

Chapter 1 Introduction and Scope

Overview

On August 18, 1998, the U.S. Department of Agriculture (USDA) Food Safety and Inspection Service (FSIS) announced plans to conduct a farm-to-table risk assessment for *Escherichia coli* O157:H7 in beef with a focus on ground beef. At that time, the agency also announced a public meeting to be held October 28, 1998 to solicit from the public scientific information and data that would be relevant to conducting the risk assessment (*Fed. Reg.*, Vol. 63, p. 44232).

The overall goals of the assessment are as follows: 1. To quantitatively model, with attendant uncertainty, human illnesses caused by *E. coli* O157:H7 in beef in the United States and to compare these results with national estimates of illnesses derived from observed epidemiological data. 2. To identify the occurrence and levels of the pathogen at points along the farm-to-table continuum and the contribution of these points to the number of human illnesses. 3. To quantify the effects of various mitigation strategies in reducing the number of human illnesses. 4. To identify future research needs. 5. To document risk assessment methods and evidence for future assessments. 6. To document changes in the risk assessment model and its inputs. 7. To effectively communicate the results to all interested parties--government, consumer groups, industry, the scientific community and the general public.

Since 1994, FSIS has treated various raw chopped or ground beef products that bear or contain *E. coli* O157:H7 as adulterated under the Federal Meat Inspection Act unless they are further processed in a manner that destroys this pathogen. In the same year, the agency won a court challenge of the policy. On October 17, 1994, FSIS initiated a microbiological testing program for *E. coli* O157:H7 in raw ground beef in meat plants and retail stores. The testing program operated under FSIS Notice 50-94, issued December 23, 1994, until the agency issued FSIS Directive 10,010.1 on February 1, 1998. The initial testing program was established and designed to test approximately 5000 samples, 50% from federally inspected plants and 50% from retail stores. Based on the low concentrations of *E. coli* O157:H7 recovered from samples of frozen ground beef patties identified in a 1993 outbreak,¹ FSIS increased the sample size from 25 grams to 325 grams in FY 1998 to enhance efficiency and the likelihood of detecting pathogens in raw ground beef sold to consumers. If a positive sample is confirmed, inspectors will condemn the sampled lot, unless it is fully cooked (in accordance with 9 CFR 318.23) or processed in an equivalent manner (FSIS Directive 10,010.1). FSIS Directive 8080.1 Rev. 2 (11-3-92) outlines the basic procedures for recall of an inspected meat and poultry product. The ongoing risk assessment will assist FSIS to review and refine its integrated risk reduction strategy for *E. coli* O157:H7 in beef.

The intent in releasing this draft report is to solicit comment and input regarding the scope of the risk assessment, the analytical framework to be used in conducting the risk

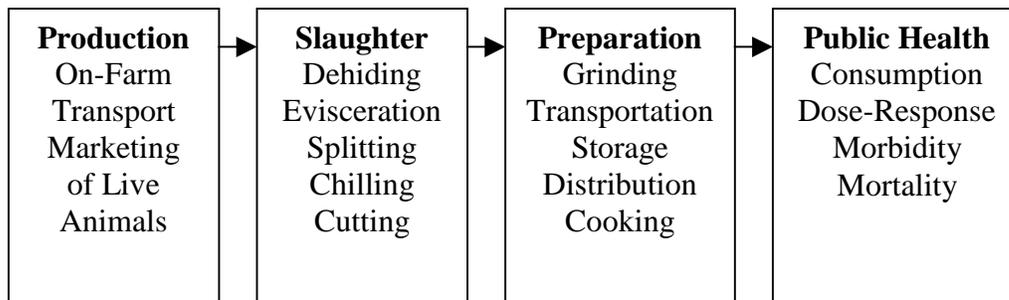
¹ The most probable number (MPN) of *E. coli* O157:H7 recovered from six samples from the 1993 outbreak ranged from 30-1500 organisms per 100 grams (Johnson *et al.* 1995, Marks *et al.* 1998).

1 assessment, the scientific evidence acquired by the risk assessment team to date from the
 2 available literature, and the existing data gaps identified by the risk assessment team. The
 3 draft report is not intended to present results, preliminary or otherwise. Comments and
 4 additional data sources identified at the technical public meeting on October 28, 1998 or
 5 submitted in response to the August 18, 1998 Federal Register Notice will be evaluated
 6 for inclusion in further risk assessment model development and refinement. (See *Fed.*
 7 *Reg.*, Vol. 63, p. 44232 for details regarding submissions to the docket.)

8
 9 In this draft report, the model for *E. coli* O157:H7 in beef contains four modules: 1) on-
 10 farm production (Ch. 2); 2) slaughter (Ch.3); 3) preparation (Ch.4); 4) public health (Ch.
 11 5) (Figure 1). (The slaughter and grinding processes may be combined as one of four
 12 modules in the final model and assessment report.) An appendix presents evidence and
 13 alternative models for predicting growth and decline of *E. coli* O157:H7 in beef that may
 14 be relevant to both the slaughter and preparation modules. The pathway models presented
 15 in chapters 2-5 are tentative, as is the application of models derived primarily from
 16 studies of broth culture media to predict microbial dynamics in various beef matrices.
 17 The risk assessment team is interested in receiving comments on its analytical framework
 18 and alternative, biologically plausible and analytically feasible modeling approaches.

19
 20 The output of the entire risk assessment model is the effect of beef products (with a focus
 21 on products containing ground beef) contaminated with *E. coli* O157:H7 on public health,
 22 in terms of the annual number of cases of illnesses and death. A baseline risk assessment
 23 will serve to identify risk factors and high-risk pathways under current practices of
 24 production, slaughter, processing, transportation, storage, preparation, and consumption.
 25 As such, the baseline, or “as is” scenario, is intended to reflect to the extent practicable,
 26 the full range of current practices and behaviors in the farm-to-fork continuum. The
 27 baseline risk assessment is intended to inform a distinct FSIS policy analysis that will
 28 identify feasible risk mitigation options for further comparative analysis. A subsequent
 29 comparative risk assessment will provide decision-makers with information concerning
 30 the efficacy of the alternative mitigation strategies and a tool to evaluate these strategies
 31 to decrease the number of human illnesses resulting from *E. coli* O157:H7 in beef. The
 32 agency’s goal is to complete the analysis during 1999.

33
 34 Figure 1. Farm-to-table risk assessment model for *E. coli* O157:H7 in beef.



1 Scope

2
3 “Ground Beef” v. “Whole Cuts” of Beef

4
5 The announcement of the risk assessment (*Fed. Reg.*, Vol. 63, p. 44232) stated that,
6 contingent on an analysis of available epidemiological data concerning outbreaks of *E.*
7 *coli* O157:H7 associated with “whole cuts” of beef (e.g. roast beef), the scope of the risk
8 assessment will be confined to “ground beef” products. During 1982-97, there have been
9 154 reported outbreaks of *E. coli* O157:H7 (Tables 5-9). In 25% of the outbreaks (39),
10 ground beef was identified as a likely vehicle of infection, whereas whole cuts of beef
11 (i.e., roast beef) have been identified as a likely vehicle in approximately 2% (3) of
12 outbreaks (Table 1). Roast beef was a likely vehicle in approximately 7% of the
13 outbreaks where beef was identified as a likely vehicle. (Contamination of other vehicles
14 by beef accounts for an uncertain proportion of the outbreaks for which the likely vehicle
15 is either unknown or identified. In addition, the likely vehicle may be misclassified in an
16 uncertain proportion of outbreaks.)
17

Likely Vehicle	No. Outbreaks	No. Ill	%Outbreaks	% Ill
Meat				
Coney dog sauce	1	10	0.65	0.28
Salami	1	19	0.65	0.53
Ground beef & Other (ranch dressing and person-to-person)	2	88	1.30	2.45
Roast beef	3	157	1.95	4.38
Venison	3	17	1.95	0.47
Ground beef	37	1179	24.03	32.87
Subtotal	47	1470	30.52	40.98
Unknown				
	40	561	25.97	15.64
Vegetables/Produce/Cider				
	17	548	11.04	15.28
Person to person				
	29	519	18.83	14.47
Water (Ice, Drinking Water, Swimming)				
	15	393	9.74	10.96
Miscellaneous (Mayonnaise, Retail foods, School lunch)				
	3	78	1.95	2.17
Milk Products (Raw milk, Ice cream bars)				
	3	18	1.95	0.50
Total	154	3587		

Compiled from data in Tables 5-9.

18
19 In discussing appropriate cooking temperatures for intact beef steaks, the National
20 Advisory Committee on Microbiological Criteria for Foods and its Meat and Poultry
21 Subcommittee stated that:

22
23 Due to a low probability of pathogenic bacteria being present in or
24 migrating from the external surface to the interior of beef muscle, cuts of
25 intact muscle (steaks) should be safe if the external surfaces are exposed to
26 temperatures sufficient to effect a cooked color change. In addition, the
27 cut (exposed) surfaces must receive additional heat to effect a complete
28 sear across the cut surfaces...
29

1 The Committee's definition of "Intact Beef Steak" limited the applicability of this
2 conclusion to "[a] cut of whole muscle(s) that has not been injected, mechanically
3 tenderized or reconstructed." (See the Subcommittee minutes, adopted by the Committee
4 on November 20, 1997.)

5
6 In light of the relative lack of outbreaks attributed to whole cut beef products and the
7 Committee's conclusions, the proposed scope of the FSIS risk assessment for *E. coli*
8 O157:H7 in beef is restricted to comminuted beef products, with a primary emphasis on
9 ground product. It may be feasible for the scope of the assessment to include comminuted
10 beef processed by means other than grinding (e.g., mechanical separation and partial
11 defatting) by considering the potential for such beef to introduce *E. coli* O157:H7 or
12 change the concentration of *E. coli* O157:H7 in ground product in the formulation of
13 hamburger or meat patties (as defined in 9 CFR 319.15). At the broadest level of
14 aggregation, the proposed scope of the assessment includes 3 classes of product: 1)
15 products consisting of 100% ground beef, 2) products containing 50% or more ground
16 beef, 3) products containing less than 50% ground beef.

