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Transmissible Spongiform Encephalopathies (TSEs), Including “Mad Cow Disease”: Public Health and Scientific Issues

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Summary

On December 23, 2003, the U.S. Secretary of Agriculture announced that a cow in Washington state had tested positive for bovine spongiform encephalopathy (BSE, or Mad Cow disease), representing the first domestic case. The Secretary announced expanded protections against BSE on December 30, 2003. On January 26, 2004, the U.S. Secretary of Health and Human Services announced additional safety measures for products regulated by the U.S. Food and Drug Administration (FDA) to protect public health. Both have stressed that the human health impact of finding one BSE positive cow is believed to be minimal.

BSE is a member of a group of diseases called Transmissible Spongiform Encephalopathies (TSEs). Although the predominant theory is that TSEs are caused by *prions* or proteinaceous infectious particles (a novel disease mechanism first described in the 1980s), some scientists believe a virus may eventually be identified as the infectious agent. While some TSEs, such as scrapie in sheep, have been known for over 200 years, others, including BSE, appear to have emerged quite recently. Some TSEs seem to affect only one species and others, like BSE, appear to have jumped the "species barrier" to infect more than one species. This event has transformed prion diseases from a rare and esoteric area of research to a matter of significant public health concern. BSE is believed to have been transmitted to people who ate contaminated beef, leading to the identification in 1996 of a new human disease, variant Creutzfeld-Jakob disease (vCJD), in the United Kingdom.

As attention has focused on the finding of BSE in the United States, government control efforts have been scrutinized. Some have argued that prevention programs, begun in 1988 and strengthened at points since then, are robust, and that the finding of a BSE-positive cow represents an isolated case and a negligible health risk to humans. Others believe that shortfalls in government prevention efforts are serious, and that BSE may be entrenched in the United States, albeit at low levels. The spectrum of opinions about the public health risk from BSE underscores the myriad uncertainties surrounding prion diseases, and especially their modes of transmission, and detection.

This report examines known and purported human health risks from BSE and related diseases, the status of efforts to detect and prevent these diseases in humans, and the scientific basis of these efforts. For a discussion of BSE prevention efforts in the agricultural sector (including FDA measures to assure the safety of animal feed, and USDA measures to assure the safety of beef), refer to CRS Issue Brief IB10127, *Mad Cow Disease: Agricultural Issues for Congress*, by Geoffrey S. Becker, and CRS Report RL32199, *Bovine Spongiform Encephalopathy (BSE, or 'Mad Cow Disease'): Current and Proposed Safeguards*, by Sarah A. Lister and Geoffrey S. Becker.

This report will be updated as circumstances warrant.

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Transmissible Spongiform Encephalopathies (TSEs), Including "Mad Cow Disease": Public Health and Scientific Issues

Introduction

Mad Cow disease, (bovine spongiform encephalopathy, or BSE), is an incurable degenerative neurologic disease of cattle. First detected in the United Kingdom (U.K.) in 1986, it was later linked to a new form of a rare, fatal human illness, Creutzfeld-Jakob disease (CJD), via consumption of beef from affected animals. When compared with the existing form of CJD, the new form, called *variant CJD* (vCJD) affects younger victims and displays a distinct microscopic pattern of brain lesions at autopsy. The suspected causal link between BSE and vCJD, announced by the British government in March 1996, had sweeping effects on global cattle markets and on cattle production and slaughtering practices in the United Kingdom as well as other countries seeking to prevent BSE. The findings of BSE in a Canadian beef cow in May 2003, and a dairy cow in Washington state in December 2003, have prompted expanded measures to guard against BSE and reassessment of existing public health safeguards by federal agencies and other interested parties.

What Are Transmissible Spongiform Encephalopathies?

