2.3.8 Poultry

Many of the same factors that make pigs an unlikely source of infectivity for cattle also make chickens an unlikely source. As a result, we do not quantitatively address this source in our risk assessment (Section 3).

As is the case with pigs, experimental data do not support the existence of a poultry-specific TSE. Experiments have subjected chickens to TSE challenge *via* both the parenteral and oral administration routes. The chickens challenged orally received five grams of brain from cattle confirmed to have BSE on three occasions at four, five, and six weeks of age. The chickens challenged i.c. received 50□l of a 10% saline suspension of brainstem material from these cattle at 1 day after birth and one ml at two weeks after birth. No evidence of transmissible encephalopathy was found (MAFF, 2000b). In addition, there is no evidence to date of residual infectivity in any tissue (Linda Detwiler, personal communication). Even if there were a poultry-specific TSE, the fact that chickens are typically slaughtered at an early age makes it unlikely that a prion disease would have time to develop.

Although chickens themselves appear to pose no substantial risk to cattle of exposure to a TSE, the use of chicken litter as a feed supplement could pose a risk (Public Citizen, 2001) that should be investigated further. It is possible that cattle-derived protein feed supplements administered to chicken could contain BSE infectivity, and that BSE infectivity could pass through chicken and become available in cattle feed supplemented with chicken litter.

2.3.9 Recycled Products

Several products that can be used in ruminant rations have the potential of harboring infectivity. The FDA does not exclude from ruminant feed the following products derived from mammals:

- Plate waste: Inspected and processed meat products that have been cooked and offered for human consumption and further heat processed for feed (such as plate waste and used cellulosic food casings);
- Gelatin,
- Milk products (milk and milk proteins),
- Blood and blood products,

- Tallow, grease, fat, oil
- Aminoacids, dicalcium phospahate, and
- Mammalian protein, which consists entirely of porcine or equine protein.

2.3.9.1 Plate Waste

Plate waste is defined to be food products that have been inspected by the FSIS or an equivalent state agency, cooked, and presented for human consumption. Plate waste often comes from large institutions, such as amusement parks or hotels. It consists of food items that have been cooked and presented for human consumption. Plate waste can undergo any of the following heat treatments: conventional rendering, extrusion and cooking at 212 °F for 30 minutes (Swine Health Protection Act), pelleting at either 190 °F (internal temperature), or pelleting at temperatures similar to those of conventional rendering. This additional treatment using high temperature and pressure may further reduce the amount of infectivity that might be in this material.

There are approximately half a dozen processors of plate waste in the United States. The final product competes with grains in the formulation of feed, although at this time, it is not a cost-effective option because of the high processing costs.

Bakery products comprise approximately 90% of all plate waste going to animal feed. The remainder consists of eggs, dairy products, fish and other products of animal origin. Therefore, plate waste consists mostly of non-meat products (Food and Drug Administration, 1997). Because plate waste is high in moisture content, vegetable proteins must be added (50% to 60%), and it must undergo further processing to aid the dehydration and extrusion process. The best estimate is that plate waste consists of between two and four percent bovine tissue. APHIS has expressed concern that plate waste could contain infective tissue, such as brain and spinal cord (Food and Drug Administration, 1997), but such tissues are unlikely to be present in any substantial quantity in plate waste.

We assume that high risk tissues (*i.e.*, brain) are extremely unlikely to be included in plate waste. Plate waste might contain on occasion spinal cord contamination or spinal cord in a T-bone steak. Because T-bone steaks originate from younger cattle, the likelihood of carrying infectivity at the time of slaughter is extremely low. In addition, spinal cord is unlikely to be

included in the product (Food and Drug Administration, 1997) because T-Bone steaks are unlikely to be included in plate waste.

In conclusion, current practices make the amount of infectivity in plate waste to which cattle could be exposed very small. Plate waste consists of little mammalian protein, and the tissues that are included in this waste are unlikely to contain BSE infectivity. Moreover, plate waste undergoes a substantial amount of heat treatment, which would further reduce the level of infectivity in this material.

