

## \*BOVINE SPONGIFORM ENCEPHALOPATHY AND NEW VARIANT CREUTZFELDT-JAKOB DISEASE

Gary C. Smith  
Center for Red Meat Safety  
Department of Animal Sciences  
Colorado State University  
Fort Collins, CO 80523-1171

What are BSE, CJD and nvCJD? The “B” in BSE means bovine (i.e., cattle), “S” stands for spongiform (i.e., sponge-like appearance under a microscope) and “E” is for encephalopathy (i.e., brain illness); thus, BSE is a disease causing a sponge-like appearance of the cattle brain (Smith, 2001a). BSE is manifested as “craziness” of cattle (vigorous and repetitive jerking of small muscles all over the body; a change in the tone of the “moo”; aimless head butting; frenzied movements) hence the name mad cow disease (Dealler and Lacey, 1990; Raiden *et al.*, 2001). The incubation period (time between exposure to the infectious agent and the display of physical symptoms) is about 3 to 6 years (Dealler and Lacey, 1990). BSE was first observed in the United Kingdom in 1972 and diagnosed/described as a cattle disease in 1986; the incidence peaked at 36,680 cases in 1992 and since has declined to 1,311 cases in 2000 and 459 cases through September 2001 (DEFRA, 2001). Because the infective agent is not considered “foreign” by the cow’s body, there is no immune response (i.e., no antibodies are made); this makes it difficult to develop a diagnostic test, and the only way to diagnose BSE with 100% certainty is by brain biopsy after death of the animal (Raiden *et al.*, 2001).

Creutzfeldt-Jakob Disease (CJD) is named for the two physicians who first diagnosed/described it (in the 1920s) in human patients (National Cattlemen’s Beef Association, 2001b). There are three types of CJD, two of which are genetic or familial (Gerstman-Straussler-Schneinker Syndrome; Fatal Familial Insomnia) and the third of which is sporadic, “classical” CJD (Rhodes, 1997; Belay, 1999). CJD is a progressive, degenerative, spongiform and fatal encephalopathy that occurs worldwide at a rate of about one case per million persons per year (U.S. Meat Export Federation, 2001a), usually in persons over the age of 55 years (Franco, 2001). nvCJD (new variant Creutzfeldt-Jakob Disease) was first diagnosed/described in 1996 and is also a progressive, degenerative, spongiform and fatal encephalopathy (Brown *et al.*, 2001). nvCJD is different, though, from classical CJD because it has largely, but not exclusively, affected much younger people; the age of the first ten known victims of nvCJD ranged from 16 to 39 years suggesting that nvCJD has a much shorter incubation time than classical CJD (Will *et al.*, 1996).

BSE, CJD and nvCJD belong (along with scrapie in sheep, chronic wasting disease in deer and elk, and kuru in humans) to a group of diseases called (Acheson, 2001) Transmissible Spongiform Encephalopathies (TSEs). Since BSE was first diagnosed/described, numerous possible causes for the anomaly have been suggested: (a) Sheep scrapie, jumping species because of changes in meat byproduct rendering practices (U.S. Meat Export

---

\* Presentation AC 02, American Society for Microbiology, Audioconference Series 2002, on February 6, 2002.

Federation, 2001a). (b) An unconventional virus (USDA-APHIS, 1999; Food Processing, 2001). (c) A “virino,” which is described as an incomplete virus composed of naked nucleic acid protected by host proteins (USDA-APHIS, 1999; Food Processing, 2001). (d) Copper/manganese irregularities in the animal’s diet (Purdey, 2001). (e) High-dose treatment of cattle with Phosmet, an organophosphate used to treat cattle for ox warbles (National Meat Association, 2001b; Render, 2001a). (f) “Molecular mimicry” by the bacteria *Acinetobacter* found in “winter feeds” for cattle (Ebringer *et al.*, 1997). (g) Occurrence of a rogue-protein, or abnormal, prion in cattle feed (USDA-APHIS, 1999). Food Processing (2001) describes a “prion” as an abnormal partially proteinase K-resistant protein devoid of nucleic acid, capable of causing a cell to produce more abnormal protein.

It is now accepted that abnormal prions are the infectious agents responsible for Transmissible Spongiform Encephalopathies (Saborio *et al.*, 2001). The principal component of prions is the glycoprotein PrP<sup>Sc</sup>, which is a conformationally modified isoform of a normal cell-surface protein called PrP<sup>C</sup> (Prusiner, 1998). Acheson (2001) says the causative agent was termed a “slow virus” in the 1950s; Raiden *et al.* (2001) says it was originally termed a “small, proteinaceous infectious particle.” Stanley Prusiner, in 1982, coined the term “prion” for this protein; he was awarded the Nobel Prize In Medicine in 1997 for his work (Franco, 2001). Prions occur normally in the brain, spinal cord and certain nervous tissues of all animals; normal prions may have a role in copper transport, nerve conduction, long-term survival of Purkinje neurons, normal synaptic function of neurons, cell signaling, regulation of circadian activity and antioxidant reactions (Liemann and Glockshuber, 1998; Mareib, 1998; Doyle, 2001). It is the occurrence of aberrant forms of prions (the so-called “rogue-protein prion” or “BSE prion”) that causes the problem. Pathogenic prions pervert normal prions by changing their structure and causing them to aggregate and interfere with brain function (Doyle, 2001). Prion disorders riddle the mammalian brain with plaques and holes, the precise pattern and resulting symptoms—dementia, extreme fatigue, or loss of balance—depend on whether one is human, bovine or ovine (Lewis, 2001).

The “aberrant” or “abnormal” or “rogue-protein” BSE prion is now—almost universally—considered to be the causative agent for BSE and nvCJD (Collinge *et al.*, 1996; Bruce *et al.*, 1997; Hill *et al.*, 1997). The infectious agent of a Transmissible Spongiform Encephalopathy is an infectious form of prion protein, called “Pr Pscrapie” (PrP<sup>Sc</sup>), named after the long-known sheep illness; in BSE and its human version, nvCJD, ingested PrP<sup>Sc</sup> converts the normal “cellular” form of PrP (PrP<sup>C</sup>) to an abnormal form (Lewis, 2001). Investigators are now seeking the site where prion pathogenesis begins; their work is converging on a little-mentioned resident of the intestinal lining called an M cell (Lewis, 2001). M cells, in Peyer’s patches, link the digestive and immune systems, provide a portal for ingested bacteria and viruses to lymphoid tissue beneath the intestinal lining, and some researchers (Beekes and McBride, 2000) believe PrP<sup>Sc</sup> traverse M cells to start development of orally-transmitted TSEs.

BSE is the most recently identified disease caused by these unique infectious proteins known as “prions” (Doyle, 2001). How rogue-protein prions originated and why animals became susceptible to them is not known. Perhaps, the original abnormal prion was from a

sheep with scrapie, or was mutated in a bovine animal (the “spontaneous rogue-protein prion generation” theory), or as has been recently suggested, was introduced into England by importation of Nyala or Kudu antelope from Africa (Wall Street Journal, 2001a). And, maybe, mineral imbalances or bad bacteria or improperly heated meat-and-bone meal in the feed, or inappropriate use of organophosphate pesticides compromised the immune system of some cattle, allowing the rogue-protein prion to gain a foothold—starting the spiral of BSE infections that were, almost certainly, spread from bovine to bovine (and, as it turns out, from cattle to meat, cats and people) by the feeding of ground-up cattle cadavers to living cattle (Smith, 2001b). Horn *et al.* (2001) have concluded that changes in rendering processes, use of meat-and-bone meal in starter calf diets and a relatively high proportion of sheep meat in rendered material probably combined to initiate the BSE epidemic in the UK.

There are two different isoforms of the prion involved in BSE: (a) The host encoded cellular prion protein ( $\text{PrP}^c$ ) that the brain makes naturally, and (b) The abnormal isoform ( $\text{PrP}^{\text{sc}}$ ) that causes the disease (Liemann and Glockshuber, 1998). There are two theories about how the  $\text{PrP}^{\text{sc}}$  actually causes the  $\text{PrP}^c$  to change (Raiden *et al.*, 2001): (1) The “conformational model,” which hypothesizes a slow change from  $\text{PrP}^c$  to  $\text{PrP}^{\text{sc}}$ , formation of a heterodimer and creation of two  $\text{PrP}^{\text{sc}}$  proteins, and (2) The “nucleation-dependent polymerization model” that hypothesizes that  $\text{PrP}^c$  is in thermodynamic equilibrium with a monomeric precursor, similar to  $\text{PrP}^{\text{sc}}$ , which acts as a nucleus to incorporate more  $\text{PrP}^{\text{sc}}$  precursors (Liemann and Glockshuber, 1998). Once present,  $\text{PrP}^{\text{sc}}$  acts as a crystal, inducing other normal prions ( $\text{PrP}^c$ ) to change their configuration, forming a precipitate that “clogs up” the cells in the brain (Klitzman, 1998).

We may never know the how or the why of what started this spiral, but this much, we now believe, we know (Smith, 2001a): (a) Prions are present normally as relatively straight molecules (with several  $\alpha$ -helical structures) in the brain, spinal cord, cornea, pituitary gland and nerve ganglia of cattle and people. (b) Rogue-protein prions are malformed, misfolded proteins that occur as bent, curved or widened molecules (with more  $\beta$ -sheet structures) that gain entry into the body through the tonsils or Peyer’s patches of the small intestine and are transported to the brain via the lymphatic system. (c) When rogue-protein prions enter the brain, these malformed prions convert normal prions into malformed prions. Smith (2001b) said “Imagine, if you will, a ballroom filled with people who are waltzing. A person enters the room, doing the twist. Every time the twister bumps into a waltzer, the waltzer starts doing the twist...and converting other waltzers to twisters. Because the malformed prions eventually aggregate (clump together) they collect in areas of the brain, kill the surrounding tissue and form holes.”

