE. March 8, 1999.
- CDC (2000). *Escherichia coli* O111:H8 outbreak among teenage campers - Texas, 1999. *MMWR* 49(15):321-324.
- CDC (2000a). Surveillance for foodborne-disease outbreaks - United States, 1993-1997. *MMWR* 49(SS-1):1-62.
- CDC (2000b). FoodNet surveillance report for 1999 (final report). November.
- CDC (2000c). Surveillance for waterborne-disease outbreaks - United States, 1997-1998. *MMWR* 49(SS-4):1-35.
- CDC (2001). Provisional cases of selected notifiable diseases, United States, weeks ending December 30, 2000 and January 1, 2000. *MMWR* 49(51 and 52):1168.
- CDC (2001a). Preliminary FoodNet data on the incidence of foodborne illnesses - selected sites, United States, 2000. *MMWR* 50(13):241-246.

CDC (2001b). Surveillance for outbreaks of *Escherichia coli* O157:H7 infection. Summary of 1999 data. Report from the National Center for Infectious Diseases, Division of Bacterial and Mycotic Diseases to CSTE. June 15, 2000.

Clarke SC, Haigh RD, Freestone PP, Williams PH (2002) Enteropathogenic *Escherichia coli* infection: history and clinical aspects. *Br. J. Biomed. Sci* 59(2):123-127.

Colwell R. (1997). Presentation: Protecting the public against food-borne pathogens: *E. coli*. September 25-26, 1997. Washington, D.C.

Cody SH, Glynn MK, Farrar JA, Cairns KL, Griffin PM, Kobayashi J, Fyfe M, Hoffman R, King AS, Lewis JH, Swaminathan B, Bryant RG, Vugia DJ (1999). An outbreak *Escherichia coli* O157:H7 infection from unpasteurized commercial apple juice. *Ann Intern Med* 130(3):202-9.

Cosio FG, Alamir A, Yim S, *et al.* (1998). Patient survival after renal transplantation: The impact of dialysis pre-transplant. *Kidney Int* 53(3):767-772.

Cray WC Jr., Casey TA, Bosworth BT, Rasmussen MA (1998). Effect of dietary stress on fecal shedding of *Escherichia coli* O157:H7 in calves. *Appl. Environ. Microbiol.* 64(5):1975-1979.

Cudjoe, K. (2001) Personal communication with United States Department of Agriculture/FSIS staff scientists.

CX/FH 03/6 "Proposed Draft Process by which the Codex Committee On Food Hygiene Could Undertake Its Work In Microbiological Risk Assessment/Risk Management"

Del Rosario BA, Beuchat LR. Survival and growth of enterohemorrhagic *Escherichia coli* O157:H7 in cantaloupe and watermelon. *J Food Prot* 1995; 58:105-107.

Doyle MP, Schoeni JL (1984). Survival and growth characteristics of *Escherichia coli* associated with hemorrhagic colitis. *Appl Environ Microbiol* 48(4):855-856.

Doyle MP, Zhao T, Meng J, *et al.* (1997) *Escherichia coli* O157:H7. In: Doyle M.P., Beuchat L.R., Montville T.J., eds., *Food Microbiology: Fundamentals and Frontiers*. American Society of Microbiology Press: Washington, D.C. pp. 171-191

Dytoc MT, Ismaili A, Philpott DJ, *et al.* (1994). Distinct binding properties of eaeA-negative verocytotoxin-producing *Escherichia coli* of serotype O113:H21. *Infect Immun.* 62(8): 3494-3505.

Elder RO, Keen JE, Siragusa GR, *et al.* (2000). Correlation of enterohemorrhagic *Escherichia coli* O157:H7 prevalence in feces, hides, and carcasses of beef cattle during processing. *Proc Natl Acad Sci* 97(7):2999-3003.