2.3.9.2 Gelatin

FDA regulations allow the feeding of gelatin to ruminants because it has not been shown to harbor infectivity. SSC considers gelatine, amino-acids and dicalcium phosphate to be safe if processing ensures that all material is subjected to degreasing, followed by acid and/or alkaline treatment, heating to 120°C, and then heating to 138-140°C for four seconds. (SSC, 1998b). We assume that recycling this material poses little risk of exposing cattle to BSE.

2.3.9.3 Milk

FDA regulations do not prohibit the use of milk in cattle feed. No infectivity has been detected in milk or in the udder (mammary gland) of cows (as measured by the mouse bioassay) (Wells et al., 1998). At this time, there is no evidence that any of the TSEs can be transmitted through milk.

SEAC considers milk to be safe and has concluded that there was no reason, following the interim results of a cohort study, to change this position (SEAC, 1999). The World Health Organization has also issued a statement that concludes that milk is safe, most recently in June 2001 (WHO, 2001). SEAC reviewed the processing and use of milk in the light of research implicating lymphocytes in the pathogenesis of TSEs (SEAC, 1999). The Committee noted that there was no evidence of infectivity in the spleen or lymph nodes of cattle infected with BSE. In an opinion on the vertical transmission of BSE, the SSC also concluded there to be no reason to restrict the use of milk. However, SSC does recommend that as a precautionary measure, milk from BSE-affected cows be kept out of the human food supply (European Commission, 1999b). We assume that recycling this material poses little risk of exposing cattle to BSE.

2.3.9.4 Blood and blood products

No detectable infectivity has been found in blood or blood components of cattle infected with BSE (Wells et al., 1998, Wells et al., 1999, MAFF, 2000b, Bradley, 1999). Unlike TSEs affecting other animals, infectivity has not been detected in spleen or lymph nodes of cattle experimentally infected with BSE during either the incubation period or after manifestation of clinical signs. Infectivity in blood has been found in sheep experimentally infected with BSE (Foster et al., 1996). It is possible that in the cases of Scrapie, CWD, vCJD, and perhaps BSE in sheep, the lymphoid tissue plays an important role in the pathogenesis of the disease (Andreoletti et al., 2000, Ironside et al., 2000, Sigurdson et al., 1999). Some have speculated that neuroinvasion can occur directly *via* peripheral nerves or the lymphoreticular system and then *via* peripheral nerves (Glatzel and Aguzzi, 2001). Even if infectivity does exist in the blood of BSE-infected cattle, the total amount of infectivity is below the level of detection of the mouse bioassay. We assume that recycling this material poses little risk of exposing cattle to BSE. We do evaluate the potential for BSE infectivity to be present in blood as CNS micro-emboli (Section 3.1.2.3). In our sensitivity analysis, we characterize the effect of assuming inherent infectivity in blood at the level of detection.

2.3.9.5 Tallow

The World Health Organization has concluded that because of the proteinaceous nature of TSE agents, they will tend to remain with the cellular residues of MBM during the extraction process, rather than being extracted with the lipids of tallow (WHO, 2001). In addition, a rendering study funded jointly by the EU and MAFF in 1997 showed that tallow can be considered to be safe even if its treatment does not achieve the 133°C/20 minutes/3 bars of pressure minimum treatment standard (Taylor et al., 1997, MAFF, 2001). We assume that recycling this material poses little risk of exposing cattle to BSE.

2.4 Measures Taken to Protect Against BSE

Protecting against the introduction of BSE into a country requires policies that are based on prohibitions and restrictions. Regulations mainly prohibit the importation of feed, feeding materials or animals from countries with BSE, and ban recycling of ruminant materials into ruminant feed. In countries with BSE, infected tissues are not allowed into the human food supply or animal feed. Minimizing the spread of disease is complicated by the fact that BSE

animals may not show clinical signs of disease for an extended period after becoming infected and the agent cannot be readily deactivated once it contaminates feed. After describing these problems (Section 2.4.1), this section discusses actions taken in the UK to address its epidemic (Section 2.4.2), actions taken in Europe to prevent the spread of BSE beyond the UK (Section 2.4.3), measures taken in the United States to prevent the introduction of BSE (Section 2.4.4), and surveillance measures in the United States (Section 2.4.5).