Evidence supporting the rogue-protein prion theory of BSE disease transmission among cattle and that BSE can be transmitted to humans (via consumption of beef or offal from BSE-infected cattle) causing nvCJD, but not classical CJD, is highly documented in the scientific literature (Scott *et al.*, 1999). A series of scientific papers, published from 1996 through 1999 (Will *et al.*, 1996; Lazmezias *et al.*, 1996; Collinge *et al.*, 1996; Hill *et al.*, 1997; Bruce *et al.*, 1997; Almond and Pattison, 1997; Scott *et al.*, 1999), provide incontrovertible evidence that: (a) nvCJD could be reproduced almost exactly in rhesus monkeys by inoculation with BSE prions; (b) the glycoform profile of the rogue-protein

prion from nvCJD cases was distinct from the prion of classical CJD and identical to that of the BSE prion; (c) nvCJD is indeed caused by the same agent that causes BSE and makes implausible any assertion that these observations are coincidental—nvCJD is human BSE, and; (d) mice injected with BSE prions developed the neurological disorder; prions from the diseased mice were injected into another group of mice and they too developed the disease. These findings argue unequivocally that BSE and nvCJD are caused by the same strain of rogue-protein prion.

Davenport (2001) reported that: (a) The sheep disease scrapie has been around for centuries without infecting humans but the strikingly similar mad cow disease (a progressive and ultimately fatal neurodegenerative condition) has apparently slipped from infected cattle into the human population. (b) Both scrapie and mad cow disease are almost certainly transmitted by an abnormally folded form of a protein, known as a prion. (c) Researchers are left with the problem of trying to figure out what determines whether a particular prion disease can spread from one species to another. (d) Research by Weissman and Chien (University of California at San Francisco) with yeast prions indicates that this species barrier can be overcome if the prion protein can adopt multiple structures and can thus interact with prion proteins from more than one species. (e) If something similar happens with the prion that causes mad cow disease, it might explain how it is able to cause disease in humans as well as cattle (Davenport, 2001).

How are BSE and nvCJD transmitted? Although it is generally believed that the BSE epidemic in the UK was a result of sheep scrapie prions surviving the rendering process and jumping species to cattle, a 2.5 year BSE Inquiry chaired by Lord Phillips argues against those hypotheses. New Scientist (2000a), in an article entitled ‘How It Went So Horribly Wrong,’ identified these key conclusions from the BSE Inquiry: (a) John Wilesmith realized BSE was spread by meat-and-bone meal (MBM) but erroneously thought it was the bovine form of scrapie and that changes in rendering processes allowed the scrapie agent to infect cattle. (b) Wilesmith’s theories were blithely accepted by many scientists and, because scrapie hadn’t posed problems in humans, it was wrongly assumed that BSE wouldn’t either. (c) Wilesmith’s conclusions were endorsed in 1989 by the Southwood Advisory Committee which said that BSE was unlikely to have any human health implications. (d) Reassurances were issued until March 20, 1996 by Chief Medical Officers that BSE could not spread to other species despite the fact that a Siamese cat developed a TSE in 1999. (e) Infectivity (a 0.5 gram dose was lethal) wasn’t recognized, Specified Bovine Offals illegally entered the human and animal food chains, and mechanically recovered meat from cow spines entered the human food chain through December 1995 (New Scientist, 2000a).

It is now believed (Brown, 2001a) that at some point in time—probably prior to 1970—cattle were given feed contaminated with rogue-protein prions; that feed most likely was, or contained, meat-and-bone meal (MBM) that was made from cadavers or other remains of sheep with scrapie, cattle with mutated prions or African antelope that had, or had died from, a TSE (Smith, 2001b). In nature, prion diseases are known to be transmitted orally and mutant genes may cause disease or an increased susceptibility to abnormal prions (Doyle, 2001). The incubation time (time required for malformed prions to convert enough normal prions to malformed prions to cause the neurological and physical symptoms of BSE)

was such (perhaps 8 to 15 years) that by the time enough “mad” cows were observed to establish a trend (in the early 1970s), the transmission cycle (feeding remains of a few cows that died of BSE to other cattle and thus infecting very many of them with BSE), the problem was out of control (Smith, 2001a). The spiral continued upward as newly infected cows were slaughtered, and brains and spinal cords were put back into animal feed; that feed was given to more cows, spreading the disease (Brown, 2001a).

The disease moved from cattle to humans when infected meat was cut-up, ground or processed (USA Today, 2001a); the vehicle could have been ground meat or sausage (which could have contained brains, spinal cords or the ileum portion of the small intestine) or it could have come from solid-muscle cuts contaminated by splitting the carcass (spreading spinal cord tissue in the process) or contaminated by butchers or meat cutters using sloppy techniques (e.g., some meat cutters in the UK purchase whole carcasses with the intact head attached, open the skull to extract and merchandise the brain—for breakfast food—and then proceed to fabricate the carcass into steaks, roasts and mince) without first cleaning their tools, cutting boards or equipment (New Scientist, 2000a, 2001b).

Professor James Ironside (vCJD Surveillance Unit, Edinburgh University) was quoted (National Meat Association, 2001e) as telling BBC Radio that there was “no clear explanation why people in the North of Britain appear to be more susceptible to BSE than people in the South; it may be genetics but it is more likely that Northerners just had more exposure to the disease by having eaten more pies and burgers containing low-grade meat.” “It is impossible to check this theory unless the food industry reveals which of its products contained low-grade meat” said Professor Ironside, “because the Spongiform Encephalopathy Advisory Committee has been continually thwarted, for 5 years, in its efforts to extract information from food companies about how much mechanically recovered meat (the meat that carries the most risk of passing on BSE) was used in the past” (National Meat Association, 2001e). Bill Jerney, President of the UK Meat Manufacturers’ Association, told the BBC that while they wished to cooperate, information on where exactly mechanically recovered meat had been supplied was not available (National Meat Association, 2001e).

Pathogenic prions are extremely resistant to heat and disinfectants, and the high concentration of pathogenic prions in central nervous system tissue makes it important to prevent these tissues from entering the food chain (Doyle, 2001). The difference in spread between BSE and nvCJD may be due to the fact that, in humans, recycling of infected tissue has not occurred, and thus the epidemic will evolve much more slowly than in cattle (Brown *et al.*, 2001). Estimated infectivity of bovine tissue containing BSE prions (FDA, 2001) is as follows: (a) One gram of nervous tissue contains 10 million infective doses of the BSE prion. (b) One gram of any of the spleen, lymph node or colon contains less than 25,000 infective doses of the BSE prion. (c) One gram of any of the pancreas, liver or lung contains less than 100 infectious doses of BSE prions. (d) One gram of any of muscle, bone or heart contains less than one-tenth of one infectious dose of BSE prions (FDA, 2001).

BSE popped up in herds all over England in 1988; by the year 2001, 180,500 cattle had been diagnosed with BSE in the UK, and other cattle with BSE had been discovered in

15 other European countries (Office International des Epizooties, 2001). In Great Britain, 106 probable and proven cases of nvCJD had been diagnosed through August 2001 (UK Department of Health, 2001) and 3 deaths due to nvCJD have occurred in other EU countries (Smith, 2001a).

Healy (2001) described the sequence of nvCJD development in a human, and its consequences, as follows: (a) Hovering silently within its victims for years, nvCJD hides in lymphoid tissue (tonsils, lymph nodes, spleens, Peyer's patches) and, at some point, within beta-lymphocytes, begins its explosive assault on the brain. This long silence raises the specter of undetected transmission to others via surgical instruments or blood transfusions. (b) Susceptibility seems limited to people with a homozygous methionine at the 129 codon of their prion gene (40% of the population). (c) We don't know how the infected prion commands host prion proteins to misfold and replicate millions of times, how it spreads to the brain and incites amyloid deposition, or why it causes seemingly indiscriminate neuronal cell death. (d) Without a blood test, scientists cannot predict whether human infection will be a small, geographically contained event or a global epidemic (Healy, 2001).

Fox (2001) said "The only surefire way now to test for BSE is to check an animal's brain after it has been killed. There is still no treatment for prion diseases, including BSE and nvCJD, but a reliable and sensitive diagnostic would permit the testing not only of cattle, but also of human blood products and tissues before they are used in medical procedures." At least six companies—Paradigm Genetics, Prion Developmental Labs, Boehringer Ingelheim, Genescan Europe AG, IDEXX Laboratories, Caprion Pharmaceuticals—are working to develop tests to detect BSE and/or nvCJD while the diseases are incubating—before physical symptoms occur (Hollingsworth, 2001; Barto, 2001; DeFrancesco, 2001; Giese, 2001).

In the meantime, it has been determined (New Scientist, 2000b) that people with other amino acids (methionine/valine or valine/valine) at the 129 codon of the prion gene are also susceptible to nvCJD—the incubation period just takes longer; and, Corinne Lasmezas, a scientist in France, has demonstrated primate-to-primate transmission of BSE via blood (Reuters, 2001). The death of a 74-year-old man in England from nvCJD raised the specter of some deaths in the elderly having been misdiagnosed as dementia (National Meat Association, 2001c). Meat Processing (2001b) reported that: (a) Older individuals are just as susceptible as younger people to contracting nvCJD, according to a new study published in Proceedings of the National Academy of Sciences. (b) Paul Brown (NIH) said "This is bad news, it makes you worry that, over the course of time, more people will come down with the disease." (c) Present estimates are that 1 million pounds of meat from BSE-infected cattle may have entered the food chain, and that up to 136,000 nvCJD cases may ultimately result from that meat. (d) It will be a while before we know how many cases will occur because nvCJD has an extremely long incubation period—from 5 to 10 years, or even longer (Meat Processing, 2001b).