Elliott EJ, Robins-Browne RM, O'Loughlin EV, Bennett-Wood V, Bourke J, Henning P, Hogg GG, Knight J, Powell H, Redmond D (2001) Nationwide study of Haemolytic uraemic syndrome: clinical, microbiological, and epidemiological features *Arch Dis. Child.* 85(2):125-31.

FDA (Food and Drug Administration) (1997). Guide to minimize microbial food safety hazards for fresh fruits and vegetables. November 25, 1997 (Draft).

Feng P, Weagant SD, Monday SR (2001) Genetic analysis for virulence factors in *Escherichia coli* O104:H21 that was implicated in an outbreak of hemorrhagic colitis. 39(1):24.

Fey PD, Wickert RS, Rupp ME, *et al.* (2000) Prevalence of non-O157 shiga toxin-producing *Escherichia coli* in diarrheal stool samples from Nebraska. *Emerg Infect Dis* 6(5):530-533.

Food Safety and Inspection Service (FSIS) (1998a). Detection, isolation and identification of *Escherichia coli* O157:H7 and O157:NM (non-motile) from meat and poultry products. FSIS Microbiology Laboratory Guidebook, 3<sup>rd</sup> ed., (Chapter 5).

Food Safety and Inspection Service (FSIS) (1999). Revision 1 (9/3/1999) to Chapter 5, Microbiology Laboratory Guidebook, 3<sup>rd</sup> edition, 1998. (Available at: <http://www.fsis.usda.gov/OPHS/microlab/mlgchpt5.htm>)

- Goldwater P.N. and Bettelheim, K.A. (1995) The role of enterohaemorrhagic *Escherichia coli* serotypes other than O157:H7 as causes of disease in Australia. *Communicable Diseases Intelligence* 19, 2-4.
- Griffin PM (1995). *Escherichia coli* O157:H7 and other enterohemorrhagic *Escherichia coli*. In: Blaser MJ, Smith PD, Ravdin JI, Greenberg HB, Guerrant RL, eds. *Infections of the gastrointestinal tract*. New York: Raven Press, Ltd., pp 739-761.
- Gutierrez E. (1997) Japan prepares as O157 strikes again. *Lancet* 349: 1156.
- Gyles CL (1992) *Escherichia coli* cytotoxins and enterotoxins. *Can J Microbiol* 38:34-746.
- Hancock DD, Besser TE, Rice DG, *et al.* (1998) Multiple sources of *Escherichia coli* O157 in feedlots and dairy farms in the Northwestern USA. *Prev Vet Med* 35:11-19.
- Hancock DD, Besser TE, Rice DH (1998a). Ecology of *Escherichia coli* O157:H7 in cattle and impact of management practices. In: *E. coli* O157:H7 and other shiga toxin-producing *E. coli* strains. Kaper JB, O'Brien AD, eds. *Am Soc for Microbiol, Washington DC*, pp 85-91.
- Hancock D, Besser T, Lejeune J, *et al.* (2001) The control of VTEC in the animal reservoir. *Internatl J Food Microbiol* 66:71-8.