2.4.1 General Issues Related to the Surveillance of BSE and the Deactivation of the BSE Agent

There is no pre-clinical or clinical test available to identify BSE in the field except when the disease is very near the end of its incubation period. Diagnosis in a live animal is based on clinical signs. Most commonly, the animal presents with changes in temperament, such as nervousness or aggression, abnormal posture, lack of coordination, difficulty in rising, or loss of body condition despite continued appetite. Specific clinical signs include abnormal head and ear position, apprehension and nervousness, apparent blindness, and exaggerated responses.

Microscopic examination is performed post-mortem and requires brain material preserved in formalin. This tissue is then stained and examined for the characteristic appearance of BSE specific changes. Microscopic examination is required by the EU Diagnostic Manual (European Commission, 1999a, European Commission, 2000) and by the OIE (OIE, 2000). The brain neuropathology of BSE resembles that of natural scrapie in sheep: astrogliosis, intracellular vacuolation affecting the gray matter neutropil and perikarya giving the distinctive appearance of spongiform changes, neuronal loss, and cerebral amyloidosis generally represent the most prominent changes (Wells et al., 1991).

Other validated tests for postmortem diagnosis include:

- The detection of disease-specific brain changes by electron microscopy (scrapie associated fibrils, SAF);
- The detection of the abnormal form (PrP^{BSE}) of the host protein (PrP^{c}) by immunological means such as immunoblotting, immunohistochemistry (used as a confirmatory diagnoses by the EU); and
- Detection of infectivity in tissues by bioassay (usually i.c. injection into mice).

Newer tests have been developed and are capable of detecting pre-clinical cases and of screening animals before slaughter. These tests have high sensitivity and specificity for detecting and confirming BSE for diagnostic purposes and can detect disease in animals not showing typical signs at slaughter (European Commission, 1999a). So far, the sensitivity and specificity of the newer tests have not been shown to be better than that of immunohistochemistry at similar preclinical stages of the disease (Linda Detwiler, personal communication). The tests include:

- An immunobloting test based on the Western Blotting procedure for the detection of Pr^{Pres} using monoclonal antibody (Prionics);
- A chemiluminescent ELISA using polyclonal anti PRP antibody for detection (Enfer); and
- A sandwich immunoassay for PRP^{res} (CEA).

All of these tests are very rapid, with results obtained within 24 hours. Results from the Swiss surveillance system show that the Prionics test could be used to target populations other than those with clinical signs of the disease (European Commission, 1999a, Schaller et al., 1999, Doherr et al., 1999). Although these tests can detect PrP^{res} before the animal shows clinical signs of the disease, it is not clear at what point during the incubation period the test would reliably yield positive results. It appears that their utility is primarily near the end of the disease progression.

There are no commercially available methods for the detection of the BSE agent in food. On the other hand, food and food products can be screened to detect high risk tissues, such as brain in sausages (SSC, 1999a, Lucker et al., 2000), spinal cord in ground beef (Schmidt et al., 1999); (Schmidt et al., 2001) or Advanced Meat Recovery (AMR) product (Kelley et al., 2000); (Schmidt et al., 2001), and central nervous system tissue in the blood of animals stunned with pneumatic stunners (Garland et al., 1996, Schmidt et al., 1999, Anil et al., 1999).

TSE agents are known for their capacity to survive severe environmental conditions such as desiccation, thermal extremes and UV exposure. Autoclaving, sodium hydroxide and sodium hypochlorite can achieve some level of inactivation but only under the most severe conditions. Currently there is no method to inactivate BSE that may be present in food for human consumption.