New Scientist (2001a) recently reported that: (a) Mad cow disease scandals just don't stop. In a week when Great Britain recorded 6 new cases of nvCJD—the biggest real monthly increase so far—it has become clear that it most certainly inflicted the curse on the

rest of the world. (b) Great Britain continued to export animal feed made from ground-up remains of infected cattle long after it knew that the pellets spread BSE to other cattle; the rest of the EU was still exporting it in January 2001. (c) Great Britain insists that the feed was meant only for pigs and chickens but you can bet this message didn't reach farmers in places like Southeast Asia. Even restricting the feed to pigs and chickens may not be safe because these animals end-up in cattle feed and could pass the infection on. (d) Great Britain exported meat-and-bone meal (containing brains until 1991) from 1980 through 1996, to more than 80 countries; the rest of the EU more than trebled MBM exports during the 1980s to non-EU countries (New Scientist, 2001a). USA Today (2001b) reported that the first indication that MCD may have spread to Eastern Europe was reported on June 6, 2001 by agriculture officials in the Czech Republic; tests have not yet confirmed the disease which is suspected in a 6-year-old animal in Jihlava but the European Commission said in April that the Czech Republic is at risk of BSE because it has imported live cattle and MBM from EU countries. No MBM was exported to the U.S. between 1988 and 2001 (National Cattlemen's Beef Association, 2001b); it is believed that no MBM was exported to either Canada or Mexico during that same time period, but we are not certain that is correct (Smith, 2001b).

What measures are being taken to minimize risk that BSE will enter the U.S.? An agency of our federal government, the Animal and Plant Health Inspection Service (APHIS) of the U.S. Department of Agriculture (USDA), is charged with responsibility for preventing entry of Foreign Animal Diseases (FADs), including BSE, into our country and is especially vigilant regarding those FADs which would have potentially catastrophic effects on farm-animal populations, the agricultural economy and/or the public (human) health. Activities of APHIS specifically related to FADs include (USDA-APHIS, 2001a): (a) Guarding our borders against foreign agricultural pests and diseases through activities at U.S. ports and overseas in foreign countries. (b) Detecting and monitoring animal and plant diseases in this country. (c) Carrying out emergency operations if foreign pests or diseases get past our border defenses. Horn (2001) described our concerns about FADs as: (a) These diseases are common overseas. (b) Because these diseases are spread by natural means, constant efforts are needed to exclude their entry into the USA. (c) Our livestock would be unbelievably susceptible to these FADs. (d) An outbreak of an FAD would cripple agricultural trade, would be devastating economically and would have psychologically depressing societal effects.

According to American Meat Institute (2001), Beef Business Bulletin (2001a), Texas Cattle Feeders Association (2001a,b), National Cattlemen's Beef Association (2001b), Murphy (2001) and Lazar (2001a): (1) The U.S. has not imported beef from the U.K. since 1985; the U.S. has not imported ruminant animals or at-risk ruminant products from countries with confirmed cases of BSE since 1989. (2) More than 60 veterinary diagnostic laboratories throughout the U.S. participate in a BSE surveillance program with the National Veterinary Services Laboratory (Ames, IA). (3) In 1997, a Food and Drug Administration (FDA) regulation banned the use of at-risk, mammalian-derived animal protein byproducts in cattle feed (Meat Processing, 1997) to ensure that, if the rogue-protein prion causing BSE ever entered the U.S., it would be prevented from spreading through cattle feed. (4) In 1997, the USDA banned imports of all live ruminants and certain ruminant products from European countries until BSE is more fully understood. (5) In 1998, the USDA asked the School of

Public Health, Harvard University to analyze and evaluate the USDA's BSE prevention measures. (6) In 2000, APHIS prohibited all imports of rendered animal protein products, regardless of species, from Europe. (7) In 2000, the USDA issued a Declaration of Extraordinary Emergency, obtained some sheep from three flocks imported from Europe, euthanized these sheep and examined—diagnostically—their brains. (None had BSE.) (8) In 2000, APHIS prohibited all imports of rendered animal protein products from Europe, regardless of species. (9) In 2001, USDA seized the remaining sheep imported from Europe, euthanized them and examined their brains. (None had BSE; National Cattlemen's Beef Association, 2001b). (10) In 2001, President George Bush signed the Mad Cow and Related Disease Prevention Act of 2001 (S.700) which established an interagency task force with oversight by USDA Secretary Ann Veneman, to prevent the introduction of foreign animal diseases—particularly BSE and FMD—into the U.S. (11) In 2001, NCBA President Lynn Cornwell and Secretary Joaquin Ponce de Leon of the Confederacion Nacional Ganadera of Mexico signed an agreement expressing the intent of their organizations to keep North American free of FMD and other FADs. (12) In September 2001, as an outgrowth of the U.S/Mexico agreement, cattlemen's organizations from North and Central American countries (Belize, Costa Rica, Guatemala, Honduras, Panama, Canada, Mexico, USA) pledged to work together to ensure appropriate measures to prevent FADs are in place and enforced.

Salvage (2001) reported that BSE has not been detected in the U.S. and that the USDA says we have a “Triple Firewall System” in place to keep it out: (a) Firewall #1—A series of import bans dating back to 1985 ensures that no live cattle or at-risk cattle products are imported from any European country. (b) Firewall #2—FDA banned at-risk animal protein in cattle feed in 1997. (Feeding animal protein to cattle doesn't cause BSE unless the animal protein includes BSE prions, but the ban would keep the disease from spreading should it ever occur in the U.S.) (c) Firewall #3—USDA has had an active surveillance program for the past ten years that has found no sign of the disease in U.S. cattle herds (Salvage, 2001).

In February 2001, New Scientist (2001c), Fulmer (2001) and Dairy, Food and Environmental Sanitation (2001) identified several vulnerabilities relative to potential spread of BSE prions in the U.S.; included were concerns about: (a) Potential feed-mixing errors and MBM diversions. (b) Inadequate testing and surveillance, depending too much on farmers and abattoirs to report sick cows. (c) Related TSEs—scrapie in sheep and chronic wasting disease in deer and elk. With regard to item (a), above, American Feed Industry Association has developed a Facility Certification Institute to provide third-party certification for compliance with the federal government's mammalian protein regulation at feedmills (Feedstuffs, 2001b). Suppliers of ground beef products to McDonald's, Inc. require their packer suppliers to sign “letters of compliance” that the materials fed to cattle from which the meat is derived are in compliance with FDA, CFR 21 Part 589.2000 which prohibits the feeding of ruminant meat-and-bone meal to ruminant animals (National Meat Association, 2001f). Beef packing companies (North American Meat Processors Association, 2001) now require “producer-affidavits” attesting to the fact that slaughter cattle have not been fed MBM. With regard to item (b), above, Detwiler (2001b) said: (a) Through March 2001, USDA has examined 12,341 brains, largely from “fallen stock” (“downers”) but lately from

both downers and animals 20 months of age or older with “neurologically ill” symptoms. (b) From 1990 through 2001, the number of brains examined each year increased from 300, to 600, to 1,895, to 2,700, to 5,000. (c) Prior to 2000, we (USDA) could say “With this level of surveillance, we will find BSE if it occurs in the U.S. cattle population at a rate of 1.3 infected cows per thousand”; with the new surveillance plan proposed by USDA for 2002, “we will find it if BSE occurs in the U.S. cattle population at a rate of 0.15 infected cows per thousand” (Detwiler, 2001b). And, with regard to item (c) above, FDA has heightened efforts to learn more about CWD (Regaldo, 2001); and, USDA has instituted a National Sheep Scrapie Eradication Program (USDA-APHIS, 2001b). Because Jean Phillippe Deslys, a French scientist, has demonstrated that sheep scrapie can cause sporadic CJD (classical CJD but not nvCJD) in mice, he has surmised that the sheep scrapie prion may cause classical CJD in humans (New Scientist, 2001d).

What Can U.S. Beef Producers Do To Help Prevent Entry/Spread Of BSE?  
Producers must comply with the Food and Drug Administration (FDA) requirement that anyone feeding ruminant animals must save copies of invoices and labeling of all feed they receive that contains animal protein (National Cattlemen’s Beef Association, 2001a); feed that does not have an invoice or label from the manufacturer or distributor does not comply with the law, and the feed cannot be fed to cattle. National Cattlemen’s Beef Association (2001a) urges that: (a) Producers have written documentation from their feed suppliers that the premixes, supplements and complete feeds they buy are free of prohibited materials. (b) Cattle feeders/producers should consider buying feeds exclusively from feed mills that do not handle prohibited materials. While this is not a part of FDA regulations, NCBA believes this is a reasonable step to reduce the risk of prohibited materials being incorporated in premixes, supplements and complete feeds destined for cattle. Wren (2001) quoted Dr. Linda Detwiler of USDA-APHIS as responding to the question “What can the U.S. meat protein industry do to help prevent BSE from occurring?” with the answer “Compliance. Any person or company that imports products should strictly comply with the regulations for importation. Domestically, producers should comply with feed ban regulations, as they are critical. If we can learn nothing else from the situation in Europe, it is that compliance with live animal and feed ban regulations is essential.