TSEs in Livestock and Other Animals. BSE belongs to a group of diseases called transmissible spongiform encephalopathies (TSEs). On microscopic examination, the diseased brain is permeated with holes like a sponge, hence the name "spongiform." TSEs are considered to be transmissible because feeding, injecting or transplanting tissues containing the agent will transmit the disease. TSEs are not new and are known to affect several other species besides cattle. **Scrapie**, which affects sheep, has been known for over 200 years. **Chronic Wasting Disease (CWD)**, which affects deer and elk, has existed in Colorado and Wyoming for 40 to 50 years and has since been found in 11 other states and two provinces in Canada. TSEs also affect mink, a number of domestic and zoo cats, and other ruminants such as goats and antelope. There is a long incubation period (two to eight years in cattle) during which no signs are apparent. Length of the incubation period depends on the species affected, the dose and the mode of infection.

TSEs are thought to be caused by "proteinaceous infectious particles," or *prions*. Prion protein is found in many body cells, especially on the surface of nerve cells in the brain. Its normal function is poorly understood. Current theory is that TSEs result when prion protein changes into an abnormal shape and aggregates into long fibrils or clumps of fibrils called plaques. The abnormal prion can induce normal

prions to change to the aberrant form. This remarkable ability allows the prion to replicate and behave as an infectious agent. The aberrant prion is not broken down and eliminated by the body, leaving deposits that accumulate within the brain. Scientists speculate that the loss of normal brain cell prions or the toxicity of the aggregated abnormal prions causes nerve cell death which eventually leads to the characteristic holes that are a trademark of the disease. Initially it was thought that a "slow virus" caused TSEs. When the prion theory was first proposed in 1982, it was viewed with considerable skepticism. Further studies have supported the prion theory, which is now predominant. Debate continues, however, and the heart of the controversy is the role of the prion protein in causing TSEs: is it the transmissible agent, or just a pawn in a viral-mediated disease?

Human TSE Diseases. In humans, four related spongiform encephalopathies have been identified. These diseases appear similar to each other on microscopic examination of the brain, but may differ in the way they are acquired, their clinical symptoms (such as dementia or insomnia), or their pattern of distribution throughout the world. **Kuru** is found only in one tribe in Papua New Guinea. Affected individuals contract the disease either through ritual cannibalism or preparation of the dead for burial. **Fatal familial insomnia (FFI)** and **Gerstmann-Straussler-Scheinker disease (GSS)** are inherited (familial) with cases occurring in families; symptoms appear in mid-life.

The fourth disease, **Creutzfeldt-Jakob disease (CJD)**, usually strikes people over 65. It occurs worldwide at an estimated annual rate of one case per million population. Since U.S. CJD surveillance was begun in 1997, 732 cases have been identified. Worldwide, about 10-15% of CJD cases are inherited, but for most cases the cause is unknown. Less than 1% of CJD cases are *iatrogenic*: they occurred as the result of various medical treatments or procedures which inadvertently transferred the CJD agent (e.g., during transplantation of nervous system tissue). The incubation period ranges from 15 months to more than 30 years for iatrogenic CJD cases. Although they do not have an inherited mutation, individuals who have developed iatrogenic CJD have a genetic feature which may make them more susceptible to developing the disease following exposure. Studies of blood donors in three European countries indicate that this feature is present in 49% of donors in Finland, 42% in Britain, and 34% in Ireland.

The first cases of vCJD were announced in March 1996 in the United Kingdom. According to the UK Department of Health, as of February 2, 2004, the total number of definite or probable cases of vCJD in the UK is 146, of which seven are still alive.¹ In addition, six cases of vCJD have been reported in France and one each in Canada, Ireland, Italy and the United States. The U.S. case lived in the United Kingdom in the 1980s and is thought to have acquired the disease there.² All vCJD cases have the same genetic feature that is associated with iatrogenic CJD and most sporadic CJD cases. (Sporadic CJD is discussed further below.) It is unknown if those who

¹ Monthly CJD Statistics, U.K. Department of Health, at [http://www.doh.gov.uk/cjd/cjd_stat.htm].