2.4.2 Actions to Address BSE in the UK

Soon after the BSE epidemic emerged in the UK, several measures were taken to decrease the incidence of the disease in animals and the potential exposure of humans to potentially infected meat products (MAFF, 2000b). The disease became notifiable in 1988, requiring that all cattle suspected of having BSE be destroyed and sent for diagnosis. Upon confirmation of the role of animal feed in the epidemic in 1988, the UK banned the use of MBM as ingredient in feed produced for ruminants. In September 1990, there was a ban on the use of Specified Bovine Offals (SBO) as an ingredient in feed stuff for any species. This legislation identified tissues with the highest concentration of infectivity (Hadlow et al., 1980, Hadlow et al., 1982) and removed them from the animal feed chain. Feed-borne BSE infections continued even after the imposition of the feed ban, but at a much lower rate (Anderson et al., 1996). In March 1996, the government of the UK imposed a total ban on the use of mammalian proteins in feed produced for farm animals. As a result of these ever more stringent bans to reduce the recycling of infectivity, the annual incidence of BSE fell by 90% between 1992 and 1997.

During the first few years following the initial identification of BSE in Britain, the epidemic was primarily an animal health concern. That focus reflected the experience with scrapie, which despite its presence in the human food supply for hundreds of years, had never lead to a known case of human illness. Precautionary measures where nonetheless put into place to protect the human food supply, including a ban on the sale of brain and spinal cord from cattle older than 6 months (material designated as specified bovine offal or SBO) for human consumption.

In 1990 a domestic cat was diagnosed as suffering from a 'scrapie-like' spongiform encephalopathy. This event generated concern that BSE might also be transmissible to other species, including humans. In 1994 the Spongiform Encephalopathy Advisory Committee (SEAC) judged the risk of transmissibility to humans to be remote only because precautionary measures had been put into place. Scientists theorized that if BSE were transmitted to humans, it would be likely to resemble CJD and suggested that surveillance be put into place to identify atypical cases or changing patterns of the disease.

In 1996 a new variant of the human Creutzfeldt-Jakob disease (now known as variant CJD or vCJD) was announced in the United Kingdom. It was identified in a small group of

people, all of whom were much younger than most individuals who develop CJD (Will et al., 1996, CJD Surveillance Unit, 2001). These cases shared clinical and neuropathological features that differed from those of CJD. As of August 31, 2001, the total number of definite and probable cases of vCJD reported in the United Kingdom was 106, including 12 probable vCJD deaths from which neuropathological confirmation will never be possible (CJD Surveillance Unit, 2001). Outside the UK, four vCJD cases have been reported in France, one in Ireland, and one in Hong Kong. Clinical, pathological and molecular studies provide compelling evidence that the agent that causes vCJD is the same as that which causes BSE (Will et al., 1996, Collinge et al., 1996, Bruce et al., 1997, Hill et al., 1997, Scott et al., 1999).

Following the announcement by the UK government that there appeared to be a link between BSE and vCJD, several additional measures were taken to reduce human exposure to the infective agent. SEAC recommended in March, 1996 that carcasses from cattle aged over 30 months be deboned in licensed plants and that the trimmings be classified as SBO. SEAC's suggestion was implemented in a 1997 regulation requiring the deboning of all beef from cattle over six months old. The ban on retail sales of bone-in beef was lifted in 1999 following a continued decline in the incidence of BSE and the implementation of other control measures to protect against the introduction of BSE into the human food supply.

Among other measures introduced were the compensation of producers for the loss of animals due to regulations related to the protection of public health and the eradication of BSE. Regulations aimed at eradicating BSE included the "selective cull" (implemented in 1997), which targeted for eradication animals that were the same age as an identified BSE case from their herd. Another regulation aimed specifically at protecting human health was the so-called "over 30 month scheme" (implemented in 1996), which prohibited the sale of beef from cattle over the age of thirty months for human consumption. The rational for this ban was that cattle over the age of 30 months could carry potentially substantial levels of infectivity in different tissues without having yet developed clinical signs of the disease. Table 2-2 outlines the chronology of the regulations implemented in the UK following the initial outbreak of BSE in 1986.