What Can U.S. Packers And Processors Do To Help Prevent Entry/Spread Of BSE?  
Concern that the stunning of cattle with captive-bolt devices could, if used on an animal with BSE, cause embolism of infective brain tissue and, thus, contamination of the carcass and meat with BSE prions is supported by research of Bauer *et al.* (1996), Garland *et al.* (1996), Scientific Committee On Veterinary Measures Relating To Public Health (1998), Anil *et al.* (1999), Schmidt *et al.* (1999a), Love *et al.* (2000) and Horlacher *et al.* (2001). Garland *et al.* (1996) found visible pieces of brain tissue in the pulmonary arteries of 2.5 to 5.0% of cattle that had been stunned by use of a pneumatic captive-bolt device with a hollow bolt; after the hollow bolt entered the brain cavity, highly compressed air was blown through it—into the skull—destroying the brain structure. Anil *et al.* (1999) found no brain tissue particles in jugular veins after stunning cattle with a solid bolt, captive-bolt device but about 6% of cattle had brain tissue in their jugular veins if they were pithed (insertion of a long cylindrical cane through the opening in the skull, through the brain, and into the vertebral canal, to destroy the spinal cord) after stunning.

Schmidt *et al.* (1999a) concluded that potential for disruption of central nervous system (CNS) tissue when stunning beef cattle was greatest with pneumatic-powered air injection stunners, intermediate with pneumatic-powered stunners, and least—but present—with cartridge-fired stunners. Horlacher *et al.* (2001) found CNS tissue in 0.63% of cattle stunned with a mechanical captive-bolt device (the Schermer Stunner™) but, because the quantities of CNS were so small, they considered the human exposure risk to be slight. The Scientific Committee On Veterinary Measures Relating To Public Health (1998) concluded that: (a) BSE infectivity is, by far, the highest in the CNS of ruminants; less than 1 gram of infected brain can infect a cow by the oral route. (2) Because of “blow back” of brain tissue onto workers and into the slaughter premises, and the finding of fragments of brain tissue in the right-side heart and lungs with possible entry into the left side heart, arterial circulation and, hence, distribution throughout the carcass, we (the Committee) consider it wrong at present (February 17, 1998) to use pneumatic stunners with air injection in the slaughtering process of ruminants. Meat & Poultry (2001) reported that Patrick Boyle, president of the American Meat Institute (AMI), said “A 2001 survey demonstrated that no AMI member was using air-injected pneumatic cattle-stunning devices; in addition, stunner manufacturers ceased making air-injected pneumatic stunners in 1997.

Food Marketing Institute (FMI) which represents most of the U.S. supermarket industry, requested that the U.S. beef industry “establish a voluntary program to assure that bovine brain and spinal cord are not incorporated into products where they are not an expected ingredient”; National Meat Association and American Meat Institute co-signed a letter to FMI agreeing that such materials should not be found in products where consumers would not readily recognize their presence, and outlining a series of principles and Good Manufacturing Practices that will aid processors in avoiding pitfalls in this regard (National Meat Association, 2001d).

Troeger (2001) said “The usual slaughtering process for cattle very probably leads to the transfer of risk material, especially from the spinal cord, to the meat; this is, above all, the case when the spine is sawn lengthways. The most promising methods available at present for minimizing the risk appear to be in manual cattle-slaughtering, boning the entire carcass, either still warm or refrigerated (where necessary for reasons of meat hygiene law) with subsequent lengthways splitting of the boned spine, and—in industrial beef cattle slaughtering—extraction of the spinal cord by vacuum from the whole carcass followed by conventional sawing or completely sawing out the spine, including the spinal ganglia. Additional risk is incurred with captive bolt stunning and removing the head of the animal during slaughter.”

The disease agent (i.e., the BSE prion) has been found in brain tissue, the spinal cord and the retina of naturally infected cattle, and—in experimentally inoculated cattle—BSE infectivity has been demonstrated for the dorsal root ganglia, trigeminal ganglia, distal ileum and bone marrow (National Cattlemen’s Beef Association, 2001b). Detwiler (2001a) says “Specific procedures have been linked to humans contracting BSE from infected tissues, and include pneumatic stunning, advanced-meat-recovery systems, mis-splitting of carcasses (splitting that spreads contaminated tissues) and ingestion of high-risk tissues.” According to Heim (2001), the routine use in meat products (particularly sausage) of brain, trigeminal

ganglia, spinal cord, dorsal root ganglia, distal ileum, retina and, perhaps, bone marrow spread the disease in the U.K. Brown (2001b) concluded that the use of mechanically recovered meat contaminated with compressed spinal cord and paraspinal ganglia nervous tissue used in food for humans moved the BSE problem into the human population of the U.K. Hueston (2001b) identified the six meat products of greatest concern for BSE-prion contamination and—parenthetically—the possible contaminants in each as: (1) rib roast; t-bone steak (dorsal root ganglion), (2) bone-in meat (bone marrow), (3) mechanically recovered meat (spinal cord, dorsal root ganglion), (4) head meat (brain leak, trigeminal ganglion), (5) sausage casing (distal ileum) and (6) ground meat (brain, spinal cord). Lazar (2001b) said “BSE infectivity can be found in the brain, trigeminal ganglia, spinal cord, dorsal root ganglia, distal ileum, retina, and perhaps in bone marrow; that is why bone-in beef cuts such as t-bone steaks have been banned in the UK (Moore, 1997) and EU. European Commission (2001b) adopted a proposal on February 7, 2001 that was intended to further combat any risk related to exposure to BSE; it made obligatory the removal of the vertebral column from carcasses and meat of all cattle over 12 months of age at harvest and forbade use in food of mechanically recovered meat generated from any bone from a ruminant animal.

The presence of dorsal root ganglion, bone marrow and/or spinal cord as an inadvertent contaminant of meat may result from generation of advanced-meat-recovery tissues from the vertebral column (Schmidt, 2001; USDA-FSIS, 1998). Because then-current methods for detecting central nervous system (CNS) tissue in meat were cumbersome, time-consuming and costly, Schmidt *et al.* (1999b) used glial fibrillary acidic protein (GFAP), which is restricted to CNS tissue, in an enzyme-linked immunosorbent assay (ELISA) for the detection of CNS tissue in blood and muscle from cattle. In the latter study, no GFAP was detected in skeletal muscle, trace amounts were present in the sciatic nerve and high levels of GFAP were present in spinal cord, cerebral cortex and whole brain (Schmidt *et al.*, 1999b). In a subsequent study (Schmidt *et al.*, 2001), less than 1 nanogram of GFAP per milligram of tissue was found in most subprimals and advanced-meat-recovery product; occasional samples contained higher levels of GFAP, probably because of contamination by the carcass-splitting saw, incomplete removal of the spinal cord, or a chance sampling of a major nerve.

Actions that have been taken by U.S. packers and processors (Schmidt, 2001; Rucks, 2001) to reduce potential for presence of BSE prions in beef products include: (a) Packers—Prohibited use of air-injection cattle stunners; much more careful carcass splitting; use of spinal cord removal (from beef sides and cuts) procedures employing vacuuming, scraping and Jarvis powered spinal-cord removers. (b) Packers—“Zero Tolerance” standard operating procedures (SOPs) for spinal cord; continuous monitoring, ink-marking and redirecting (to inedible use) of mis-split vertebrae; verification as part of in-plant Good Manufacturing Practices (GMPs). (c) Packers—Two inspectors of the raw material that enters advanced-meat-recovery equipment; routine analysis for glial fibrillary acidic protein (GFAP) in finished goods. (d) BPI, Company—Prohibited all bones as raw material; routine testing for GFAP; changed product name from “Lean Finely Textured Beef” to “Lean Beef Trimmings” (Schmidt, 2001; Rucks, 2001). National Meat Association (2001g) has released “Good Manufacturing Guidelines” for the removal of spinal cord during slaughter operations and

sampling and testing of advanced-meat-recovery product for glial fibrillary acidic protein analysis.

What Can Be Done By Those In The U.S. Beef Industry—In General—To Minimize Presence/Spread Of BSE? Smith (2001e) identified the following Critical Control Points (CCPs) for implementation by those in the beef industry to minimize risk of having and/or spreading rogue-protein prions that cause BSE, in beef tissues and products: (1) Assure, absolutely, that cattle are not fed meat-and-bone meal. (2) Do not allow use of air-injection cattle stunning devices. (3) Assure complete removal of the spinal cord from beef carcasses. (4) If tissues recovered by use of advanced-meat-recovery (AMR) equipment are generated or purchased, do not use tissues recovered from the vertebral column. (5) If AMR tissues or Lean Finely Textured Beef (LFTB) tissues are to be purchased and used, secure affidavits from suppliers regarding which raw materials are, or are not, to be used as sources of these tissues and randomly test tissues for presence of glial fibrillary acidic protein (GFAP)—a substance found uniquely in central nervous system cells—for validation. (6) Have an individual animal identification (IAID) “traceback” system in place, so that, if the anomaly of BSE occurs, it can be contained (Smith, 2001e).

Texas Cattle Feeders Association (2001c) announced that the USDHHS will expand its efforts to keep BSE out of the U.S. while stepping up surveillance and research at home. The plan is composed of four parts: (1) Surveillance; the Centers for Disease Control and Prevention will enhance its current program to identify and investigate possible causes of nvCJD and will increase its technical assistance to state and local health personnel. To date, no cases of nvCJD have been diagnosed in the United States. (2) Protection; FDA and USDA will review and expand import inspection programs and the animal feed inspection program. FDA will also continually review and upgrade policies to prevent potential exposure to nvCJD and similar diseases through blood transfusion and tissue transplantation. (3) Research; the National Institutes of Health will more than double current spending for research on diseases like BSE and nvCJD by the end of fiscal 2002. (4) Oversight; USDHHS will take any steps necessary to assure the public with timely, accurate and thorough information about the potential threats of BSE and nvCJD and about the actions each agency is taking to protect the public from these threats.