17
18 Beyond the proposed scope of the present risk assessment are cuts of beef in which
19 pathogens may be introduced below the surface by means of injection, mechanical
20 tenderizing, or reconstruction (e.g., beef that has been scored to incorporate a marinade or
21 that has been cubed and mechanically tenderized and restructured beef products such as
22 gyros) or by a comminution process such as chopping, flaking, or mincing (e.g., fresh
23 veal sausage and fabricated beef steak), unless such a comminuted product is combined
24 with ground beef in the formulation of a food product. These beef products that are
25 beyond the proposed scope of the present assessment may, however, be incorporated
26 within the scope of future iterations of the risk assessment model to address all beef
27 products other than cuts of intact muscle.

28
29 As suggested by the public announcement of the FSIS risk assessment for *E. coli*
30 O157:H7 in beef (*Fed. Reg.*, Vol. 63, p. 44232), the scope of the analysis does not extend
31 beyond beef as a vehicle of infection. In order to keep the scope of the assessment
32 manageable, to make the analysis tractable, and in light of time and resource constraints,
33 there are currently no plans to quantitatively model cross-contamination from or to non-
34 beef food products, water, fomites, etc. Similarly, there are currently no plans to
35 quantitatively model secondary infections resulting from person-to-person contact. The
36 risk assessment may, however, treat these issues qualitatively or semi-quantitatively since
37 contamination of non-meat vehicles by beef products may be a significant factor. The
38 delimited scope of the analysis will be taken into account in comparing the results
39 predicted by the baseline risk assessment model with estimates of illnesses derived from
40 observed epidemiological data. The epidemiological evidence acquired to date by the risk
41 assessment team for the purpose of ground-truthing the baseline model results is
42 introduced in this chapter and summarized in chapter 5, the public health module.

1 Risk Assessment Endpoints

2

3 The risk assessment model will yield intermediate and final outputs in the form of
 4 distributions that characterize the variability and uncertainty in national annual estimates
 5 of a variety of risk assessment endpoints, including but not limited to those listed in Table
 6 2.

7

8 Table 2. *E. coli* O157:H7 Risk assessment endpoints

Module	Endpoints
Production	Herd and within herd prevalence rates
	Prevalence of GI, hide, and GI/hide positive live animals at the knock box
	Concentration of <i>E. coli</i> O157:H7 in the GI tract and on the hide of positive live animals at the knock box
Slaughter	Prevalence of contaminated carcasses
	Concentration of <i>E. coli</i> O157:H7 on contaminated carcasses
	Prevalence of contaminated lots of trim
	Concentration of <i>E. coli</i> O157:H7 in lots of contaminated trim
Grinding and Preparation	Prevalence of contaminated lots of ground product
	Likelihood that <i>E. coli</i> O157:H7 positive ground beef would pass undetected through a random microbial monitoring program at various levels of sampling intensity
	Concentration of <i>E. coli</i> O157:H7 in lots of contaminated ground product
	Prevalence of contaminated cooked product
	Concentration of <i>E. coli</i> O157:H7 in cooked product
Public Health	Probability of <i>E. coli</i> O157:H7 infection at varying dose levels
	Number of <i>E. coli</i> O157:H7 infections (symptomatic and asymptomatic colonization) associated with ground beef consumption
	Number of normal diarrheal cases
	Morbidity and mortality from hemorrhagic colitis
	Morbidity and mortality (acute and premature) from HUS/TTP

9

10 Hazard Identification

11

12 Emergence 1982-93

13

14 *E. coli* O157:H7 was first recognized as a human pathogen in 1982, when it was
 15 associated with two outbreaks of hemorrhagic colitis (bloody diarrhea) in Oregon and
 16 Michigan associated with eating hamburgers from a particular fast-food chain (Riley *et*
 17 *al.*, 1983). Evidence indicating that rare sporadic infection occurred prior to 1982 comes
 18 from a retrospective review by the Centers for Disease Control and Prevention (CDC) of
 19 over 3,000 *E. coli* serotypes identified from 1973-1983, in which O157:H7 was detected
 20 only once in a 1975 isolate from a 50 year old California woman (Riley *et al.*, 1983). The
 21 subsequent occurrence of large outbreaks and the widespread distribution of cases has led
 22 to the designation of *E. coli* O157:H7 as an emerging pathogen. During the period 1982-
 23 1993, 39 outbreaks were documented in 22 states (Table 5).

1 Enterohemorrhagic *E. coli*

2

3 *E. coli* strains are a normal part of the intestinal bacteria of humans and warm-blooded
4 animals. Most do not cause disease. Distinct *E. coli* strains are serologically differentiated
5 on the basis of three major surface antigens, which enable serotyping: the O (somatic), H
6 (flagella), and K (capsule) antigens. *E. coli* strains that cause diarrheal illness are
7 categorized into specific groups based on virulence properties, mechanisms of
8 pathogenicity, clinical syndromes, and distinct O:H serogroups. These categories include:
9 enteropathogenic *E. coli* (EPEC), enterotoxigenic *E. coli* (ETEC), enteroinvasive *E. coli*
10 (EIEC), diffuse-adhering *E. coli* (DAEC), enteroaggregative *E. coli* (EaggEC), and
11 enterohemorrhagic *E. coli* (EHEC). *E. coli* O157:H7 belongs to the EHEC group (Levine
12 1987). EHECs are defined as Shiga toxin-producing *E. coli* which have been
13 demonstrated to cause diarrhea in man. Other virulence attributes associated with EHEC
14 include adherence factors (*eaeA* gene) and enterohemolysin. EHEC appear to cause
15 disease by adherence to human intestinal cells and the release of potent cytotoxins. The
16 role of virulence factors, such as intimin and enterohemolysin, are not yet fully
17 understood (WHO 1997).

18

19 Since *E. coli* O157:H7 was first identified as a human pathogen in 1982, other strains and
20 serogroups of *E. coli* have been identified as EHEC: ON:H-, O26:H11, O11:H8, and
21 sorbitol-positive O157:H- (Whittam 1998). (*E. coli* ON refers to serotypes for which the
22 somatic (O) antigen is nontypeable with standard antisera. Non-motile *E. coli* are
23 designated as O:H- or O:NM). Griffin (1995) suggested that although the absence of a
24 biochemical marker likely leads to underrecognition of non-O157 EHECs, the paucity of
25 reported outbreaks due to non-O157 EHECs, combined with the higher isolation rates of
26 serotype O157:H7 in prospective studies, indicates that the non-O157 EHECs do not
27 attain the public health importance of *E. coli* O157:H7 in the U.S. Therefore, the
28 proposed scope of the present assessment is limited to *E. coli* O157:H7. We invite,
29 however, additional or more current scientific evidence regarding the public health
30 impact of non-O157 EHECs.

31

32 Microbiology and Evolution of *E. coli* O157:H7

33

34 Most strains of *E. coli* O157:H7 possess microbiological characteristics uncommon to
35 most other *E. coli*. O157:H7 does not grow well, if at all, at 44-45.5°C, the usual
36 temperature for recovery of *E. coli* from food samples (Doyle and Schoeni 1984).
37 Raghubeer and Matches (1990) found that *E. coli* O157:H7 is excluded using standard
38 fecal coliform enumeration procedures for foods and water.

39

40 Unlike most *E. coli* strains, O157:H7 does not ferment sorbitol (a sugar alcohol) rapidly
41 (within 24 h). Therefore, MacConkey agar containing sorbitol (SMAC) instead of lactose
42 provides a differential medium for detection of *E. coli* O157:H7 (March and Ratnam
43 1986). (Because most *E. coli*, including O157:H7, ferment lactose, O157:H7 is
44 indistinguishable from other fecal flora grown on MacConkey agar containing lactose.
45 When grown on SMAC, sorbitol-negative colonies appear white, whereas sorbitol-
46 positive colonies appear blue or purple (USDA/FSIS (1998).) Further sensitivity

1 improvements resulted from the addition of rhamnose to SMAC medium. Rhamnose is
2 not fermented by *E. coli* O157:H7 as it is by most sorbitol-negative *E. coli* serotypes
3 (Chapman *et al.* 1993). Low concentrations of the antibiotic cefixime added to SMAC
4 media inhibit the growth of *Proteus* species, which are often sorbitol negative and can be
5 confused with *E. coli* O157:H7 on SMAC (Sanderson *et al.* 1995). Other growth media
6 were developed (e.g., 4-methylumbelliferyl- β -D-glucuronide (MUG) by Thompson *et al.*
7 (1990)) to exploit the finding that, unlike most other *E. coli* strains, O157:H7 is unable to
8 produce β -glucuronidase (GUD) (i.e., O157:H7 is unable to hydrolyze 4-
9 methylumbelliferyl-D-glucuronide, an assay normally used in verifying the presence of
10 *E. coli*). Ongoing developments in analytical procedures for *E. coli* O157:H7 continue to
11 improve the sensitivity and specificity of detection methods, as well as operational
12 attributes (cost, time, and training requirements). For the current FSIS laboratory methods
13 for detection, isolation and identification of *E. coli* O157:H7 from meat and poultry
14 products, see USDA/FSIS (1998).