Table 2-2
Chronology BSE-Related Regulatory Actions in the UK

Year	Regulatory Action
1988	Compulsory notification Ruminant feed ban Slaughter compensation
1989	Bovine offal prohibition: banned the use of SBO for human consumption
1990	Bovine identification Marking and breeding records Selective culling Ban on the feed of SBO to any animals
1991	Control exports of bovine offal proteins and feeds containing such proteins
1994	Extended control of SBO Prohibition on the use of mammalian proteins in ruminant feeds
1995	Removal of spinal cord from bovine over 6 months
1996	Prohibition on the use of mammalian MBM in feed for livestock, fish and horses The over 30 months scheme
1997	Beef-bone regulations
1998	EU lifted ban on the export of UK beef
1999	Prohibition on the retail sale of bone-in beef lifted
2000	EU decision to test all cattle aged over 30 months presented for human consumption (implemented in 2001).

2.4.3 Actions to Address BSE in Europe

Other countries that have reported cases of BSE imported either animals or animal feed from the UK. It is estimated that a total of 58,000 adult breeding cattle were exported from the UK between 1985 and 1990. The UK also exported MBM during the years that the BSE agent is thought to have been present in rendering products from the UK. For example, because the price of MBM in England fell in 1989, exports of MBM doubled during that year (*e.g*, 15,000 tons of MBM were exported to France alone in 1989) (Taylor and Woodgate, 1997).

Cases of BSE have been reported in several countries. Some of these cases occurred in animals directly imported from the UK or in cattle fed with feed containing UK MBM. Following export of the disease from the UK, small epidemics were observed in Northern Ireland, Switzerland, France, and Portugal, presumably caused by the rendering and feeding of material from diseased animals. Few countries in Europe have not reported any BSE cases. Since the detection of BSE depends on the characteristics of the surveillance system, the absence of a reported case does not rule out the presence of the disease.

Due to the potential spread of BSE to other countries, the European Union and other international organizations have taken a wide range of measures to protect human and animal health and to stop the spread of the epizootic (European Commission, 2001). Some of the most important measures that have been taken by the international community include the following:

- The World Health Organization (WHO) in 1996 recommended that all countries ban the use of ruminant tissues in ruminant feed.
- In 1996, the European Commission banned the export of British live cattle, beef, semen, embryos, and all products produced from slaughter in the United Kingdom.
- The Office International des Epizzoties (OIE), the world organization for animal health, has codified the requirements for member countries to be considered BSE free. A risk assessment of the potential hazards is a pre-requisite.
- Feed bans in other countries: Since 1996, many countries started implementation of feed bans.
- In 2000, the Scientific Steering Committee of the EU reported the assessment of the geographical risk of BSE for 25 countries. This assessment considers the stability of the system and the likelihood of BSE occurring in the country (SSC, 2000c).
- In 2000, the European Commission adopted the decision to remove specified BSE risk materials from the feed chain and from human food.
- In 2000, the European Commission prohibited the use of certain animal by-products, including MBM, and blood meal (but excluding milk, or fish meal) from non-ruminants in feed for any farm animal species (effective January 1, 2001).
- In 2000, the European Commissions extended the SRM list to include bovine intestines.

- In 2000, the European Commission adopted the decision to test all cattle over 30 months of age. All animals over 30 months that cannot be tested or that test positive for BSE must be destroyed.

2.4.4 Measures to Prevent the Establishment of BSE in the United States Cattle Population

After more than 11 years of surveillance of high-risk animals, no confirmed cases of BSE have been reported in the United States. In cooperation with USDA's Food Safety and Inspection Service (FSIS), the Animal and Plant Health Inspection Services (APHIS) has taken measures in prevention, education, surveillance, and response to reduce the risk of the introduction of BSE into the U.S. cattle population.