- Heuvelink AE, Zwartkruis-Nahuis JT, van den Biggelaar FL, *et al.* (1999) Isolation and characterization of verocytotoxin-producing *Escherichia coli* O157 from slaughter pigs and poultry. *Int J Food Microbiol* 52(1-2):67-75.
- Heuvelink AE, van den Biggelaar FL, Zwartkruis Nahuis J, Herbes RG, Huyben R, Nagelkerke N, *et al.* (1998) Occurrence of verocytotoxin-producing *Escherichia coli* O157 on Dutch dairy farms. *J Clin Microbiol* 36:3480-3487.
- Hilborn ED, Mermin JH, Mshar PA, Hadler JL, Voetsch A, Wojtkunski C, Swartz M, Mshar R, Lambert-Fair MA, Farrar JA, Glynn MK, Slutsker L. (1999) A multistate outbreak of *Escherichia coli* O157:H7 infections associated with consumption of mesclun lettuce. *Arch Intern Med* 159:1758-64.
- IASR (Infectious Agents Surveillance Reports) "Verotoxin-producing *Escherichia coli*, January 1991-November 1995, Japan" Vol.17 No.1 (No.191).
- Jackson LA, Keene WE, McAnulty JM, Alexander ER, Diermayer M, Davis MA, Hedberg K, Boase J, Barrett TJ, Samadpour M, Fleming DW (2000) Where's the Beef? The Role of Cross-Contamination in 4 chain Restaurant-Associated Outbreaks of *Escherichia coli* O157:H7 in the Pacific Northwest. *Arch. Intern. Med.* 160:2380-2385.
- Jordan D., McEwen, S.A., Lammerding, A.M., McNab, W.B. and Wilson, J.B., 1999a. A simulation model for studying the role of pre-slaughter effects on the exposure of beef carcasses to human microbial hazards. *Prev. Vet. Med.*, 41: 37-54.
- Jordan D., McEwen, S.A., Lammerding, A.M. McNab, B., and Wilson, J.B., 1999b. Pre-slaughter control of *Escherichia coli* O157 in beef cattle: a simulation study. *Prev. Vet. Med.*, 41: 55-74.
- Kai A.; Obata, H.; Hatakeyama, K.; Igarashi, H.; Itoh, T.; Kudoh, Y. "A 13- year study of enterohaemorrhagic *Escherichia coli* (EHEC) infections in Tokyo (1984-1996)" presented at 3<sup>rd</sup> International Symposium and Workshop on Shiga Toxin (Verocytotoxin) – Producing *Escherichia coli* (STEC) Infections June 22<sup>nd</sup>-26<sup>th</sup> 1997.
- Karmali MA (1989) Infection by verocytotoxin-producing *Escherichia coli*. *Clin Microbiol Rev* 2(1): 15-38.
- Kassenborg H, Hedberg C, Hoekstra M, *et al.* (2001) Farm visits and undercooked hamburgers as major risk factors for sporadic *Escherichia coli* O157:H7 infections - data from a case-control study in five FoodNet sites. Manuscript in preparation.
- Keene WE, Sazie E, Kok J, Rice DH, Hancock DD, Balan VK, *et al.* (1997) An outbreak of *Escherichia coli* O157:H7 infections traced to jerky made from deer meat. *JAMA* 277:1229-1231.