15

16 All EHEC strains produce Shiga toxin 1 and/or Shiga toxin 2. Shiga toxin 1 is similar to
17 the Shiga toxin produced by *Shigella dysenteriae* type 1. The ability of *E. coli* O157:H7
18 to produce Shiga toxins was first reported in 1983. The structural genes for Shiga toxins
19 are encoded on bacteriophages; in contrast, those for the Shiga toxin of *S. dysenteriae*
20 type 1 are on the chromosome (Griffin 1995).² Toxin production alone, however, is not
21 sufficient to make *E. coli* O157:H7 pathogenic, since some Shiga toxin-producing *E. coli*
22 (STEC) do not appear to be human pathogens (Griffin 1995). Adherence appears to be
23 another critical virulence factor.

24

25 The adherence factors of *E. coli* O157:H7 have not been completely elucidated, however.
26 Like other EHEC, O157:H7 contains a plasmid in the 60-Mega Dalton (MDa) range
27 which encodes the production of enterohemolysin. At this point, the plasmid is regarded
28 as a virulence marker only, because there is no direct evidence that it or enterohemolysin
29 contributes directly to virulence. It is suspected that the plasmid is involved in adherence,
30 perhaps by mediating the initial contact, but reports of its exact role are conflicting
31 (Griffin 1995). *E. coli* O157:H7 also possesses an attaching and effacing (*eaeA*) gene that
32 encodes production of intimin, a 94-kDa outer membrane protein that enables intimate
33 adherence of the bacterium subsequent to initial, localized adherence to intestinal cells.
34 The attaching and effacing gene of *E. coli* O157:H7 is homologous to the *eaeA* gene of
35 EPEC, which is associated with infant diarrhea, but the *eaeA* gene is not sufficient for the
36 production of attaching and effacing lesions. For example, serotype O113:H21 is a

² Because the toxins are cytotoxic to African green monkey kidney (Vero) cells, they also have been described as verotoxins (VTs). The toxin is composed of a single A subunit that blocks protein synthesis and five B subunits that bind to globotriaosylceramide (Gb₃) receptors on cell surfaces (Griffin 1995). Differences in receptor distribution in endothelial cells in various tissues may be responsible for differences in target organs (e.g., the colon and renal glomeruli) and clinical syndromes (e.g., hemorrhagic colitis and hemolytic uremic syndrome (HUS), respectively) (Gyles 1992). VT binds to cells within the glomerulus of kidneys in children, but not in adults, implying that Gb₃ is present in the renal glomerulus of children but that it declines with development. This explains the age-related incidence of HUS, which is primarily a condition of young children (Lingwood *et al.* 1998). The lack of glomerular damage, the hallmark of HUS, in animal models is likely due at least in part to the absence of the Gb₃ receptor. It is absent in rabbit kidneys, for example (Griffin 1995).

1 verocytotoxin-producing *E. coli* eliciting clinical features comparable to O157:H7, but
2 O113:H21 is *eaeA*-negative, suggesting distinct adhesion factors (Dytoc *et al.* 1994).

3
4 Feng *et al.* (1998) assessed the genetic relationships among Shiga toxin-producing O157
5 strains to elucidate stages in the evolutionary emergence of *E. coli* O157:H7. The results
6 support a model in which O157:H7 evolved sequentially from a GUD-positive and
7 sorbitol-positive EPEC strain of serotype O55:H7, first by acquiring the Shiga toxin 2
8 gene and then by dividing into two branches; one became GUD-negative and sorbitol-
9 negative, resulting in the O157:H7 clone that spread worldwide, and the other lost
10 motility, leading to the sorbitol-fermenting O157:H- clone that has been identified in
11 Europe.

12 13 Low Infectious Dose of *E. coli* O157:H7

14
15 CAST (1994, p. 12) estimated that the infectious dose for *E. coli* O157:H7 is in the range
16 of 10 to 1,000 colony forming units. The American Gastroenterological Association
17 estimated the infectious dose of *E. coli* O157:H7 to be less than 1,000 organisms (AGA
18 1995). Based on retrospective analysis of foods associated with outbreaks, the capability
19 of person-to-person transmission, and the ability of the pathogen to tolerate acidic
20 conditions, which enables survival in the acidic environment of the stomach, Doyle *et al.*
21 (1997) estimated the infectious dose of *E. coli* O157:H7 to be less than a few hundred
22 cells. The infectious dose of *E. coli* O157:H7 remains uncertain, however, due to
23 uncertainties and variability in detection and enumeration of microbes recovered from
24 food outbreak samples and due to the variability in response to given dose levels within
25 the population and for an individual over time.

26 27 Health Outcomes Associated with *E. coli* O157:H7

28
29 Infection with *E. coli* O157:H7 presents a wide spectrum of clinical manifestations,
30 including asymptomatic carriage, nonbloody diarrhea, hemorrhagic colitis, hemolytic-
31 uremic syndrome (HUS), and thrombotic thrombocytopenic purpura (TTP). Cases of
32 asymptomatic *E. coli* O157:H7 colonization have occasionally been detected in
33 outbreaks, even among children, but the incidence rates are difficult to estimate because
34 stool samples from asymptomatic persons are rarely obtained. In one fourth to three
35 quarters of patients, the diarrhea remains nonbloody and the illness is mild. However, in
36 most cases that come to medical attention, the diarrhea becomes bloody on the second or
37 third day of illness (Griffin 1995). Ostroff *et al.* (1989), for example, found that 95% of
38 the 93 reported sporadic cases of *E. coli* O157:H7 in Washington State in 1987 had
39 bloody diarrhea. Nonbloody diarrhea progressing to hemolytic-uremic syndrome also has
40 been reported (Su and Brandt 1995). In Seattle, Washington, in a one-year prospective
41 study of 445 children's stools submitted to a microbiology laboratory, *E. coli* O157:H7
42 was isolated from 13 (2.9%) (Bokete *et al.* 1993). Su and Brandt (1995) estimated that *E.*
43 *coli* O157:H7 is associated with 0.6% to 2.4% of all diarrheal cases.

44
45 Hemorrhagic colitis was first reported in 1971. Its symptoms include severe abdominal
46 cramps followed by bloody diarrhea; edema (swelling), erosion, or hemorrhage of the

1 mucosal lining of the colon; and the absence of conventional enteric organisms in the
2 stool (Su and Brandt 1995). A large, multistate outbreak investigation found that 451
3 (90%) of 501 cases of diarrhea caused by *E. coli* O157:H7 were bloody (Bell *et al.* 1994).
4 In 93 outbreaks occurring during 1982-96, investigations reported 54% of diarrhea cases
5 caused by *E. coli* O157:H7 were bloody (CDC, unpublished data). Thirty-eight percent to
6 61% of *E. coli* O157:H7 infections result in hemorrhagic colitis, and *E. coli* O15:H7 is
7 estimated to cause 15% to 36% of all cases of bloody diarrhea or hemorrhagic colitis.
8 Symptoms of hemorrhagic colitis generally persist for several days to a few weeks (Su
9 and Brandt 1995). Hospitalization rates associated with outbreaks occurring during 1982-
10 96 have ranged from 0% to 100% (CDC, unpublished data). Most hospitalized patients
11 recovered within 1 week without specific therapy; however, complications (e.g., upper-
12 gastrointestinal bleeding, stroke) from hemorrhagic colitis associated with *E. coli*
13 O157:H7 have been reported (Su and Brandt 1995). Roberts *et al.* (1998, citing Boyce *et*
14 *al.* 1995a, Ryan *et al.* 1986) estimate the mortality rate of those suffering hemorrhagic
15 colitis without progression to HUS to be one percent.

16
17 Hemorrhagic colitis may be the only manifestation of *E. coli* O157:H7, or it may precede
18 development of hemolytic uremic syndrome. HUS is characterized by microangiopathic
19 hemolytic anemia (intravascular destruction of red blood cells), thrombocytopenia
20 (depressed blood platelet counts—platelets, or thrombocytes, are the clotting agent in
21 blood), and acute renal (kidney) failure. Several different pathogens are suspected of
22 causing HUS, but *E. coli* O157:H7 is the most common pathogen isolated from patients
23 with HUS (Neill *et al.* 1987). Siegler *et al.* (1994) found that 140 (89%) of 157 HUS
24 cases in Utah between 1971-90 were post-diarrheal. In the U.S., nearly all cases of post-
25 diarrheal HUS are caused by infection with enterohemorrhagic *E. coli* (EHEC) (Mahon *et*
26 *al.* 1997). (*Shigella dysenteriae* type I has long been recognized as a major cause of HUS
27 in developing countries with inadequate sanitation.) Griffin (1995) estimates that *E. coli*
28 O157:H7 is likely responsible for 85-95% of HUS cases in the U.S. HUS occurs most
29 commonly in children under the age of 10 but also has been reported in adults (Neill, *et*
30 *al.* 1985). During 1996, the first year of national reporting, 18 states reported 102 cases of
31 post-diarrheal HUS. Median age of patients was 5 years (range: 1-79) (CDC 1996).

32
33 The proportion of all patients who develop HUS following *E. coli* O157:H7 infection
34 varies widely among studies and outbreaks. Griffin and Tauxe (1991) estimate that,
35 overall, 2% to 7% of *E. coli* O157:H7 infections progress to HUS. Griffin (1995)
36 estimates the rate of HUS in sporadic *E. coli* O157:H7 cases with bloody diarrhea to be
37 about 5% to 10%. Clinical data indicate that approximately 10% of children under the
38 age of 10 infected with *E. coli* O157:H7 receive medical attention for overt HUS (Tarr
39 1995).