What is the general prospect of BSE occurring in cattle in the United States? Groppe (2001) said “A panel of animal health experts told a U.S. Senate subcommittee (on April 4) that the chance of a Mad Cow Disease outbreak in the United States is extremely rare.” Smith (2001c,d) said “Having recently spoken to Dr. Will Hueston (University of Minnesota), who is one of the most respected experts on the subject: (a) I do not believe we will have a BSE outbreak within the next 12 months, and perhaps never, and (b) If either BSE or nvCJD does occur in the U.S. during the next year, or ever, I believe the response to the incident by those in industry and government will be so rapid that it will be of minimal consequence to the livestock industry, but of variable consequence to the meat and food industries—depending on how the media reports the incident and how consumers react to such reports.”

What have been the consequences of the BSE outbreak in the European Union? Meat Processing Global (2001) reported that EU Agriculture Commissioner Franz Fischler

reported that beef consumption in the EU is down 25% (comparing October 2000 vs. March 2001 data) and that EU export performance is down to 10,000 to 15,000 tonnes per week; he said “Coping with the BSE crisis or FMD separately would already be an enormous challenge for the European agriculture sector. Now they are striking at the same time. And, the silver lining on the horizon of the beef market might turn out to be an illusion if consumers turn their back on meat altogether.” At the time of Fischler’s report, in June 2001, changes in EU beef consumption by country ranged from highs of –60% (Germany), -42% (Italy), -35% (Spain) and –30% (Greece and Luxembourg), to lows of 0% (Denmark, Netherlands, Ireland, Finland and Sweden) and +3% (United Kingdom) with the latter (+3% in the UK) suggesting no negative effect of the February 2001 outbreak of FMD in the UK on beef consumption (Meat Processing Global, 2001; U.S. Meat Export Federation, 2001b).

EU farm commissioner Franz Fischler announced that, after falling sharply following BSE, FMD and other food crises, beef consumption in EU countries is showing signs of increasing (Meat Processing, 2001c). Demand for beef in the EU was (in October, 2001) about 5.7% below levels of a year ago but much improved (e.g., five-fold better in Germany and, actually up 3% in Britain) over the low ebb—at the height of the FMD crisis—in the first few months of 2001 (Meat Processing, 2001c). Associated Press (2001) reported in late December that retail sales of beef rose 1.8% in Britain during calendar year 2001.

If BSE were to breach our defenses, how damaging could this be to the U.S. meat supply and what would be the impact on consumer buying decisions? An example of the catastrophic effects on domestic and export demands for beef that can result from occurrence of BSE (4 cases have been discovered) in a country occurred in Japan during 2001 (National Meat Association, 2001a). Japan announced on September 10, 2001 that a Holstein dairy cow tested positive for MCD in an area near Tokyo. Three weeks later, Junichiro Koizumi (Japan Prime Minister) said: “People are saying they don’t want to even eat safe beef products. This is a frightening thing!” Confusion over the disposal of the infected cow, which was ground into meat-and-bone meal (MBM), deepened consumer mistrust, with some 2,000 schools nationwide clearing beef from their lunch menus. Widespread news coverage of the BSE outbreak has taken a toll on the shares of some restaurant chains, as well as beef prices and sales in Japan, possibly denting the outlook for its Kobe beef exports. Photographs have circulated of workers standing next to literally tons and tons of unused beef product (National Meat Association, 2001a). Domestic prices for beef in Japan have fallen about 60% (Reuters, 2001). And, Clayton (2001) reported that demand for U.S. beef in Japan has declined by 50%. Meat Processing (2001d) reported that major Japanese supermarket chain beef sales in October were down 70% from a year earlier and that U.S. beef exports to that country had dropped 50% since the BSE crisis reached Japan. Several meat industry groups are urging USDA to include a “BSE-free” statement on all export certificates issued for shipments of U.S. beef for Japan; belief is that appropriate language would assist in restoring confidence in U.S. beef (Southwest Meat Association, 2001). U.S. Meat Export Federation has requested \$8 million to conduct a consumer promotion in Japan aimed at restoring confidence in U.S. beef (Beef Business Bulletin, 2001b).

The lesson learned from the BSE incident in Japan (National Meat Association, 2001a) was the extent of the danger associated with feeding at-risk animal protein (meat-and-bone meal) imported from a country that had an epidemic of mad cow disease. Obviously, traffic across the borders of the USA from Canada or Mexico creates opportunities for inadvertent entry of FAD-infected foods that could trigger potentially catastrophic effects on our food-animal and human populations; Horn (2001) reported that, in 1999, 475 million people, 125 million vehicles and 21.4 million import shipments crossed U.S. borders.

Smith (2001c) reported that “We do not believe we have BSE in the USA and we have not had a human death attributable to nvCJD. The federal government has erected three firewalls to preclude entry, and prevent spread—if it does occur—of BSE: (1) The U.S. bans cattle and beef products from countries where BSE has been detected. (2) The U.S. bans the feeding of certain animal products back to animals. (3) The U.S. has a surveillance program that includes examination of brain tissue from suspected animals.” Chandler (2001) reported that Dr. George Gray (School of Public Health, Harvard University) said “Mad Cow Disease is not likely to occur here. And, even if it does occur, it is virtually impossible to imagine how we could have a UK-like epidemic. So long as brain, spinal cord and ileum (which carry the rogue-protein prions of BSE) are carefully avoided, only small incremental changes in government policy and regulations will be needed.” Gray (2001) reiterated those conclusions in late 2001 and said the final report of their risk assessment would be released in the next few months.

“Mad Cow Disease has not been detected in the USA, but more than half of Americans are afraid it will be” said a USA Today (2001c) poll of 1,015 adults. Ninety-six percent of those polled had heard of the disease; of those, 36% were “somewhat concerned” and 29% were “very concerned” that the disease will become a problem in the USA. Feedstuffs (2001a) reported that fully 60% of American consumers now say they are concerned that BSE may breach all firewalls in the U.S. and get into the American cattle herd and beef supply” said a Roper Starch Worldwide survey for Gardenburger, Inc. Fifteen percent of American consumers said they already have reduced their beef consumption and 3% have stopped eating beef entirely; 76% of American consumers said they would reduce or stop their beef consumption if the disease was even suspected in the U.S. herd (Feedstuffs, 2001a). A Wall Street Journal/Harris Interactive Poll of 2,584 people (Wall Street Journal, 2001b) asked respondents several questions about MCD, FMD and beef consumption; findings were that: (a) 49% said their beef consumption had decreased over the past 10 years. (b) 98% had heard of MCD, 77% had heard of FMD and 2% had heard of neither MCD nor FMD. (c) Of those who had heard of MCD, 11% said they were “very” familiar with it, 19% said they were “very” concerned about the possibility of MCD spreading to the U.S. and 19% said “I eat less beef” because of knowing about MCD (Wall Street Journal, 2001).

An April 2001 Porter Novelli consumer survey revealed consumer misconceptions about BSE and FMD that may be having an impact on purchases of beef and other animal products, and reported (Render, 2001b) that, among primary food shoppers: (a) 14% said they had changed their food purchase or eating habits based on reports about BSE or FMD they had recently seen or heard. (b) 80% and 71%, respectively, said they would eliminate or reduce ground beef in their diet if BSE or FMD, respectively, were found in U.S. livestock.

(c) 19% incorrectly thought that BSE and FMD were the same. (d) 27% incorrectly thought there was a direct link between BSE and FMD. (e) 46% incorrectly thought that cows with FMD could infect humans (Render, 2001b).

Would an actual outbreak of BSE—or even concern about such outbreak—have the eventual impact of promoting greater use of food safety programs throughout the meat supply chain?” Hueston (2001a) has said that “Healthy livestock is the basis for a safe food supply.” Drovers Journal (2001) reported that the case is made that U.S. beef consumption could drop by 50% and major export markets (U.S. beef export values, including variety meats, totaled more than \$4 billion in 2000) could suddenly close if either BSE or FMD were to occur in this country. Because these diseases have wreaked such havoc in other parts of the world, it is imperative that we do everything possible to prevent entry into the U.S. But, if they do, what will be the most valuable arrow in our quiver to minimize spread of the disease? It is “traceability” (Smith, 2001a).

Stanley (1999) reported that fears about BSE and its link to the fatal human brain ailment, nvCJD, have caused Britain to require that: (a) Each cow, bull and calf in Britain must have a “passport”—a barcode and two identification tags (one attached to each ear). (b) Farmers can’t sell cattle that are more than 30 months old. (c) Meat packers can no longer sell organs and fat for use in animal feeds for domestic use. (d) Meat packers must get a special permit to prepare beef for export. (e) Farmers spend two hours each day—at a personal computer—updating data on the weight, diet, health, movement and reproductive habits of each animal in the herd (Stanley, 1999).

Smith (2001a) reported that: (a) Traceability, or trace-back, in this context refers to the ability to identify the source of meat from farm-to-fork and/or from fork, back to the farm on which the animal source originated. (b) It is now possible to follow cattle, through harvest, to the carcass form by using retinal scanning, plastic/metal tags and trolley-tracking. (c) It is more difficult to follow carcasses through fabrication (into primal/subprimal cuts and trimmings), distribution and retail-cut preparation in foodservice and supermarket operations. (d) Meat at retail can though—as is being done in Ireland, New Zealand and Australia—be traced back to carcasses of origin by use of DNA-fingerprinting technology (Smith, 2001a).

Meghen (2001) described DNA traceability of meat as follows: (a) The integrity of the food chain is now a dominant issue for consumers, and of necessity therefore also for regulators, producers, processor and retailers. (b) Because of the BSE crisis, this has been most sharply felt in the beef sector; at the center of any response is the idea of product traceability. (c) Using DNA, it is possible for a meat processor to guarantee to the retailer, and for the retailer to guarantee to the consumer, traceability to the source of origin of all meat products. (d) Because the product becomes in effect, its own label, the need for proliferating paper chains and changes in work practices can be avoided (Meghen, 2001).