- Kinney J, Gross T, Porter C, et al. (1988) Hemolytic-uremic syndrome: a population-based study in Washington, DC and Baltimore, Maryland. *Am J Public Health* 78:64-65.
- Kudva IT, Hatfield PG, Hovde CJ (1996). *Escherichia coli* O157:H7 in microbial flora of sheep. *J Clin Microbiol* 34: 431-433.
- Kudva IT, Blanch K, Hovde CJ (1998) Analysis of *Escherichia coli* O157:H7 survival in ovine or bovine manure and manure slurry. *Appl Environ Microbiol* 64(9):3166-3174.
- Lammerding A, Fazil, A, Paoli, G, Vanderlinde, P., Desmarchelier, P. 1999 Risk assessment case studies for selected meat products, Report No MSRC.002, Meat and Livestock Australia.
- LeJeune J, Hancock DD and Besser TE (1997) *Escherichia coli* O157 in cattle water troughs: A possible on-farm reservoir. Abstracts of the Fifth Annual Food Safety Farm to Table Conference, Northwest Food Safety Consortium, Moscow, ID.
- LeJeune, Besser, TE, Hancock DD (2001) Cattle Water Troughs as Reservoirs of *Escherichia coli* O157. *Appl. Environ. Microbiol.* 67:3053-3057.
- Le Saux N, Spika JS, Friesen B, et al. (1993) Ground beef consumption in noncommercial settings is a risk factor for sporadic *Escherichia coli* O157:H7 infection in Canada. *J Infect Dis* 167:500-2 (letter).
- Lingwood CA, Mylvaganam M, Arab S, et al. (1998) Shiga toxin (verotoxin) binding to its receptor glycolipid. In: J.B. Kaper and A.D. O'Brien, eds. *Escherichia coli* O157:H7 and other Shiga toxin-producing *E. coli* strains, Washington, DC: ASM Press, pp 129-139.
- Lung AJ, Lin CM, Kim JM, Marshall MR, Nordstedt R, Thompson NP, Wei CI (2001) Destruction of *Escherichia coli* O157:H7 and *Salmonella enteritidis* in cow manure composting. *J. Food Prot.* 64(9):1309-1314.
- MacDonald KW, O'Leary MJ, Cohen ML, et al. (1988) *Escherichia coli* O157:H7, an emerging gastrointestinal pathogen: results of a one-year, prospective, population-based study. *JAMA* 259(24):3567-3570.
- Mahon BE, Griffin PM, Mead PS, et al. (1997) Hemolytic uremic syndrome surveillance to monitor trends in infection with *Escherichia coli* O157:H7 and other shiga toxin-producing *E. coli*. *Emerg Infect Dis* (letter) 3(3):409-411.
- March SB and Ratnam S (1986) Sorbitol-MacConkey medium for detection of *Escherichia coli* O157:H7 associated with hemorrhagic colitis. *J Clin Microbiol* 23(5):869-872.
- Martin D, MacDonald K, White K, et al. (1990) The epidemiology and clinical aspects of the hemolytic uremic syndrome in Minnesota. *New Engl J Med* 323:1161-1167.
- Mead PS et al. (1997) Risk factors for sporadic infection with *Escherichia coli* O157:H7. *Arch Intern Med* 157:204-208.
- Mead P and Griffin P (1998) *Escherichia coli* O157:H7. *Lancet* 352:1207-1212.
- Mead PS, Slutsker L, Dietz V, et al. (1999) Food-related illness and death in the United States. *Emerg Infect Dis* 5(5):607-25.
- Meng J, Doyle MP (1998) Microbiology of shiga toxin-producing *Escherichia coli* in foods. In: J.B. Kaper and A.D. O'Brien, eds. *Escherichia coli* O157:H7 and other Shiga toxin-producing *E. coli* strains, Washington, DC: ASM Press, pp 92-108.
- Mermin J, Hilborn E, Voetsch A, Swartz M, Lambert Fair M, Farrar J, et al. A multistate outbreak of *Escherichia coli* O157:H7 infections associated with eating mesclun mix lettuce, abstract V74/I. In: Anonymous 3rd International symposium and workshop on Shiga toxin (verotoxin)-producing *Escherichia coli* infections. Melville, N.Y., United States: Lois Joy Galler foundation for Hemolytic-Uremic Syndrome Inc. 1997:9.