40
41 HUS is one of the most common causes of acute renal failure in children. Siegler *et al.*
42 (1994) found that HUS causes chronic renal sequelae, usually mild, in 51% of survivors
43 (48% of all cases). Neurological complications may occur in 30% to 50% of HUS
44 patients. Common neurological symptoms are mild, but serious complications, such as
45 seizure and coma, can occur (Su and Brandt 1995). In Martin *et al.*'s (1990) study of 117
46 children in Minnesota who had HUS, 9 children (7.7%) had renal failure and survived,

1 and one child required a kidney transplant. Siegler *et al.* (1994) found that severe kidney
2 or neurological impairments (end stage renal disease or stroke) occurred in 9 (6%) of 157
3 HUS cases over a 20-year period in Utah. Based on 1990 Medicare data on survival rates
4 after kidney transplantation and survival rates on dialysis for pediatric patients, Buzby *et*
5 *al.* (1996) estimate that approximately 60% of pediatric HUS patients that develop
6 chronic kidney failure die prematurely.³

7
8 Based on long-term studies in Minnesota (Martin *et al.* 1990) and King County,
9 Washington (Tarr and Hickman 1987) and a two-year, nation-wide study in Canada
10 (Rowe *et al.* 1991), Mahon *et al.* (1997) estimate the acute mortality rate for HUS at 3%
11 to 5%. A long-term study in Utah also reported 5% mortality (Siegler *et al.* 1994). (Su
12 and Brandt (1995) reported the HUS mortality rate as 5%-10%, but cited a review article
13 Karmali (1989), which preceded publication of most of the long-term studies.)

14
15 TTP means bleeding from tiny blood vessels in the skin and mucous membranes
16 (purpura) occurring with deficiency of blood platelets (thrombocytes). Prior to the 1980s,
17 gastrointestinal infections had not been strongly implicated in the pathogenesis of TTP
18 (CDC 1986). Clinical findings include HUS (thrombocytopenia, microangiopathic
19 hemolytic anemia, and renal failure) plus fever and neurologic symptoms (Su and Brandt
20 1995). (There is currently some debate within the public health community over whether
21 TTP should be considered a syndrome distinct from HUS.) The vascular tissue damage
22 associated with TTP resembles a more extensive form of that produced by HUS. Many
23 agents or conditions have been implicated as causing TTP, including *E. coli* O157:H7
24 infection (Su and Brandt 1995). TTP primarily affects the elderly. The case-mortality rate
25 for TTP varies among outbreaks and is uncertain.

26 27 Epidemiological Summary

28 29 Temporal and Geographic Distribution

30
31 The reported number of cases of *E. coli* O157:H7 has increased since the first recognized
32 U.S. outbreak in 1982, but some of the increase in reported cases is likely due to
33 improved surveillance, detection, and reporting. Although a small minority of those
34 infected with *E. coli* O157:H7 develop HUS, because the pathogen is the predominant
35 cause of the syndrome in the U.S., HUS can serve as a sentinel for *E. coli* O157:H7.
36 However, data that would permit analysis of temporal trends in HUS are limited and
37 inconsistent. Martin *et al.* (1990) reported a statistically significant increase in the
38 incidence of HUS in children less than 18 years old in Minnesota from 0.5 to 2.0 per
39 100,000 child-years between 1979 and 1988. Tarr and Hickman (1987) also reported that
40 between 1976 and 1980, HUS incidence among children under age 15 in King County,
41 Washington was significantly (about 2.5 times) higher than between 1971 and 1976. In
42 contrast, Siegler *et al.* (1994) found that the incidence of HUS in Utah ranged from 0.2 to
43 3.4 per 100,000 children-years during 1971-90 but found no evidence of an overall

³ More recently, Cosio *et al.* (1998) found that 28% of the kidney transplant patients died and 23% lost their grafts. In addition, 44% of those who were on dialysis for three or more years died after kidney transplant.

1 sustained increase in incidence. Since 1994, the number of *E. coli* O157:H7 outbreaks
2 reported per year has declined 30% (from 32 to 22), and the number of ill persons per
3 year due to outbreaks has declined 45% (from 543 to 298) (Tables 6-9).

4
5 Outbreaks and clusters of *E. coli* O157:H7 peak during the warmest months of the year.
6 In 1996, 75% of reported HUS cases in the US occurred from June through October
7 (CDC 1996). The reasons for this seasonal pattern are unknown. On the other hand, some
8 large outbreaks have occurred during the winter months (Tables 5-9).

9
10 Kinney *et al.* (1988) demonstrated that the incidence of HUS is not unique to a specific
11 geographic region within the U.S; however, sporadic cases of *E. coli* O157:H7 are more
12 frequently reported from northern than southern states (Griffin 1995). Rowe *et al.* (1991)
13 investigated the epidemiology of HUS in children across Canada. Outside of N. America,
14 *E. coli* O157:H7 has been isolated from humans in: Argentina, Australia, China, Chile,
15 Czechoslovakia, France, Germany, India, Ireland, Italy, Japan, South Africa, and the
16 United Kingdom (Griffin 1995). Illustrating the global distribution of *E. coli* O157:H7,
17 the largest reported outbreak, which caused thousands of illnesses, occurred in Japan in
18 1996. This outbreak, and a second one a year later, was associated with radish sprouts
19 (Buchanan and Doyle 1997). Genetically indistinguishable strains of *E. coli* O157:H7 are
20 commonly found in cattle herds hundreds or thousands of kilometers apart, and subtyping
21 of *E. coli* O157:H7 isolates suggests some regional transmission unrelated to cattle
22 movement (Hancock 1998).

23 24 Animal and Environmental Reservoirs

25
26 Animals other than cattle and humans that have been observed to shed *E. coli* O157
27 include sheep, horses, deer, dogs, and birds (Kudva *et al.* 1996, Rice and Hancock 1995,
28 Hancock *et al.* 1998). *E. coli* O157:H7 has not been observed in surveys of hog or poultry
29 farms, but experimentally, chicks have been readily colonized by small doses of *E. coli*
30 O157:H7 (Doyle *et al.* 1997). Isolates from non-bovine species may be closely related or
31 identical to bovine isolates. Long-term carriers have not been reported in any species, but
32 only cattle, sheep, and humans have been sampled with sufficient intensity to assess
33 duration of carriage (Hancock 1998).

34
35 Besides animal manure, *E. coli* O157:H7 has been detected in the environment in soil,
36 water, and water trough sediments. Although *E. coli* O157:H7 has not yet been detected
37 in commercially purchased cattle feeds, it should be able to survive in a dry feed and
38 multiply on addition of moisture (Hancock 1998).

39 40 Factors Affecting Survival and Growth

41
42 Temperature: Variable response to environmental conditions is inherent in
43 microorganisms. For example, Whiting and Buchanan found that the variations in rates of
44 growth, inactivation, and thermal inactivation among 19 strains of *E. coli* O157:H7 were
45 highly variable under identical circumstances. Four-fold ranges in survival and
46 inactivation times and two-fold ranges in growth rates were typically observed (ARS

1997). Despite the observed variability among strains in thermal inactivation rates, 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 heating ground beef sufficiently to kill typical strains of *Salmonella* will also kill *E. coli* O157:H7. Thermal pasteurization of milk has also been determined to be an effective treatment (Doyle *et al.* 1997). Doyle and Schoeni (1984) found that *E. coli* O157:H7 in ground beef was more sensitive to heat than salmonellae, but survived for 9 months at -20° C with little change in number. Optimal growth temperature was 37° C (98.6° F). The minimum temperature for *E. coli* O157:H7 growth is approximately 8-10° C (Buchanan and Doyle 1997).

Acid: Unlike most foodborne pathogens, *E. coli* O157:H7 is tolerant to acidic environments. Outbreaks have been associated with consumption of acidic foods such as dry salami and apple cider. Inoculation studies have shown that *E. coli* O157:H7 can survive fermentation, drying, and storage of fermented sausage (pH 4.5) for up to 2 months at 4°C with only a 100-fold reduction in cell populations. Hot acid sprays have been demonstrated ineffective in decontaminating *E. coli* O157:H7 on beef. The mechanism of acid tolerance appears to be associated with a protein(s) that can be induced by preexposing the bacteria to acid conditions (Doyle *et al.* 1997).

Environmental Persistence: *E. coli* O157:H7 has been observed to remain viable in soils and water for considerable periods (Colwell 1997). The bacteria can survive in inoculated soil samples for at least 18 weeks. *E. coli* O157:H7 has also been shown to persist in drying manure and to be present in incompletely composted dairy and feedlot waste. Some researchers have found that *E. coli* O157:H7 may survive in dairy cattle manure for at least 70 days, depending on temperature and, perhaps, available moisture (FDA/CFSAN 1997). Kudva *et al.* (1998) found that *E. coli* O157:H7 may survive in an unaerated sheep manure pile incubated outside under fluctuating environmental conditions for 21 months with concentrations ranging from 10² to 10⁶ colony forming units per gram (CFU/g). An *E. coli* O157:H7 cow manure pile was culture positive for 47 days. *E. coli* O157 is able to survive in water troughs sediments for at least four months and appears to multiply in this environment (LeJeune *et al.* 1997).

Drug Resistance and Antibiotic Treatment

Early surveys of antibiotic resistance revealed that *E. coli* O157:H7 isolates were sensitive to most antibiotics. However, recent studies show a trend toward increased resistance to antibiotics (Doyle *et al.* 1997). Treatment for *E. coli* O157:H7 infections is primarily supportive, including management of dehydration and complications such as anemia and renal failure (hemodialysis). The use of antibiotic treatments is controversial. Antibiotic treatment does not appear to diminish the severity of illness or prevent the development of HUS. Potential explanations for the lack of benefit for antibiotic treatment are: 1) elimination of bowel flora by the antibiotic giving a competitive advantage to *E. coli* O157:H7, and 2) lysis/death of *E. coli* O157:H7 leading to increased release of toxin (Su and Brandt 1995).