The Scientific Steering Committee (SSC) of the European Commission (2001a) has recently developed a “Rapid Response” program of action, in the event that BSE occurs in the sheep population of the EU; included in that program are: (1) An EU-wide culling program. (2) A long list of BSE-risk parts which should be removed from carcasses. (3)

Culling of all suspect animals, their offspring, all traceable relatives and all animals with TSE susceptibility in the affected and contact flocks. “Traceability of individual animals is an essential part of the plan, hopefully also enabling identification of the parents; certification of flocks as TSE-free would then be possible” (Fleischwirtschaft International, 2001).

Where Are We On A Test For “Incubating” (In Cattle Or Humans) BSE And/Or nvCJD? Shaked *et al.* (2001) reported that a protease-resistant PrP isoform can be detected in the urine of hamsters, cattle and humans suffering from TSEs. Most important, this PrP isoform (UPrP<sup>sc</sup>) was also found in the urine of hamsters inoculated with prions long before the appearance of clinical signs. Shaked *et al.* (2001) propose that the detection of UPrP<sup>sc</sup> can be used to diagnose humans and animals incubating prion diseases.

Where Are We On A Cure For nvCJD? Researchers at the University of California at San Francisco, led by Stanley Prusiner, are studying use of quinacrine and chlorpromazine—drugs presently used to treat malaria and schizophrenia in human patients—on two patients (one American; one British) who are terminally ill with nvCJD (Meat Processing, 2001a).

What Is The Position Of The U.S. Beef Industry Relative To BSE? National Cattlemen’s Beef Association (2001b) said: (1) BSE has not been identified in the United States. (2) USDA has monitored cattle in the U.S. for 10 years and has tested 11,700 brain specimens from cattle displaying any neurological symptoms that might indicate BSE. All tests have been negative. (3) CDC examined 94 deaths due to CJD that occurred between 1991 and 1995, including clinical and neuropathological review of 9 cases in patients under the age of 55. There was no indication of nvCJD. (4) University of California at San Francisco separately evaluated 67 CJD brain specimens between 1991 and 2000. There was no sign of nvCJD in any brain specimen. (5) CDC continues national surveillance of CJD cases in patients less than 55 years of age. (6) CDC and the American Association of Neuropathologists have established a National Prion Disease Pathology Surveillance Center. No cases of nvCJD have been detected in the United States (National Cattlemen’s Beef Association, 2001b).

The BSE risk assessment study commissioned by USDA and conducted by the Harvard Center for Risk Analysis was released in December 2001; results (Meat & Poultry, 2001) revealed that: (a) The risk of BSE occurring in the U.S. is extremely low. (b) Early protection systems put into place by USDA and USDHHS have been largely responsible for keeping BSE out of the U.S. and would prevent it from spreading if it ever did enter the country. (c) George Gray (Deputy Director, Harvard Center for Risk Analysis) said “Based on three years of study, we are confident BSE will not become an animal or public health problem in America.” (d) “We found that even if BSE were ever introduced, it would not become established” said Dr. Gray “with the government programs already in place, even accounting for imperfect compliance, the disease in the cattle herd would quickly die out, and the potential for people to be exposed to infected cattle parts that could transmit the disease is very low” (Meat & Poultry, 2001). In response to the report, USDA Secretary Ann Veneman said “The study clearly shows that the early actions taken by the federal government to safeguard consumers have helped keep BSE from entering the U.S.; even if BSE were to ever be introduced, it would be contained, according to the study. However, we cannot let down

our guard or reduce our vigilance. We must continue to strengthen these critical programs” (Meat & Poultry, 2001).

In response to release of results of the Harvard BSE risk assessment study, USDA Secretary Ann Veneman announced a series of actions USDA will take, in cooperation with USDHHS, to strengthen its BSE prevention programs and maintain the government’s vigilance against the disease (Meat & Poultry, 2001); these actions are: (1) USDA will have results of the Harvard BSE risk assessment study peer-reviewed to ensure its scientific integrity. (2) USDA will double the number of BSE tests it will conduct this fiscal year, with over 12,500 cattle samples targeted in 2002, up from 5,000 in 2001. (3) USDA will publish a policy options paper outlining additional regulatory actions that may be taken to reduce the potential risk of exposure and to ensure potential infectious materials are kept out of the U.S. food supply. Options to be considered will include prohibiting the use of brain and spinal cord, from specified categories of animals, in human food; prohibiting the use of CNS tissue in boneless beef products, including meat, from advanced-meat-recovery (AMR) systems; and prohibiting the use of vertebral column from certain categories of cattle, including downed animals, in the production of meat from AMR systems. (4) USDA will issue a proposed rule to prohibit the use of certain cattle-stunning devices. (According to AMI, USDA will propose a ban on use of air-injected pneumatic stunners.) (5) USDA will publish an advance notice of proposed rulemaking to consider additional regulatory options for the disposal of dead stock on farms and ranches because such cattle are considered a potential pathway for the spread of BSE in the animal chain (Meat & Poultry, 2001).

Consumer confidence that U.S. beef is safe from BSE rose to a record high 89% in December, while consumer awareness of BSE in the U.S. dropped over the last six months (Beef Business Online, 2002a). A previous survey found that in July 2001 nearly nine of 10 respondents had heard something about “mad cow disease” in the previous month; in December 2001, that figure had dropped to 70%—but was still higher than the 58% awareness measured in December 2000. Despite a higher awareness of BSE than a year ago, the number of respondents who said they were confident that U.S. beef is safe rose from 82% in December 2000 to 89%. National Cattlemen’s Beef Association said: (a) These results suggest that the triple firewalls of import bans, active surveillance and the ban on feeding ruminant-derived protein supplements to ruminants have been effective in preventing BSE problems in the U.S., and (b) A comprehensive, three-year risk analysis study by Harvard University recently confirmed the effectiveness of the prevention and risk management programs in the U.S. (Beef Business Online, 2002a).

Beef Business Online (2002b) announced that cattlemen have answered a challenge grant for BSE research from the McDonald’s Corporation with a \$600,000 investment of their own. The McDonald’s Corporation on December 13, 2001 announced that it had awarded a \$500,000 challenge grant to the National Cattlemen’s Foundation for BSE research. “While a recent report from Harvard said the U.S. was at low risk for a BSE outbreak, cattlemen and allied industries must move to strengthen the proven firewalls,” said National Cattlemen’s Foundation President Don Butler, “this grant is important for research initiatives that continue to keep American BSE-free” (Beef Business Online, 2002b).

The U.S. position is, then, that: (a) We have never had a case of BSE in our cattle population; we have never had a case of nvCJD in our resident human population. (b) We are exceptionally vigilant—searching for evidence of occurrence of either disease. (c) If BSE occurs in our cattle supply, we will quickly find it and eliminate it. And, we will prevent its prions from infecting those who eat our beef. (d) We are taking every precaution to prevent its occurrence in our cattle, to identify affected cattle before their products enter the food supply, and—if it is present and we don't yet know it—to prevent its spread to our cattle or people.

## REFERENCES

Acheson, D. 2001. Yooo Are What I Eat. *Food Quality* 8:22-33.

Almond, J. and J. Pattison. 1997. Human BSE. *Nature* 389:437-438.

American Meat Institute. 2001. Questions And Answers On Bovine Spongiform Encephalopathy (BSE). Memorandum for AMI Members, January 23.

Anil, M., S. Love and S. Williams. 1999. Potential contamination of beef carcasses with brain tissue at slaughter. *Veterinary Record* 145:460-462.

Associated Press. 2001. Beef Sales Within Britain Up 1.8% For The Year. (December 28 Issue).

Barto, D. 2001. On Patrol For BSE. *Beef* (September Issue).

Bauer, N.E., T. Garland and J.F. Edwards. 1996. Brain emboli in slaughtered cattle. *Veterinary Pathology* 33:600.

Beef Business Bulletin. 2001a. Countries Will Work To Prevent Foreign Animal Diseases. (September 28 Issue).

Beef Business Bulletin. 2001b. USMEF Seeks \$8 Million For Promotion. (November 23 Issue).

Beef Business Online. 2002a. Consumers Remain Confident That U.S. Beef Is Safe. [http://www.beef.org/bbbonline/2001\\_stories/0112\\_archives/0112\\_21a.htm](http://www.beef.org/bbbonline/2001_stories/0112_archives/0112_21a.htm)

Beef Business Online. 2002b. McDonald's Contributes To BSE Research. [http://www.beef.org/bbbonline/2001\\_stories/0112\\_archives/0112\\_21b.htm](http://www.beef.org/bbbonline/2001_stories/0112_archives/0112_21b.htm)

Beekes, M. and P.A. McBride. 2000. Early accumulation of pathological PrP in the enteric nervous system and gut-associated lymphoid tissue of hamsters orally infected with scrapie. *Neuroscience Letters* 278:181-184.

Belay, E.D. 1999. Transmissible Spongiform Encephalopathies In Humans. Annual Reviews of Microbiology.

Brown, P. 2001a. Bovine Spongiform Encephalopathy And variant Creutzfeldt-Jakob Disease. British Medical Journal 322:841-844.

Brown, P. 2001b. Human Health: What Is nvCJD And How Did It Happen? Presented at the BSE Briefing, sponsored by the American Meat Institute Foundation (Washington, DC).

Brown, R., R.G. Will, R. Bradley, D.M. Asher and L. Detwiler. 2001. Bovine Spongiform Encephalopathy And variant Creutzfeldt-Jakob Disease: Background, Evaluation And Current Concerns. CDC Emerging Infectious Diseases. 7:1-17.