- Mermin JH and Griffin PM. (1999) Invited commentary: Public health in crisis: Outbreaks of *E. coli* O157:H7 infections in Japan. *Am J Epidemiol* 150:797-803.
- Michino H, Araki K, Minami S, Nakayama T, Ejima Y, Hiroe K, et al. Recent outbreaks of infections caused by *Escherichia coli* O157:H7 in Japan. In: Kaper JB, O'Brien AD, editors. *Escherichia coli* O157:H7 and other Shiga toxin-producing *E. coli* strains. Washington, D.C., United States: ASM Press, 1998:73-81.
- Michino H, et al. (1999) Massive outbreak of *E. coli* O157:H7 infections in school children in Sakai City, Japan, associated with consumption of white radish sprouts. *Am J Epidemiol* 150:787-796.
- MMWR (1997a) Outbreaks of *Escherichia coli* O157:H7 infection associated with eating alfalfa sprouts--Michigan and Virginia, June-July 1997. 46:741-744.
- MMWR (1997b) Outbreaks of *Escherichia coli* O157:H7 infection and cryptosporidiosis associated with drinking unpasteurized apple cider--Connecticut and New York, October 1996. 46:4-8.
- Morgan GM, Newman C, Palmer SR, Allen JB, Shepherd W, Rampling AM, et al. First recognized community outbreak of haemorrhagic colitis due to verotoxin-producing *Escherichia coli* O157:H7 in the UK. *Epidemiol Infect* 1988; 101:83-91.
- Nataro JP, Kaper JB (1998) Diarrheagenic *Escherichia coli*. *Clin Microbiol Rev* 11:142-201.
- Neill MA, Agosti J and Rosen H. (1985) Hemorrhagic colitis with *Escherichia coli* O157:H7 preceding adult hemolytic uremic syndrome. *Arch Intern Med* 145(12):2215-2217.
- OCD (Oregon Health Division, Center for Disease Prevention & Epidemiology) (1998). Sporadic cases of hemorrhagic escherichiosis. *CD Summary* 47(6) (March 17, 1998).
- Okrend AJG, Rose BE, Matner R (1990) An improved screening method for the detection and isolation of *Escherichia coli* O157:H7 from meat, incorporating the 3M Petrifilm™ test kit - HEC - for hemorrhagic *Escherichia coli* O157:H7. *J Food Protect* 53(11):936-40.
- Ostroff SM, Kobayashi JM and Lewis JH (1989) Infections with *Escherichia coli* O157:H7 in Washington State: The first year of statewide disease surveillance. *JAMA* 262(3):355:359.
- Paton A.W., Ratcliff, R.M., Doyle, R.M., Seymour-Murray, J., Davos, D., Lanser, J.A. and Paton, J.C. (1996) Molecular microbiological investigation of an outbreak of hemolytic-uremic syndrome caused by dry fermented sausage contaminated with Shiga-like toxin-producing *Escherichia coli*. *Journal of clinical Microbiology* 34:1622-1627.
- Paton JC, Paton AW (1998) Pathogenesis and diagnosis of shiga toxin-producing *Escherichia coli* infection. *Clin Microbiol Rev* 11:450-479.
- Paton AW, Woodrow MC, Doyle RM, et al (1999). Molecular characterization of a shiga toxigenic *Escherichia coli* O113:H21 strain lacking eae responsible for a cluster of cases of hemolytic-uremic syndrome. *J Clin Microbiol* 37(10):3357-61.
- Pierard D.; Cornu, G.; Proesmans, W.; Dediste, A.; Jacobs, F.; Van de Walle, F.; Mertens, A.; Ramet, H.; Lauwers, S.; BVIKM/SBIMC HUS Study Group "Incidence of HUS and role of O157 and non-o157 VTEC infection in HUS in Belgium" presented at 3<sup>rd</sup> International Symposium and Workshop on Shiga Toxin (Verocytotoxin) – Producing *Escherichia coli* (STEC) Infections June 22<sup>nd</sup>-26<sup>th</sup> 1997.
- Proctor ME, Davis JP (2000) *Escherichia coli* O157:H7 infections in Wisconsin, 1992-1999. *Wisconsin Med J* 99(5):32-7.
- Reilly W. J.; Carter, F. T. "Surveillance of *E. coli* O157 in Scotland" presented at 3<sup>rd</sup> International Symposium and Workshop on Shiga Toxin (Verocytotoxin) – Producing *Escherichia coli* (STEC) Infections June 22<sup>nd</sup>-26<sup>th</sup> 1997.