1 Incidence and Outcome Estimates

2

3 Outbreak data may be useful for identifying trends in the sources of infection, but
4 outbreak investigations miss small clusters of infections and sporadic cases not clearly
5 linked to a common source. Small clusters and sporadic cases may be captured by passive
6 or active surveillance. Passive surveillance paints a slightly different picture from the
7 outbreak data. In 1994, *E. coli* O157:H7 was designated by the Council of State and
8 Territorial Epidemiologists as reportable to the Centers for Disease Control and
9 Prevention (CDC) under the National Notifiable Diseases Surveillance System (NNDSS).
10 During 1994-96 (the most recent years for which data are currently available), the
11 number of reported cases of *E. coli* O157:H7 increased from 1420 to 2741, and the rate of
12 reported cases increased from 0.82 to 1.18 per 100,000 person-years (CDC 1997a). Some
13 of the reported increase is undoubtedly due to improved passive surveillance. The
14 investigation of a pseudo-outbreak of *E. coli* O157:H7 in New Jersey during 1994, for
15 example, indicated that the number of clinical laboratories culturing all diarrheal
16 specimens for *E. coli* O157:H7 had increased from 10% in 1993 to 90% in 1994 (CDC
17 1995). Passive surveillance, however, is also known to underestimate the actual number
18 of cases for a variety of reasons discussed below.

19

20 In comparison to the NNDSS data, a prospective, population-based study conducted in
21 Washington during 1985-86 estimated the incidence of culture-confirmed *E. coli*
22 O157:H7 infection to be 8 per 100,000 person-years (MacDonald *et al.* 1988). Ostroff *et*
23 *al.* (1989) estimated an incidence of 2.1 per 100,000 person-years during the first year of
24 statewide surveillance in Washington in 1987. Based on testing conducted in 1996, the
25 Foodborne Diseases Active Surveillance Network (FoodNet), a collaborative program
26 initiated in 1995 among the Centers for Disease Control and Prevention (CDC), the
27 USDA, the Food and Drug Administration (FDA), and the California, Connecticut,
28 Georgia, Minnesota, and Oregon state health departments, estimated a rate of 2.9 cases
29 per 100,000 person-years (CDC 1997b). Rates at the FoodNet sites ranged from 0.6 for
30 Georgia to 5 for Minnesota. Extrapolating to a U.S. population of 260 million yields a
31 rough national estimate of 7540 cases per year for 1996. In 1997, the average rate for all
32 FoodNet sites was 2.1 cases per 100,000 person-years (CDC 1998). Rates at the FoodNet
33 sites ranged from 0.2 for Georgia to 4.2 for Minnesota. Extrapolating to a U.S. population
34 of 260 million yields a rough national estimate of estimate 5,460 cases per year for 1997.
35 Both estimates, however, are unadjusted for recognized sources of underestimation.

36

37 The number of cases from passive or active surveillance systems may underestimate the
38 actual incidence of infection because some infected persons are asymptomatic or do not
39 seek medical care, physicians do not obtain cultures from all patients presenting
40 symptoms of infection, some persons who obtained medical care do not provide a stool
41 specimen, laboratories do not culture all stool samples for *E. coli* O157:H7 (although
42 routine culturing of bloody diarrhea for *E. coli* O157:H7 is increasingly common,
43 particularly in FoodNet sentinel site areas), some proportion of the lab results are false
44 negatives, and not all culture-confirmed infections are reported to public health
45 authorities. For example, in a 1994 national survey 70 (54%) of 129 randomly selected

1 clinical laboratories reported that they did not routinely test all stools or all bloody stools
2 for *E. coli* O157:H7 (Boyce *et al.* 1995b).

3
4 CDC (1993) investigators estimated that from 10,000 to 20,000 cases of *E. coli* O157:H7
5 occur in the U.S. each year (see also, Boyce *et al.* 1995a, AGA 1995). This is equivalent
6 to a rate of approximately 4 to 8 cases per 100,000 person-yrs, assuming a population of
7 250 million. The estimated number of cases was based, however, on patients who seek
8 medical care. An investigation of an unnoticed outbreak of *E. coli* O157:H7 in Las Vegas
9 in 1993 revealed that 45% of ill persons had not sought medical care (Cieslak *et al.*
10 1997). Assuming that 50% of infected persons do not visit a physician and recover fully,
11 Roberts *et al.* (1998) estimate the total number of *E. coli* O157:H7 infections per year to
12 be 20,000-40,000. CDC is currently revising the estimated national annual incidence of
13 *E. coli* O157:H7.

14
15 The incidence of HUS in North America is approximately 1 to 3 cases per 100,000
16 children-years for children under 5 years of age; the rate among older children is
17 somewhat lower, 1 to 2 cases per 100,000 children-years (Martin *et al.* 1990, Rowe *et al.*
18 1991, Kinney *et al.* 1988, Tarr and Hickman 1987, Siegler *et al.* 1994). For 41 outbreaks
19 occurring during 1982-98 for which preliminary disaggregated health outcome data are
20 currently available (i.e., outcomes are broken down into four categories: affected,
21 hospitalized, HUS or TTP, and dead), 94 out of 1855 cases (5%) progressed to HUS or
22 TTP, and 19 out of 1855 cases (1%) resulted in death (Table 10). For 1982-96, 139
23 outbreak investigations reported that 22% of cases were hospitalized, 5.6% developed
24 HUS/TTP, and 0.7% died (CDC, unpublished data).

25
26 Table 1 above summarized reported outbreaks of *E. coli* O157:H7 during 1982-97 by
27 vehicle category. CDC has identified ground beef as the likely vehicle of infection for
28 25% of the outbreaks and 33% of the illnesses associated with outbreaks during this
29 period. Table 3 summarizes reported outbreaks of *E. coli* O157:H7 during 1994-97 by
30 vehicle category. As illustrated in Figure 2, during this period, there is a declining
31 proportion of illnesses associated with outbreaks identified ground beef was identified as
32 the likely vehicle of infection.

1

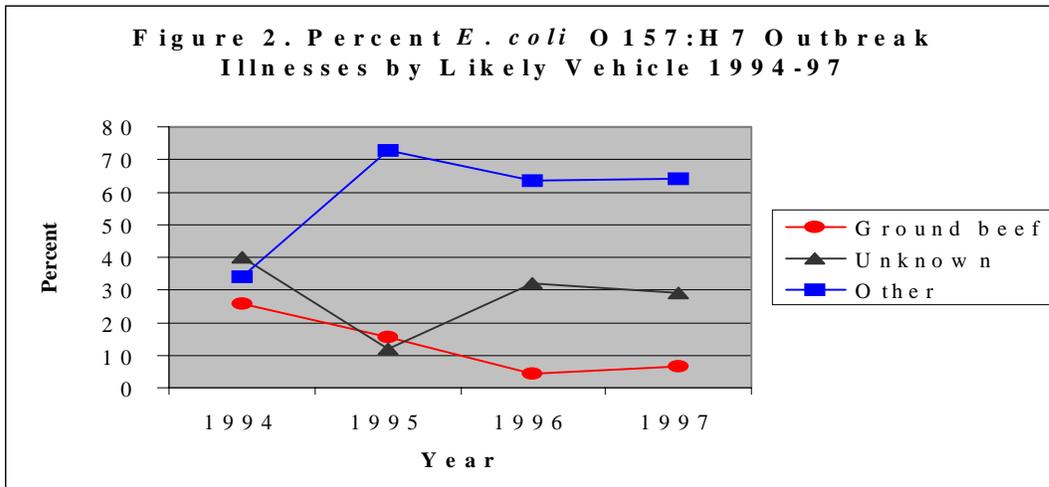
Table 3. *E. coli* O157:H7 Outbreaks 1994-97 by Vehicle Category

1994				1996			
Likely Vehicle	Outbreaks	No. Ill	% Ill	Likely Vehicle	Outbreaks	No. Ill	% Ill
Ground beef	9	140	25.8	Ground beef	4	21	4.3
Unknown	13	219	40.3	Unknown	7	157	32.2
Other	10	184	33.9	Other	18	310	63.5
Total	32	543	100.0	Total	29	488	100.0
1995				1997			
Likely Vehicle	Outbreaks	No. Ill	% Ill	Likely Vehicle	Outbreaks	No. Ill	% Ill
Ground beef	10	67	15.4	Ground beef	2	20	6.7
Unknown	5	52	12.0	Unknown	7	87	29.2
Other	17	316	72.6	Other	13	191	64.1
Total	32	435	100.0	Total	22	298	100.0

2

Compiled from data in Tables 6-9.

3



4

5

Risk Factors

6

Data from many studies suggest that cattle manure in one form or another is the most common source of human infections. As indicated in Table 1, ground beef is the most frequently identified source of outbreaks. Surveillance data indicate, however, that the majority of *E. coli* O157:H7 infections are sporadic, with no identified link to any other case (Ostroff *et al.* 1989, MacDonald *et al.* 1988). For example, only 25% of the cases reported in Oregon from 1991-97 were outbreak-associated (OCD 1998). Furthermore, sporadic disease may reflect entirely different food vehicles, mechanisms, or sources of infection than those responsible for outbreaks. Because the specific exposures responsible for sporadic infections are rarely confirmable, the principal source of infection remains uncertain. In a one-year case-control study conducted in Oregon during 1996-97, only

16

1 two potential exposures from a long list were associated with increased risk of infection:
2 visiting or living on a farm and, more specifically, visiting or living on a farm where
3 there are cows (OCD 1998). Only a minority of cases had these risks, however, making
4 the population attributable risk low. It may be that the small numbers of cases (74) in the
5 Oregon study prevented the detection of a significant association with other factors, such
6 as eating hamburger, eating in restaurants or fast-food outlets, or spending time in day-
7 care facilities (OCD 1998). In the first reported nationwide case-control study of *E. coli*
8 O157:H7 infection conducted in 1990-92, consumption of “undercooked” (described as
9 pink in the middle) ground beef was the only dietary factor independently associated with
10 diarrhea in multivariate analysis. However, the population-attributable risk for this
11 behavior was only 34% (Slutsker *et al.* 1998).⁴ The case-control findings suggest that the
12 *E. coli* O157:H7 story is more complicated than just rare hamburgers, and the source of
13 most sporadic infections remains unknown.