Bruce, M.E., R.G. Will, J.W. Ironside, I. McConnell, D. Drummond, A. Suttie, L. McCardle, A. Chree, J. Hope, C. Birkett, S. Cousens, H. Fraser and C.J. Bostock. 1997. Transmissions To Mice Indicate That 'new variant' CJD Is Caused By The BSE Agent. Nature 389:498-501.

Chandler, D.L. 2001. Study: U.S. Mad Cow Outbreak Is Unlikely. The Boston Globe. (February 6 Issue).

Clayton, P. 2001. Personal Communication. (Paul Clayton is a Vice President of the U.S. Meat Export Federation, Denver, CO).

Collinge, J., K.C. Sidle, J. Meads, J. Ironside and A.F. Hill. 1996. Molecular Analysis Of Prion Strain Variation And The Aetiology Of 'new variant' CJD. Nature 383:685-690.

Dairy, Food and Environmental Sanitation. 2001. FAO: Countries Around The World Should Be Concerned About "Mad Cow Disease" And Should Take Action To Reduce And Prevent Risks. Dairy, Food and Environmental Sanitation 21:216-217.

Davenport, R.J. 2001. Getting Yeast Prions To Bridge The Species Gap. Science 291:1881.

Dealler, S.F., and R.W. Lacey. 1990. Transmissible Spongiform Encephalopathies: The Threat Of BSE To Man. Food Microbiology 7:253-279.

DEFRA. 2001. BSE Statistics. Department of Environment, Food and Rural Affairs. United Kingdom. <http://www.doh.gov.uk/cjd/>

DeFrancesco, L. 2001. Quickening The Diagnosis Of Mad Cow Disease. The Scientist. (June 11 Issue).

Detwiler, L. 2001a. The U.S. Government Response: BSE Surveillance And Response. Presented at the BSE Briefing, sponsored by the American Meat Institute Foundation (Washington, DC).

Detwiler, L. 2001b. Personal remarks made during a conference call organized by National Meat Association in April. (Dr. Detwiler is an official of USDA-APHIS, Washington, DC).

Doyle, D. 2001. Bovine Spongiform Encephalopathy—Scientific Literature Review. Food Research Institute, University of Wisconsin, Madison, WI.

Drovers Journal. 2001. Keeping Devastating Diseases At Bay, Everyone's Help Is Needed To Prevent Foreign Animal Diseases From Entering The United States. (January Issue).

Ebringer, A., C. Thorpe, J. Pirt, C. Wilson, P. Cunningham and C. Ettelaie. 1997. Bovine Spongiform Encephalopathy: Is It An Autoimmune Disease Due To Bacteria Showing Molecular Mimicry With Brain Antigens? Environmental Health Perspectives 105:1172-1174.

European Commission. 2001a. Rapid Response Program Of Action In The Event That BSE Occurs In The Sheep Population Of The EU. Scientific Steering Committee of the European Commission. (May Release).

European Commission. 2001b. BSE Controls In The European Union.  
[http://www.europa.eu.int/comm/dgs/health\\_consumer/library/press/press106\\_en.html](http://www.europa.eu.int/comm/dgs/health_consumer/library/press/press106_en.html)

FDA. 2001. Estimating Risks For vCJD In Vaccines Using Bovine-Derived Materials.  
<http://www.fda.gov/cber/bse/risk.htm>

Feedstuffs. 2001a. Consumers Worry About BSE In U.S. Herd. (March 12 Issue).

Feedstuffs. 2001b. AFIA Announces Facility Certification Institute. (March 19 Issue).

Fleischwirtschaft International. 2001. Traceability And Certification Of TSE-Free Flocks. (May Issue).

Food Processing. 2001. Clinical Signs Of BSE; Causative Agent Of BSE. (March Issue).

Fox, M. 2001. Companies Race to Develop Better Mad Cow Disease Test. Reuters Science News. (February 5 Issue).

Franco, D.A. 2001. BSE: Just The Facts. Render. (June Issue).

Fulmer, Melinda. 2001. "Mad Cow" Risk Tiny But Real, Experts Say. Los Angeles Times (February 20 Issue) pp. A1, A6.

Garland, T., N. Bauer and M. Bailey. 1996. Brain emboli in the lungs after stunning. Lancet 348:610-612.

Giese, J. 2001. It's A Mad, Mad, Mad, Mad Cow Test. Food Technology 55:60-62.

- Gray, G. 2001. Analysis Of The Harvard Risk Assessment. Proc. 2001 Meat Industry Research Conference (Chicago, IL). pp. 9-18.
- Groppe, M. 2001. Mad Cow Disease Unlikely In US, Expert Tells Congress. Gannett News Service, The Coloradoan. (April 5 Issue).
- Healy, B. 2001. vCJD: Broad U.S. Response Required. Science 291:1859.
- Heim, D. 2001. The European Situation: What Happened And Why? Presented at the BSE Briefing, sponsored by the American Meat Institute Foundation (Washington, DC).
- Hill, A.F., M. Desbruslais, S. Joiner, K.C.L. Sidle, I. Gowland, J. Collinge, L.J. Doey and P. Lantos. 1997. The Same Prion Strain Causes vCJD And BSE. Nature 389:448-450.
- Hollingsworth, P. 2001. Hot Topics Address Today's Issues. Food Technology 55:61-68.
- Horlacher, S., E. Lucker, E. Eigenbrodt and S. Wenisch. 2001. Kontamination der Rinderlunge mit ZNS. Proc. 41. Arbeitstagung des Arbeitsgebietes Lebensmittelhygiene, Teil I; Vortrage 168-173. Deutsche Veterinarmedizinische Gesellschaft e. V. Gieben (cited by Klaus Troeger, Fleischwirtschaft International 2/2001:49-51).
- Horn, F. 2001. Bio Security And Animal Disease. Proc. 2001 Meat Industry Research Conference (Chicago, IL). pp. 21-22.
- Horn, G., M. Bobrow, M. Bruce, M. Goedert, A. McLean and J. Webster. 2001. Review Of The Origin Of BSE. <http://www.defra.gov.uk/animalh/bse/bseorigin.pdf>
- Hueston, W. 2001a. Bovine Spongiform Encephalopathy: Update. Presented at the Annual Meat Marketing Conference (Charlotte, NC).
- Hueston, W. 2001b. The U.S. Situation: It's Not Here, Why? Presented at the BSE Briefing, sponsored by the American Meat Institute Foundation (Washington, DC).
- Klitzman, R. 1998. The Trembling Mountain: A Personal Account Of Kuru, Cannibals And Mad Cow Disease. Plenum Trade Publishing, New York, NY.
- Lazar, V. 2001a. Should You Worry About BSE? Meat Processing. (February Issue).
- Lazar, V. 2001b. What To Say About BSE? Meat Processing. (May Issue).
- Lazmezas, C.I., J.P. Deslys, R. Demaimay, I.T. Adjou, F. Lamoury, D. Dormont, O. Robain, J. Ironside and J.J. Hauw. 1996. BSE Transmission To Macaques. Nature 381:743-744.
- Lewis, R. 2001. Portals For Prions? Investigators Look At Potential Pathway For Prions. The Scientist 15:1, 21-23.

Liemann, S., and R. Glockshuber. 1998. Transmissible Spongiform Encephalopathies. *Biochem. Biophys. Research Communications* 250:187-193.

Love, S., C.R. Helps, S. Williams, A. Shand, J.L. McKinstry, S.N. Brown, D.A. Harbour and M.H. Hanil. 2000. Methods For Detection Of Haematogenous Dissemination Of Brain Tissue After Stunning Of Cattle With Captive Bolt Guns. *J. Neuroscience Methods* 99:53-58.

Marieb, E.N. 1998. Fundamentals Of The Nervous System And Nervous Tissue. pp. 362-400. In: *Human Anatomy & Physiology*. 4<sup>th</sup> Ed. Benjamin/Cummings Publishing Company, Menlo Park, CA.

Meat & Poultry. 2001. Assessment Indicates Risk Of BSE Occurring In US Is Low. (December Issue).

Meat Processing. 1997. FDA Bans Mammalian Protein From Feed. (July Issue).

Meat Processing. 2001a. Drugs May Combat BSE-Type Disease In Humans. (September Issue).

Meat Processing. 2001b. Elderly At Risk For vCJD. (April Issue).

Meat Processing. 2001c. European Beef Consumption Recovering. (December Issue).

Meat Processing. 2001d. Dashed Hopes For U.S. Beef Exports. (December Issue).

Meat Processing Global. 2001. EU Beef Consumption Falls By 25 Per Cent. (May/June Issue).

Meghen, C. 2001. DNA Traceability Of Meat. Monograph prepared by IdentiGEN, Ltd. Smurfit Institute of Genetics, Trinity College, Republic of Ireland. pp. 1-9.

Moore, E. 1997. Butchers Have Beef With Ban: British Mad Cow Fears Lead Government To Halt Sale Of Meat Bearing Bone. *Houston Chronicle* (September 11 Issue).

Murphy, D. 2001. U.S., Latin American Cattlemen Cooperating On FMD, BSE Prevention. [www.meatingplace.com](http://www.meatingplace.com)

National Cattlemen's Beef Association. 2001a. FMD & BSE: What Every Producer Needs To Know. National Cattlemen's Beef Association, Englewood, CO.

National Cattlemen's Beef Association. 2001b. CJD, BSE, vCJD Information. National Cattlemen's Beef Association, Englewood, CO.

National Meat Association. 2001a. Japan BSE Worries Grow. *NMA/Lean Trimmings*. (October 1 Issue).

National Meat Association. 2001b. BSE Update. NMA/Lean Trimmings. (June 18 Issue).