- Rice DH, Hancock DD (1995) Non-bovine sources of *Escherichia coli* O157:H7/Epidemiology. Conference of Research Workers in Animal Diseases: November 13-14, 1995. Chicago, IL. Abstract #66.
- Riley LW, Remis RS, Helgerson SD, et al. (1983) Hemorrhagic colitis associated with a rare *Escherichia coli* serotype. *New Engl J Med* 308:681-685.
- Roberts T, Buzby J, Lin J, et al. (1998) Economic aspects of *E. coli* O157:H7: disease outcome trees, risk, uncertainty, and the social cost of disease estimates. In: Greenwood B and DeCock K, eds. *New and resurgent infections: Prediction, detection and management of tomorrow's epidemics*. London School of Hygiene & Tropical Medicine. Seventh Annual Public Health Forum. John Wiley & Sons, Ltd: West Sussex, England, pp 155-172.
- Robins-Browne R. M., Elliott, E. and Desmarchelier, P. (1998) Shiga toxin-producing *Escherichia coli* in Australia. In *Escherichia coli O157:H7 and Other Shiga Toxin-Producing E. coli strains* ed. Kaper, J.B. and O'Brien, A.D. pp. 66-72. Washington, D. C.: ASM Press.
- Rowe PC, Orrbine E, Well GA, et al. (1991). Epidemiology of hemolytic-uremic syndrome in Canadian children from 1986 to 1988. *J Pediatr* 119(2):218-224.
- Ryan CA, Tauxe RV, Hosesk GW, et al. (1986). *Escherichia coli* O157:H7 diarrhea in a nursing home: clinical epidemiologic and pathological findings. *J Infect Dis* 154: 631-638.
- Saari, M.; Keskimake, M.; Puohiniemi, R.; Siitonen, A. "Shiga toxin – producing *Escherichia coli* (STEC) in gastrointestinal infections in Finland" presented at 3<sup>rd</sup> International Symposium and Workshop on Shiga Toxin (Verocytotoxin) – Producing *Escherichia coli* (STEC) Infections June 22<sup>nd</sup>-26<sup>th</sup> 1997.
- Schlundt J (2001) Emerging food-borne pathogens. *Biomed. Environ. Sci.* 14(1-2):44-52.
- Siegler RL, Pavia AT, Christofferson RD, et al. (1994) A 20-year population-based study of postdiarrheal hemolytic uremic syndrome in Utah. *Pediatrics* 94: 35:40.
- Slutsker L, Ries AA, Maloney K, et al. (1998) A nationwide case-control study of *Escherichia coli* O157:H7 infection in the United States. *J Infect Dis* 177:962-966.
- Solomon EB, Potenski CJ, Matthews KR (2002) Effect of irrigation method on transmission to and persistence of *Escherichia coli* O157:H7 on lettuce. *J. Food Prot.* 65(4):673-676.
- Solomon EB, Yaron S, Matthews KR (2002b) Transmission of *Escherichia coli* O157:H7 from Contaminated Manure and Irrigation Water to Lettuce Plant Tissue and Its Subsequent Internalization App. *Environ. Microbiol.* 68(1):397-400.
- Steele BT, Murphy N, Arbus GS, Rance CP. An outbreak of hemolytic uremic syndrome associated with ingestion of fresh apple juice. *J Pediatr* 1982; 101:963-965.
- Su C, Brandt LJ (1995) *Escherichia coli* O157:H7 infection in humans. *Ann Intern Med* 123:698-714.
- Swerdlow DL, Griffin PM (1997) Duration of faecal shedding of *Escherichia coli* O157:H7 among children in day-care centres. *Lancet* 15;349(9054):745-746.
- Tarr PI (1995) *Escherichia coli* O157:H7: clinical, diagnostic, and epidemiologic aspects of human infection. *Clin Infect Dis* 20(1):1-8.
- Tarr PI, Hickman RO (1987) Hemolytic uremic syndrome epidemiology: A population-based study in King County, Washington, 1971 to 1980. *Pediatrics* 80:41-45.
- Tauxe R. V. (1997) Emerging Foodborne Diseases: An Evolving Public Health Challenge *Emerging Infect. Dis.* 3(4).
- Thompson JS, Hodge DS, Borczyk AA (1990). Rapid biochemical test to identify verotoxin-positive strains of *Escherichia coli* serotype O157. *J Clin Microbiol* 28:2165-2168.