14
15 Host susceptibility factors, inoculum size, virulence of the strain, or other unknown
16 factors may account for the selective development of HUS among those infected with *E.*
17 *coli* O157:H7. Patients at extremes of age (very young, very old) may be at increased risk
18 for *E. coli* O157:H7-associated diarrhea as well as for HUS, TTP, and death. (See Ch. 5,
19 Figures 11 and 12.) The prolonged use of antimotility or antidiarrheal agents has also
20 been proposed as a risk factor in HUS. Strains that produce relatively more Shiga toxin 2
21 also are suspected to be more virulent than those that produce relatively more Shiga toxin
22 1. In one outbreak, antibiotic treatment during the exposure period and before symptom
23 onset was reported to be a risk factor for person-to-person transmission of *E. coli*
24 O157:H7 (Su and Brandt 1995).

25
26 The disproportionate number of cases of HUS that occur in children younger than 5 years
27 of age further suggests that host factors may be important. Tarr and Hickman (1987)
28 found that the highest annual incidence of HUS in children younger than 15 years of age
29 was in children less than 3 years of age. Rowe *et al.* (1991) found that the peak age-
30 specific HUS incidence rate in children younger than 15 years was for children younger
31 than 5 years. Martin *et al.* (1990) identified day-care attendance as a risk factor in the
32 incidence of HUS.

33 34 Assessment Methodology

35 36 Probabilistic Risk Analysis

37
38 The FSIS risk assessment for *E. coli* O157:H7 in beef will be conducted using
39 probabilistic risk analysis (PRA) methods. In contrast to deterministic modeling methods,
40 which use a singular point estimate of each variable within a model to determine the
41 model’s outcome(s), PRA accounts for uncertainty and variability by modeling each

⁴ More recently, Kassenborg *et al.* (1998) also found that consumption of pink hamburgers or pink ground beef was a statistically significant risk factor in a case-control study conducted at 5 FoodNet sites. However, the final report has not yet been published, and an estimate of the population risk attributable to consumption of pink ground beef is not yet available (Kassenborg 1998).

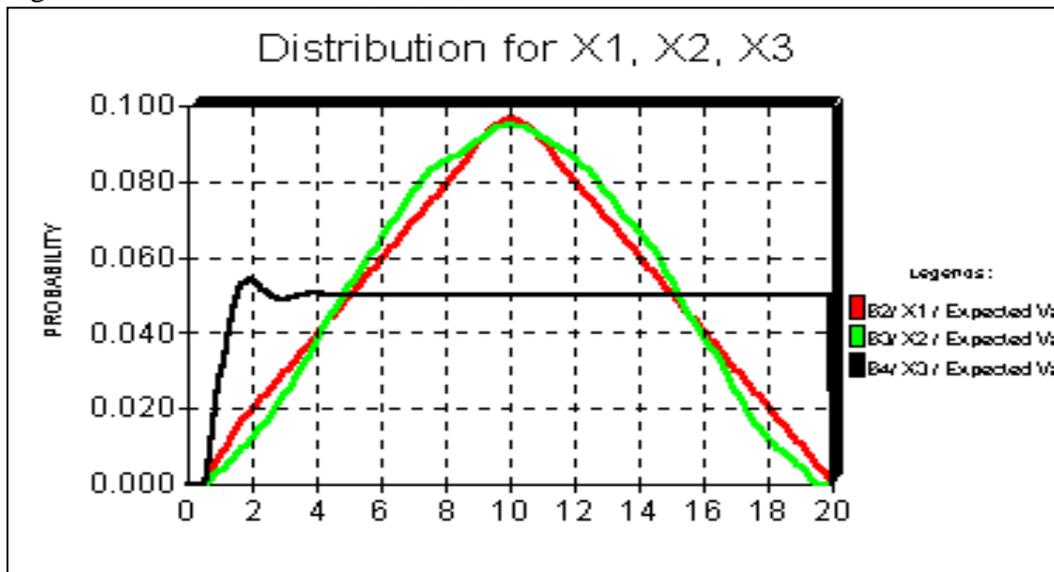
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1 variable within a model by a probability or uncertainty distribution. A few hypothetical
 2 examples help to demystify PRA methods.

3
 4 Figure 3 provides examples of some distributions that are commonly used in PRA. The x
 5 (horizontal) axis covers the range of possible values that the variable could take, and the
 6 y (vertical) axis gives each value within that range a probability weighting. In each case
 7 in Figure 3, the average, or expected, value of the distribution of X_1 , X_2 , and X_3 is 10,
 8 while the minimum and the maximum are 0 and 20, respectively. Differences stem from
 9 the various statistical distributions assumed to represent the variability and/or uncertainty
 10 in the x variable (Triangular, BetaPERT, or Uniform).

11
 12 Figure 3. Distribution for X_1 , X_2 , X_3 .



13
 14 Deterministic modeling permits sensitivity analysis. This is achieved by evaluating
 15 various combinations of “what if” scenarios, e.g., changing the value of one variable
 16 from one extreme (the minimum) to the other (the maximum) while holding all other
 17 variables constant at a nominal value (the mean). For anything but the simplest
 18 deterministic models, however, the number of possible combinations of values comprises
 19 too large a set of scenarios to have any practical use. PRA is similar to “what if”
 20 scenarios in that it generates a number of possible scenarios. However, it surpasses
 21 deterministic methods by accounting for all possible values that each variable could take
 22 and weights each possible scenario by the probability of its occurrence. PRA achieves
 23 this by employing simulation methods, which are generically referred to as Monte Carlo
 24 analysis.

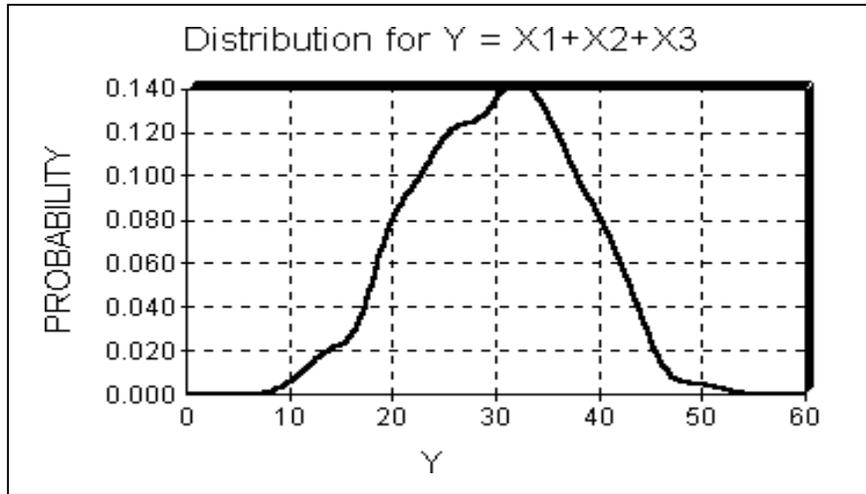
25
 26 The structure of a PRA model is very similar to a deterministic model, with variables
 27 linked together by mathematical functions (addition, multiplication, exponents, etc.),
 28 except that each uncertain variable is represented by a probability distribution instead of a
 29 single value. Consider the following expression: $Y = X_1 + X_2 + X_3$. The expected value of
 30 the probabilistic model is identical to the simple output of the deterministic model
 31 ($Y=10+10+10=30$), but the complete output of the probabilistic model shows the range of

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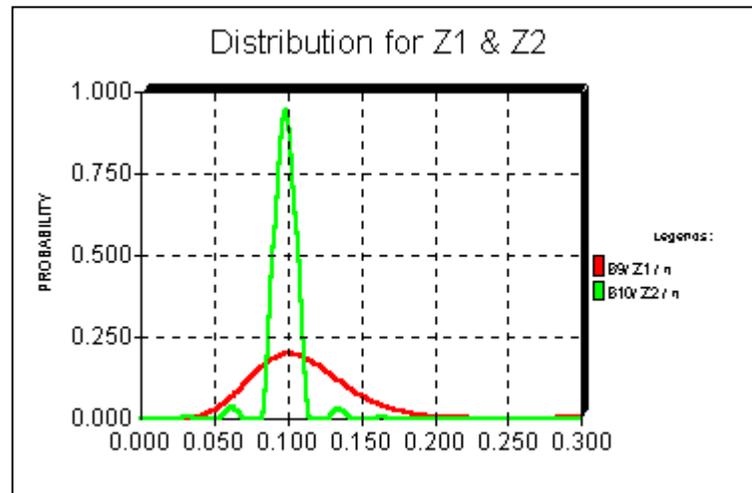
1 values that Y can take and the likelihood of the occurrence of each of the possible Y
 2 values (Figure 4).

3
 4 Figure 4. Distribution for Y.



5
 6 Figure 5 illustrates that as more data become available, PRA estimates become more
 7 precise. Consider the hypothetical example in which Z is the proportion of contaminated
 8 product. One estimate of the true proportion (Z_1) comes from a sample of 100 units, of
 9 which 10 are contaminated. Another estimate (Z_2) comes from a sample of 10,000 units,
 10 of which 1,000 are contaminated. In both cases, the estimated proportion is centered
 11 about 0.1, but Z_2 is characterized by a much tighter uncertainty distribution, and reflects
 12 increased confidence that extreme values, although possible, are less likely to occur.
 13 Vose (1996) provides a practical introduction to probabilistic risk analysis modeling.