National Meat Association. 2001c. First Elderly vCJD Victim. NMA/Lean Trimmings. (April 30 Issue).

National Meat Association. 2001d. NMA, AMI Respond To FMI Request On BSE. NMA/Lean Trimmings (September 24 Issue).

National Meat Association. 2001e. BSE Update. NMA/Lean Trimmings (September 10 Issue).

National Meat Association. 2001f. Compliance With FDA MBM Requirements. NMA Extra Trimmings FAX ALERT! (February 16 Issue).

National Meat Association. 2001g. Good Manufacturing Guidelines For The Removal Of Spinal Cord During Slaughter Operations And Sampling And Testing Of Advanced Meat Recovery Product For Glial Fibrillary Acidic Protein Analysis. NMA Resource (December 13 Issue).

New Scientist. 2000a. How It Went So Horribly Wrong. (November 4 Issue).

New Scientist. 2000b. Lying In Wait: It May Be That Nobody's Genes Can Protect Them From BSE. (November 18 Issue).

New Scientist. 2001a. The Madness Spreads; Hungry Children Around The World Could Bear The Brunt of BSE. (February 10 Issue).

New Scientist. 2001b. Suspect Steak; Meat Butchered The Traditional Way Could Have Killed Five People. (March 31 Issue).

New Scientist. 2001c. Mad Cow USA: America Denies Having BSE, But Has Yet To Prove It. (February 10 Issue).

New Scientist. 2001d. Like Lambs To The Slaughter: What If You Can Catch Old-Fashioned CJD By Eating Meat From A Sheep Infected With Scrapie? (March 31 Issue).

North American Meat Processors Association. 2001. IBP Initiates Feeding Certification Program. Newsfax (February 12 Issue).

Office International des Epizooties. 2001. Number Of Reported Cases Of BSE Worldwide. [http://www.oie.int/eng/info/en\\_esbmonde.htm](http://www.oie.int/eng/info/en_esbmonde.htm)

Prusiner, S.B. 1998. Prions. Proc. National Academy Sciences 95:13363-13383.

- Purdey, M. 2001. Does An Ultraviolet Photo-Oxidation Of The Manganese-Loaded/Copper-Depleted Prion Protein In The Retina Initiate The Pathogenesis Of TSE? *Medical Hypotheses* 57:29-45.
- Raiden, R.M., S.S. Sumner and M.D. Pierson. 2001. Bovine Spongiform Encephalopathy: A Brief Summary. *Dairy, Food and Environmental Sanitation* 21:685-690.
- Regaldo, A. 2001. FDA Will Weight Risk Of "Mad Deer" Disease To Humans. *Wall Street Journal* (January 8 Issue).
- Render. 2001a. Researcher Claims Animal Feed To Blame For BSE. (June Issue).
- Render. 2001b. Consumers Confused About Livestock Diseases. (June Issue).
- Reuters. 2001. Study Points To "Mad Cow" Blood Risk For Humans. *Reuters Online*. (April 6).
- Rhodes R. 1997. *Deadly Feasts: Tracking The Secrets Of A Terrifying New Plague*. Simon and Schuster, New York, NY.
- Rucks, M. 2001. Personal Communication. (Michael Rucks is employed by BPI, Inc., Dakota Dunes, SD).
- Saborio, G.P., B. Permanne and C. Soto. 2001. Sensitive Detection Of Pathological Prion Protein By Cyclic Amplification Of Protein Misfolding. *Nature* 411:810-813.
- Salvage, B. 2001. Facts About Mad Cow, FMD Now Available In Fact Sheet Form. <http://www.meatingplace.com>
- Schmidt, G. 2001. Detection Of Central Nervous System Tissue In Meat Products. *Proc. 2001 Meat Industry Research Conference* (Chicago, IL). pp. 23-39.
- Schmidt, G.R., K.L. Hossner, R.S. Yemm and D.H. Gould. 1999a. Potential For Disruption Of Central Nervous System Tissue In Beef Cattle By Different Types Of Captive Bolt Stunners. *J. Food Prot.* 62:390-393.
- Schmidt, G.R., K.L. Hossner, R.S. Yemm, D.H. Gould and J.P. O'Callaghan. 1999b. An Enzyme-Linked Immunosorbent Assay For Glial Fibrillary Acidic Protein As An Indicator Of The Presence Of Brain Or Spinal Cord In Meat. *J. Food Prot.* 62:394-397.
- Schmidt, G.R., R.S. Yemm, K.D. Childs, J.P. O'Callaghan and K.L. Hossner. 2001. The Detection Of Central Nervous System Tissue On Beef Carcasses And In Comminuted Beef. *J. Food Prot.* 64:2047-2052.
- Scientific Committee On Veterinary Measures Relating To Public Health. 1998. Outcome Of Discussions: Opinion Of The Scientific Committee On Veterinary Measures Relating To

Public Health—Safety Of Slaughter Practices And Methods: Risk Of Spread Of BSE Infectivity Through Cross Contamination Of Different Tissues By Using Pneumatic Stunning During The Slaughtering Process Of Ruminants—17 February 1998. [http://europa.eu.int/comm/food/fs/sc/sev/out02\\_en.html](http://europa.eu.int/comm/food/fs/sc/sev/out02_en.html)

Scott, M.R., R. Will, J. Ironside, H.O.B. Nguyen, P. Tremblay, S.J. De Armond and S.B. Prusiner. 1999. Compelling Transgenetic Evidence For Transmission Of Bovine Spongiform Encephalopathy Prions To Humans. Proc. National Academy of Sciences 96:15137-15142.

Shaked, G.M., Y. Shaked, Z. Kariva, M. Halimi, I. Avraham and R. Gabizon. 2001. A Protease Resistant PrP Isoform Is Present In Urine Of Animals And Humans Affected With Prion Diseases. J. Biochemistry, Manuscript C100278200 (In Press).

Smith, G.C. 2001a. The Likelihood And Consequences Of Occurrence of “Mad Cow Disease” And “Foot-And-Mouth Disease” In The United States. pp. 1-22. Packaging Strategies, West Chester, PA.

Smith, G.C. 2001b. BSE, CJD And nvCJD. Presented at the American Society of Microbiology (Orlando, FL).

Smith, G.C. 2001c. What’s Hot And What’s Not In U.S. Supermarkets. Presented at the Wakefern Food Corporation Food Show (Edison, NJ).

Smith, G.C. 2001d. Should U.S. Supermarkets Fear Outbreaks Of Either BSE Or FMD In the USA? Presented at the Annual Meat Marketing Conference (Charlotte, NC).

Smith, G.C. 2001e. Critical Control Points For Minimizing Risk Of BSE Prions In Beef Tissues/Products. Presented at the Food Brands America Microbiological Seminar (Fort Worth, TX).

Southwest Meat Association. 2001. Industry Requests “BSE-Free” Labels. InfoMeat (December 17 Issue).

Stanley, B. 1999. British Cows Must Have A Passport. Associated Press (August 9 Edition).

Texas Cattle Feeders Association. 2001a. Bush Signs BSE Bill. TCFA Newsletter (June 1 Issue).

Texas Cattle Feeders Association. 2001b. Nations Stand Strong Against BSE, FMD. TCFA Newsletter (October 12 Issue).

Texas Cattle Feeders Association. 2001c. Federal Government To Step Up BSE Surveillance. (August 31 Issue).

Troeger, K. 2001. Alternative Methods Of Slaughtering And Cutting: More Safety In Critical Process Stages In The Slaughtering Of Cattle. *Fleischwirtschaft International* 2/2001:49-51.

U.K. Department of Health. 2001. Creutzfeldt-Jakob Disease (CJD) And Bovine Spongiform Encephalopathy (BSE). <http://www.doh.gov.uk/cjd/>

USA Today. 2001a. How The Disease Is Transmitted. (January 29 Issue).

USA Today. 2001b. Eastern Europe Fears Mad Cow Outbreak. (June 7 Issue).

USA Today. 2001c. Specter Of Mad Cow Frightens American. (March 15 Issue).

USDA-APHIS. 1999. Fact Sheet: Veterinary Services: Bovine Spongiform Encephalopathy. [www.aphis.usda.gov/oa/pubs/fsbe.html](http://www.aphis.usda.gov/oa/pubs/fsbe.html)

USDA-APHIS. 2001a. APHIS Activities. Animal and Plant Health Inspection Service, United States Department of Agriculture, Washington, DC.

USDA-APHIS. 2001b. National Sheep Scrapie Eradication Program. Animal and Plant Health Inspection Service, United States Department of Agriculture, Washington, DC.

USDA-FSIS. 1998. Proposed Rules: Meat Produced By Advanced Meat/Bone Separation Machinery And Recovery Systems. *Federal Register* 63:17959-17965.

U.S. Meat Export Federation. 2001a. BSE—Frequently Asked Questions. U.S. Meat Export Federation, Denver, CO.

U.S. Meat Export Federation. 2001b. EU Beef Consumption To Fall 10-12% In 2001. *Export Newsline—European Union*. U.S. Meat Export Federation, Denver, CO.

Wall Street Journal. 2001a. ‘Mad Cow’ Disease Linked To Antelope, Researchers Say. (April 23 Issue).

Wall Street Journal. 2001b. Wall Street Journal/Harris Interactive Poll. (March 8 Issue).

Will, R.G., M., Zeidler, P. Brown, M. Harrington, K.H. Lee and K.L. Kenney. 1996. Cerebrospinal-Fluid Test For new-variant Creutzfeldt-Jakob Disease. *Lancet* 348:955-957.

Wren, G. 2001. BSE: How Safe Is Our Beef? *Food Systems Insider*. (May Issue).