- Tilden J Jr., Young W, McNamara A-M, Custer C, Boesel B, Lambert-Fair MA, Majkowski J, Vugia D, Werner SB, Hollingsworth J, Morris JG. (1996) A new route of transmission for *Escherichia coli*: Infection from dry fermented salami. *American Journal of Public Health* 86(8):1142-1145.
- USDA; Food Safety Inspection Service (2001) "Draft Risk Assessment of the Public Health Impact of *Escherichia coli* O157:H7 in Ground Beef" available at: [www.fsis.usda.gov/OPPDE/rdad/FRPubs/00-023NReport.pdf](http://www.fsis.usda.gov/OPPDE/rdad/FRPubs/00-023NReport.pdf)
- Van de Kar NC, Roelofs HG, Muytjens HL, Tolboom JJ, Roth B, Proesmans W, *et al.* (1996) Verocytotoxin-producing *Escherichia coli* infection in hemolytic uremic syndrome in part of western Europe. *Eur J Pediatr* 155:592-595.
- Van Duynhoven YTHP, de Jager CM, Heuvelink AE, *et al.* Enhanced laboratory-based surveillance of Shiga toxin-producing *Escherichia coli* O157 in the Netherlands. *Eur J Clin Microbiol Infect Dis* (accepted for publication).
- Wachtel MR, Whitehand LC, Mandrell RE (2002) Prevalence of *Escherichia coli* Associated with a Cabbage Crop Inadvertently Irrigated with Partially Treated Sewage Wastewater 65(3):471-475.
- Wachtel MR, Whitehand LC, Mandrell RE (2002b) Association of *Escherichia coli* O157:H7 with Preharvest Leaf Lettuce upon Exposure to Contaminated Irrigation Water *J. Food Prot.* 65(1):18-25.
- Wang G, Doyle MP (1998) Survival of enterohemorrhagic *Escherichia coli* O157:H7 in water. *J Food Protect* 61(6):662-667.
- Wells JG, Davis BR, Wachsmuth IK, *et al.* (1983) Laboratory investigation of hemorrhagic colitis outbreaks associated with a rare *Escherichia coli* serotype. *J Clin Micro* 18(3):512-20.
- Whiting RC, Buchanan R (1997) Predictive microbiology: Implications for assessing the risk of food-borne disease. Abstract: International Life Science Institute Risk Science Institute Seminar, Washington, D.C. May 8, 1997.
- Whittam TS (1998) Evolution of *Escherichia coli* O157:H7 and other shiga toxin-producing *E. coli* strains. In: J.B. Kaper and A.D. O'Brien, eds. *Escherichia coli* O157:H7 and other Shiga toxin-producing *E. coli* strains, Washington, DC: ASM Press, pp 195-209.
- Wong CS, Jelacic S, Habeeb RL, Watkins SL, Tarr PI (2000) The risk of the hemolytic-uremic syndrome after antibiotic treatment of *Escherichia coli* O157:H7 infections. *N. Engl. J. Med.* 342(26):1930-1936.
- WHO Consultation "Prevention and Control of Enterohaemorrhagic *Escherichia coli* (EHEC) Infections" WHO/FSF/FOS/97.6
- WHO (1998) "Zoonotic non-O157 Shiga toxin-producing *Escherichia coli* (STEC). Report of a WHO Scientific working group meeting. Berlin, Germany 23-26 June.
- Zhao, T, Doyle MP, Harmon BG, Brown CA, Mueller PO, Parks AH (1998) Reduction of carriage of enterohemorrhagic *Escherichia coli* O157:H7 in cattle by inoculation with probiotic bacteria. *J. Clin. Microbiol.* 36(3):641-647.