14
 15 Figure 5. Effect of increased sample size on uncertainty.

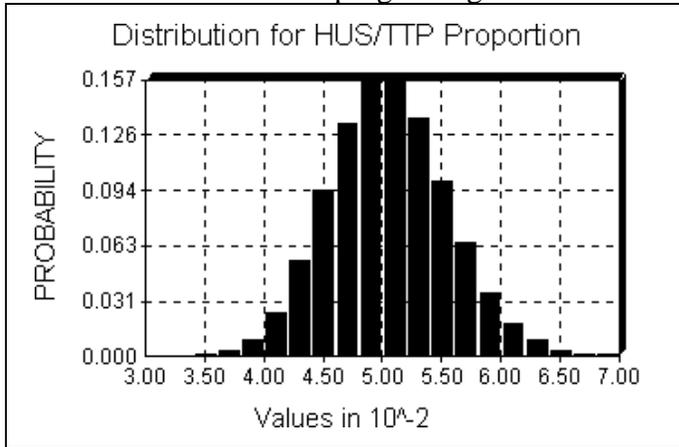


16
 17 To better motivate the methodological discussion, some concrete examples in the context
 18 of the *E. coli* O157:H7 risk assessment examples are provided.

19

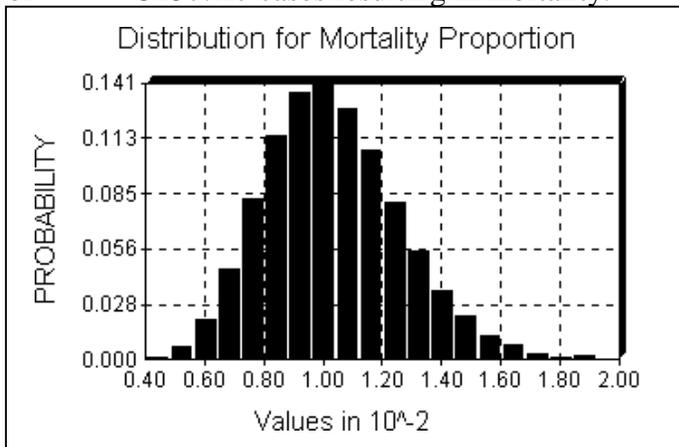
1 Example A: If 94 out of 1855 cases of *E. coli* O157:H7 progress to HUS or TTP (Table
 2 10), then the uncertainty about the true proportion of cases that progress to HUS or TTP
 3 can be characterized as a Beta (95, 1762) distribution (Figure 6). (If the number of events
 4 (s) in n trials follows a binomial distribution—i.e., the event either occurs or it does not
 5 occur—then the uncertainty about the probability of the event’s occurrence is
 6 characterized as a beta distribution with parameters s+1 and n-s+1 (Vose 1996). Values
 7 in 10^{-2} is equivalent to percent.)

8
 9 Figure 6. Estimated uncertainty distribution for proportion
 10 of *E. coli* O157:H7 cases progressing to HUS/TTP.



11 Example B: If 19 out of 1855 cases (1%) of *E. coli* O157:H7 cases resulted in death
 12 (Table 10), then the uncertainty about the true mortality rate can be expressed as a
 13 beta(20,1837) distribution (Figure 7). As suggested by Figure 5, forthcoming CDC data
 14 from a more complete set of outbreaks should substantially reduce the uncertainty about
 15 the rates of progression of O157 cases to health outcomes of differing severity. These and
 16 other relevant data will be evaluated for incorporation into the analysis as they become
 17 available.

18
 19
 20 Figure 7. Estimated uncertainty distribution for proportion
 21 of *E. coli* O157:H7 cases resulting in mortality.



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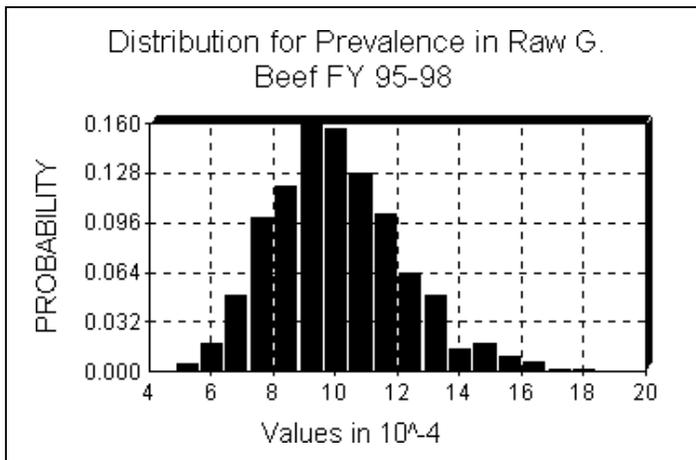
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1 Example C: During FY 94-98, 23 out of 24065 ground beef samples tested positive in the
 2 FSIS *E. coli* O157:H7 monitoring program (Table 4). The uncertainty—not accounting
 3 for analytical test sensitivity or specificity—about the true prevalence of O157 positive
 4 raw ground beef can be characterized as a beta (24, 24043) distribution (Figure 8). (Some
 5 of the observed increase in the proportion of positive samples during FY 98 is likely due
 6 to enhanced monitoring (i.e., the increased sample size—from 25 g to 325 g—and the
 7 increased rate of sampling). However, environmental and other factors may also be
 8 involved. Products sampled under the FSIS Microbiological Testing Program for
 9 *Escherichia coli* O157:H7 in Raw Ground Beef may contain beef derived from advanced
 10 meat recovery systems and/or Mechanically Separated Beef, but these products are not
 11 sampled as such, nor are products that contain another type of livestock product in
 12 addition to beef (FSIS Directive 10.010.1.)
 13

Year	FY 95	FY 96	FY 97	FY 98	Cum
No. Samples	5291	5326	5919	7529	24065
No. +ves	3	4	2	14	23
Prevalence	0.0008	0.0009	0.0005	0.0020	0.0010

Source : FSIS/OPHS Weekly *E. coli* O157:H7 Report, 10/06/98.

14
 15 Figure 8. Estimated uncertainty distribution for the
 16 prevalence of *E. coli* O157:H7 in raw ground beef.



17

1 Table 5. Reported Outbreaks of *E. Coli* O157:H7 in the U.S., 1982-1993 (These data are
2 preliminary and subject to change)

No.	State	Month/Year	Setting	Likely vehicle	No. ill
1.	OR	Feb 1982	Community	Ground beef	26
2.	MI	May 1982	Community	Ground beef	21
3.	NE	Sep 1984	Nursing home	Ground beef	34
4.	NC	Sep 1984	Day-care	Person-to-person	36
5.	NC	May 1986	Day-care	Person-to-person	15
6.	WA	Oct 1986	Community	Ground beef & Ranch dressing	37
7.	UT	Jun 1987	Custodial Institution	Ground beef & Person-to-person	51
8.	WI	May 1988	School	Roast beef	61
9.	MN	Aug 1988	Day-care centers (9)	Person-to-person	38
10.	MN	Oct 1988	School	Precooked ground beef	54
11.	WA	Aug 1989	Restaurant	Unknown	3
12.	MO	Dec 1989	Community	Drinking water	243
13.	ND	Jul 1990	Community	Roast beef	65
14.	MT	Nov 1990	School	School lunch	10
15.	OR	Jul 1991	Community	Swimming water	21
16.	WA	Aug 1991	Picnic	Ground beef	2
17.	MN	Sep 1991	Fair	Ground beef	8
18.	MA	Nov 1991	Community	Apple cider	23
19.	NY	May 1992	Unknown	Unknown	5
20.	NV	Jun 1992	Day-care	Person-to-person	57
21.	ME	Sep 1992	Home	Vegetable & Person-to-person	4
22.	OR	Dec 1992	Community	Raw milk	9
23.	CA	Jan 1993	Restaurant	Ground beef	32
	ID	Jan 1993	Restaurant	Ground beef	13
	NV	Jan 1993	Restaurant	Ground beef	58
	WA	Jan 1993	Restaurant	Ground beef	629
24.	OR	Mar 1993	Restaurant	Mayonnaise	47
25.	ME	Jun 1993	Unknown	Unknown	4
26.	OR	Jun 1993	Home	Raw milk	6
27.	NC	Jul 1993	Day-care	Person-to-person	27
28.	IL	Jul 1993	Community	Unknown	8
29.	NM	Jul 1993	Party	Unknown	4
30.	MA	Jul 1993	Community	Ground beef	10
31.	WA	Jul 1993	Church picnic	Pea salad	16
32.	CA	Jul 1993	Home	Ground beef	10
33.	OR	Aug 1993	Restaurant	Cantaloupe	27
34.	PA	Aug 1993	Community	Ground beef	3
35.	WA	Aug 1993	Restaurant	Salad bar	53
36.	CT	Sep 1993	Club BBQ	Ground beef	23
37.	MT	Sep 1993	Community	Ground beef	8
38.	WA	Oct 1993	Restaurant	Unknown	9
39.	TX	Oct 1993	Unknown	Unknown	13
				Total	1823

3 Source: Centers for Disease Control and Prevention, unpublished data.

1 Table 6. Reported Outbreaks of *E. coli* O157:H7 in the U.S., 1994 (These data are
2 preliminary and subject to change)