BSE became a reportable disease in the U.S. in 1986 (see Title 9 of the Code of Federal Regulations, Parts 71 and 161). As a result, USDA must be notified of suspect cases. Restrictions on imports from BSE countries have been in place since 1989, and active surveillance efforts began in 1990. As part of its surveillance effort, USDA has attempted to determine the disposition of cattle that were imported from the UK and the Republic of Ireland between 1980 and 1989. The Department continues to closely monitor the cattle in this group that have been located and are still alive.

In 1989, APHIS banned the import of all ruminants and restricted the importation of certain cattle products from the United Kingdom and other countries where BSE was diagnosed. In 1991, APHIS restricted the import of ruminant meat and edible products and banned most byproducts of ruminant origin from countries known to have BSE in a native animal (Title 9 Code of Federal Regulations, Part 94.18 and 95.4). Countries whose products were restricted due to BSE prior to 1997 included: the UK (1989), the Republic of Ireland (1989), Switzerland (1990), Oman (1990), France (1991), and Portugal (1994). In 1997, the US government prohibited the import of live ruminants and most ruminant products from all of Europe until a thorough assessment of the risks is conducted (USDA-APHIS, 2000b). In December, 2000, restrictions included a ban in the importation of all processed animal proteins regardless the species, offal, tankage, ruminant fat, glands, processed fats and oils, and some tallow. The importation restrictions in 2001 included a ban in the import of all ruminant meat, meat products and other edible ruminant products that were stored, processed or otherwise associated with a

facility located in Europe or Oman. In 1990, APHIS developed a plan to respond to a BSE case in the U.S. This plan was updated by the APHIS-FSIS BSE working group in 1996.

FSIS performs *ante mortem* slaughter inspections at all federally inspected slaughter establishments and veterinary medical officers and food inspectors routinely evaluate animals for central nervous system disorders. Animals exhibiting suspicious CNS signs that may be indicative of BSE or any other reportable disease are withheld from slaughter. In such cases, Veterinary Services is notified. FSIS maintains a database containing information on *ante mortem* and *post mortem* condemnations triggered by these and other conditions.

The Food and Drug Administration (FDA) controls animal feed, thought to be the main exposure medium for BSE. FDA prohibits the use of most mammalian protein in the manufacture of animal feeds administered to ruminants (Food and Drug Administration, 1997). This regulation is frequently referred to as the "feed ban." The regulation exempts the following products: blood and blood byproducts, milk products, pure porcine and pure equine proteins, plate waste, tallow, gelatin, and non-mammalian protein (poultry, marine, vegetable). Exempted products are considered to be non-prohibited material and all other mammalian protein is considered to be prohibited material.

The regulation specifies procedures for those renderers, protein blenders, feed manufacturers and distributors that produce prohibited material, non-prohibited material, or both. Firms must keep records on the origin of the materials and label prohibited material "*Do not feed to cattle or other ruminants.*" Prohibited materials intended for export are exempt from this requirement and instead must be labeled "*For export only.*" FDA requires that renderers, blenders, feed manufacturers and distributors selling both restricted and unrestricted products ensure that the two types of proteins are kept separate throughout processing. For example, there are minimum requirements for clean-out of the production line directly after the processing of prohibited material (direct cleaning, flushing, *etc.*) before subsequently manufactured material can be considered to be non-prohibited.

In early January, 2001 FDA released results of a compliance survey of 9,947 rendering and feed mills. The data demonstrated that there is significant noncompliance with the feed ban in segments of the feed industry (Food and Drug Administration, 2001b). Table 2-3 summarizes the results of this survey.