No.	State	Month	Setting	Likely vehicle	No. ill
1.	WA&OR	Jan	Home	Ground beef	21
2.	MN	Feb	Community	Ground beef	8
3.	NE	Apr	Home/camp	Ground beef	24
4.	ND	May	Restaurant	Ground beef	33
5.	CA	May	Home	Ground beef	9
6.	OH	May	Community	Coney dog sauce	10
7.	NY	Jun	Home	Ground beef	19
8.	CT	Jun	Home	Retail foods	21
9.	CT	Jun	Community	Ground beef	2
10.	PA	Jun	Home	Ground beef	4
11.	OH	Jun	Day-care	Person-to-person	8
12.	VA	Jul	Community	Unknown	7
13.	VA	Jul	Camp	Ground beef	20
14.	OH	Jul	Community	Unknown	5
15.	WI	Jul	Day-care	Person-to-person	43
16.	OK	Jul	Restaurant	Unknown	4
17.	HI	Jul	Unknown	Unknown	17
18.	NY	Jul	Day camp	Unknown	5
19.	MI	Jul	Day care	Person-to-Person	13
20.	NJ	Jul	Homes	Unknown	89
21.	NY	Jul	Community	Swimming water	12
22.	TX	Aug	Cafeteria	Salad bar	26
23.	KY	Aug	Market	Unknown	5
24.	FL	Aug	Unknown	Unknown	9
25.	OH	Aug	Day care	Person-to-person	6
26.	MN	Sep	College	Unknown	11
27.	NY	Sep	Oktoberfest	Unknown	37
28.	WA	Oct	Home	Unknown	7
29.	WI	Oct	Restaurant	Foodhandler	26
30.	WA&CA	Nov	Home	Salami	19
31.	NM	Nov	School	Unknown	20
32.	NY	Jul	Restaurant	Unknown	3
				Total	543

3 Source: Centers for Disease Control and Prevention, unpublished data.

1 Table 7. Reported Outbreaks of *E. coli* O157:H7 in the U.S., 1995 (These data are
2 preliminary and subject to change)

No.	State	Month	Setting	Likely vehicle	No. ill
1.	OR	Mar	Day-care	Person-to-person	4
2.	MN	May	Picnic	Ground beef	2
3.	NC	May	Day-care	Person-to-person	33
4.	MN	May	Home	Ground beef	4
5.	SD	Jun	Camp	Ground beef	3
6.	GA&TN	Jun	Restaurant	Ground beef	8
7.	IL	Jun	Lake	Swimming	12
8.	CO	Jun	Day-care	Person-to-person	25
9.	WI	Jun	Lake	Swimming	8
10.	MT	Jul	Community	Leaf lettuce	74
11.	NY	Jul	Day-care	Ground beef	12
12.	NY	Jul	Camp	Unknown	5
13.	CO	Jul	Camp	Ground beef	21
14.	MN	Jul	Lake	Swimming	6
15.	MN	Jul	Lake	Swimming	2
16.	MN	Jul	Camp	Water	9
17.	MA	Jul	Fair	Ground beef	8
18.	ID	Aug	Lake	Swimming	4
19.	WI	Aug	Festival	Ice	27
20.	CT	Aug	Camp	Unknown	24
21.	MN	Aug	Church	Roast beef	31
22.	ME	Sep	Camp	Lettuce	37
23.	ID	Sep	Restaurant	Lettuce	12
24.	WA	Sep	Home	Ground beef	2
25.	KS	Oct	Wedding	Punch, Fruit salad	21
26.	OH	Oct	Community	Unknown	11
27.	NY	Oct	Home	Ground beef	2
28.	OR	Nov	Home	Venison jerky	11
29.	VT	Nov	Home	Unknown	3
30.	MN	Nov	Home	Ground beef	5
31.	IL	Nov	Church	Unknown	4
32.	CA	Dec	Prison	Unknown	5
				TOTAL	455

3 Source: Centers for Disease Control and Prevention, unpublished data.

1 Table 8. Reported Outbreaks of *E. coli* O157:H7 in the U.S., 1996 (These data are
2 preliminary and subject to change)

No.	State	Month	Setting	Likely vehicle	No. ill
1.	TX	Apr	Home	Ground beef	3
2.	CT&IL	May	Home	Lettuce	47
3.	WA	Jun	Pool	Swimming	4
4.	MN	Jun	Lake	Swimming	8
5.	NY	Jun	Restaurant	Unknown	61
6.	MI&OH	Jun	Restaurant	Unknown	10
7.	NH&MA	Jun	Community	Unknown	29
8.	MN	Jun	Day-care	Person-to-person	7
9.	OR	Jun	Picnic	Unknown	38
10.	NY	Jun	Nursing home	Person-to-person	5
11.	PA	Jun	Day-care	Person-to-person	3
12.	NC	Jun	Day-care	Person-to-person	2
13.	NV	Jul	Party	Ground beef	2
14.	GA	Jul	Pool	Swimming	18
15.	MO	Jul	Community	Unknown	3
16.	PA	Aug	Party	Ground beef	9
17.	MN	Aug	Day-care	Person-to-person	8
18.	MS	Aug	School	Person-to-person	36
19.	MN	Aug	Day-care	Person-to-person	63
20.	VT	Sep	Fair/Festival	Unknown	11
21.	RI	Sep	Community	Unknown	5
22.	NY	Sep	Day-care	Person-to-person	9
23.	OR	Sep	Restaurant	Ground beef	7
24.	CA,WA,CO	Oct	Community	Apple juice	71
25.	CT	Oct	Home	Apple cider	14
26.	MN	Oct	Day-care	Person-to-person	3
27.	WA	Oct	Fair/Festival	Apple cider	6
28.	IL	Nov	Home	Venison	2
29.	OR	Dec	Home	Venison	4
				Total	488

3 Source: Centers for Disease Control and Prevention, unpublished data.

1 Table 9. Reported Outbreaks of *E. Coli* O157:H7 in the U.S., 1997 (These data are
2 preliminary and subject to change)

No.	State	Month	Setting	Likely vehicle	No. ill
1	FL	Feb	Home	Person-to-person/travel	5
2	NC	Feb	Day care	Person-to-person	5
3	FL	May	Wedding	Ground beef	5
4	OR	May	Preschool	Unknown	3
5	OR/ID	May	Home	Unknown	8
6	IL	May	School	Ice cream bars	3
7	IN	Jun	Community	Unknown	6
8	OR	Jun	Party	Melon/lemon bars	9
9	VA	Jun	Community	Alfalfa sprouts	48
10	MI	Jul	Community	Alfalfa sprouts	60
11	MN	Jul	Day care	Wading pool	17
12	MN	Jul	Day care	Person-to-person	6
13	CO/KY	Jul	Community	Ground beef	15
14	IA	Jul	Club	Person-to-person	21
15	VA	Aug	Day care	Person-to-person	2
16	WA	Aug	Camping/reunion	Person-to-person	3
17	MN	Sep	Community	Unknown	17
18	IA	Sep	School	Unknown	20
19	WA	Sep	RV Park	Water	2
20	NE	Oct	Wedding	Unknown	27
21	IN	Oct	Community	Unknown	6
22	LA	Nov	School	Person-to-person	10
				Total	298

3 Source: Centers for Disease Control and Prevention, unpublished data.

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1 Table 10. Outbreaks with Disaggregated Health Outcomes

No.	Mo. And Year	State	Affected	Hospitalized	HUS or TTP	Dead	Reference
1	Feb-82	OR	26	19	0	0	Griffin (1995)
2	May-82	MI	21	14	0	0	Griffin (1995)
3	Sep-84	NE	34	14	1	4	Griffin (1995)
4	Sep-84	NC	36	3	3	0	Griffin (1995)
5	Oct-86	WA	37	17	4	2	Griffin (1995)
6	Jun-87	UT	51	8	8	4	Griffin (1995)
7	May-88	WI	61	2	0	0	Griffin (1995)
8	Aug-88	MN	19	NR	3	0	Griffin (1995)
9	Oct-88	MN	54	4	0	0	Griffin (1995)
10	Dec-89	MO	243	32	2	4	Griffin (1995)
11	Jul-90	ND	65	16	2	0	CDC (1991)
12	Nov-90	MT	10	2	1	0	Griffin (1995)
13	Jul-91	OR	28	7	3	0	Griffin (1995)
14	Nov-91	MA	23	7	3	0	Griffin (1995)
15	Jul-92	NV	57	1	0	0	Griffin (1995)
16	Sep-92	ME	4	3	1	1	Griffin (1995)
17	Dec-92	OR	8	2	0	0	Griffin (1995)
18	Jan-93	WA,ID, NV,CA	732	195	55	4	Griffin (1995)
19	Mar-93	OR	48	12	0	0	Griffin (1995)
20	Feb-97	FL	5	2	1	0	CDC (1998)
21	Feb-97	NC	5	1	0	0	CDC (1998)
22	May-97	FL	5	1	0	0	CDC (1998)
23	May-97	OR	3	1	0	0	CDC (1998)
24	May-97	OR/ID	8	1	0	0	CDC (1998)
25	May-97	IL	3	2	0	0	CDC (1998)
26	Jun-97	IN	6	2	2	0	CDC (1998)
27	Jun-97	OR	9	1	0	0	CDC (1998)
28	Jun-97	VA	48	11	0	0	CDC (1998)
29	Jul-97	MI	60	25	3	0	CDC (1998)
30	Jul-97	MN	17	1	0	0	CDC (1998)
31	Jul-97	MN	6	1	0	0	CDC (1998)
32	Jul-97	CO/KY	15	4	0	0	CDC (1998)
33	Jul-97	IA	21	0	0	0	CDC (1998)
34	Aug-97	VA	2	0	0	0	CDC (1998)
35	Aug-97	WA	3	1	0	0	CDC (1998)
36	Sep-97	MN	17	1	0	0	CDC (1998)
37	Sep-97	IA	20	2	0	0	CDC (1998)
38	Sep-97	WA	2	1	1	0	CDC (1998)
39	Oct-97	NE	27	6	0	0	CDC (1998)
40	Oct-97	IN	6	0	0	0	CDC (1998)
41	Nov-97	LA	10	4	1	0	CDC (1998)
	TOTAL		1855	349	94	19	

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