Table 2-3
FDA Update on Ruminant Feed (BSE) Enforcement Activities (January 10, 2001)

Practice	Proportion of Firms in Compliance		
	Renders[a]	FDA Licensed Feed Mills[b]	Feed Mills not licensed by FDA[c]
Firms whose products were labeled with the required caution statement	84%	80%	59%
Firms with a system to prevent commingling of prohibited and non-prohibited products	72	91	74
Firms that followed record keeping regulations	96-98	98	91

Notes

a. For Renderers --Total number of inspections – 239, firms handling prohibited material – 180.

b. For FDA Licensed Feed Mills – 1,240 total, inspected— 846. Of those feed mills inspected, 347 were handling prohibited material.

c. For Non-FDA Licensed Feed Mills – 4,344 inspected (FDA does not know the total number because they are not required to be licensed by the Agency, but the number could be between 6,000 and 8,000). Of those feed mills inspected, 1,593 were handling prohibited material.

The Food and Drug Administration (FDA) has also taken steps to reduce the risk of contaminating with BSE pharmaceuticals that contain or are produced with materials of bovine origin. These steps include the following:

- In 1992, FDA recommended the use of scrapie/BSE-free sources for materials used in dietary supplements.
- In 1993, FDA recommended that cell lines used for biologics be BSE-free.
- In 1993, FDA requested that bovine sourced materials, except gelatin, used in manufacture of regulated products be restricted to BSE-free countries.
- In 1994, FDA requested that bovine derived material for use in cosmetics and dietary supplements not be sourced from BSE countries.
- In 1996, FDA recommended the withdrawal of plasma and plasma products made from pools of persons who later developed CJD.

- In 1997, FDA requested more restrictions on the use of bovine gelatin originated from BSE countries.
- In 1999, FDA recommended deferring the use of blood from donors with more than six months cumulative residence in UK during the period from 1980 to 1996.

2.4.5 BSE Surveillance in the United States

In addition to measures intended to mitigate the risk of BSE becoming established or propagated in the United States, the federal government has also implemented a surveillance program to help identify BSE as soon as possible if it were introduced into the U.S. Since 1986, when BSE became reportable in the U.S., USDA has encouraged the submission of brain tissue samples for testing, and has engaged in educating practitioners to look for and recognize the disease. Brain submissions are examined histologically, and immunohistochemistry has been used since 1993. USDA is considering the incorporation of rapid diagnostic tests for targeted surveillance in the future (Linda Detwiler, personal communication, 2001). Between 1990 and July 2001, over 13,900 brains were examined. For each of the last six years, the rate of surveillance has been approximately double the International Office of Epizooties (OIE) standard (OIE, 2001). In 2000 and 2001, the number of brains examined was more than five times the OIE standard.

Animals targeted for surveillance by APHIS include cattle exhibiting signs of neurologic disease in the field (*i.e.,* prior to being brought to slaughter), cattle condemned at slaughter for neurologic reasons, rabies-negative cattle submitted to public health laboratories, neurologic cases submitted to veterinary diagnostic laboratories and teaching hospitals, and a sampling of cattle that are nonambulatory ("downer cattle") at slaughter. Although the signs exhibited by downer animals are generally not typical of BSE, some have suggested that these animals are a high-risk population based on anecdotal information that a TME outbreak could be linked to feeding practices involving downer cattle (Marsh et al., 1991). In addition, U.S. cattle inoculated i.c. with North American scrapie strains developed signs inconsistent with BSE signs manifest in affected animals in Europe but similar to those of "downer" animals (Cutlip et al., 1994, Cutlip et al., 1997). The APHIS surveillance approach takes into account regional differences in the movement of animals. For example, based on movement patterns, the U.S. is divided into eight regions where adult cattle would typically live and exit the production system. Based on the adult

cattle populations in each region, APHIS has calculated regional surveillance goals for BSE based on international standards as if each region were an individual country.

In addition to surveillance for the presence of BSE, The Centers for Disease Control and Prevention (CDC) monitors the incidence of CJD in the U.S. by analyzing death certificate information from multiple-cause-of-death data compiled by the National Center for Health Statistics. This information is also used to search for possible cases of vCJD in the U.S. As of September 2001, no such cases had been identified in the United States. Nor had any change in the incidence of CJD been observed.