² *Probable Variant Creutzfeldt-Jakob Disease in a U.S. Resident — Florida, 2002*, Morbidity and Mortality Weekly Report (MMWR), vol. 51, Oct. 18, 2002, pp. 927-929.

lack this genetic feature are resistant to the development of CJD, or if there might merely be a longer incubation period prior to the development of disease.

How Are TSEs Acquired?

Several modes of TSE transmission have been described, though often only one or two of the modes has been documented for any given TSE. So far, modes described are: vertical (maternal to child) transmission, inheritance, spontaneous mutation, iatrogenic transmission, and oral ingestion of the TSE agent. Modes of transmission that have not been documented for a given TSE often cannot be ruled out. This uncertainty, and many others, lead to questions about risk and difficulty in crafting TSE preventive measures.

Vertical transmission has been demonstrated for scrapie in sheep but not for BSE in cattle.³ Inherited forms of human TSE (CJD, GSS, FFI) are caused by inherited gene mutation, often in the prion gene itself.

When the cause of a TSE is unknown, it is called “sporadic,” or sometimes “spontaneous.” Most CJD cases are sporadic. Scientists speculate that some cases of sporadic CJD may be caused by non-inherited mutations or by unidentified iatrogenic routes. Transmission of the agent may occur during procedures performed on the nervous system (including the eyes), especially when tissue transplantation is involved. Procedures linked with later development of CJD include neurosurgery, corneal transplant, and injection of growth hormone derived from the pituitary gland in the brain of human cadavers. Abnormal prions are not affected by most chemical disinfectants and the few chemicals that are effective may be too harsh for delicate surgical instruments. Prions are also very heat-resistant and are not destroyed by autoclaving (high temperature and pressure), the standard procedure for sterilizing instruments to prevent transmission of bacterial, viral and fungal agents.

BSE is believed to be transmitted orally to cattle through feed containing the abnormal prion. Animal feed is thought to have become contaminated when infected animals were rendered into a protein supplement that is often added to feed. This practice has been banned in countries affected by BSE.⁴ The oral dose can be very small: in cattle, ingestion of 10 milligrams of infectious brain tissue (less than 1/1,000th of an ounce) can cause BSE. The genesis of early cases (whether the cattle feed contained prions from sheep affected by scrapie, or a prion derived directly from cattle, or another explanation) remains a matter of speculation.

³ Nonetheless, uncertainty about the potential for vertical transmission of BSE contributed to a decision to destroy a U.S. herd containing a calf from the BSE-positive Washington state cow.

⁴ For more information on BSE control measures in cattle, see CRS Report RL32199, *Bovine Spongiform Encephalopathy (BSE, or "Mad Cow Disease"): Current and Proposed Safeguards*, by Sarah A. Lister and Geoffrey S. Becker.

For some TSEs, oral infection has been shown to cross the “species barrier.”⁵ BSE is transmissible to some other ruminants, and to cats. The BSE agent is believed to be transmitted to humans via the oral route as well, causing vCJD through consumption of beef contaminated with abnormal prions from the brains and spinal cords of affected cattle. Nervous system tissue may be present in beef products. For example, a USDA survey of meat from Advanced Meat Recovery (AMR) systems in 2003 showed that 35% of it contained nervous system tissue.⁶ AMR uses high pressure to strip edible materials from bone, yielding a meat paste used in products such as hot dogs and sausages. Since the finding of BSE in the United States, USDA announced measures to keep nervous tissue out of AMR products, but it is still permissible to market the brains of healthy young cattle for human consumption in this country.

Because the BSE agent has not been found in beef muscle, meat from affected cattle is not felt to pose a threat. (However, prions have been found in small amounts in the human muscle tissue of CJD patients and in the muscle tissue of experimental mice.) Following the announcement of the U.S. cow with BSE, USDA launched a voluntary recall (Class II — low health risk) of meat from the animal and those slaughtered with it on December 9, 2003, and all downstream meat processed in the same lots (about 10,410 pounds of raw beef).

According to USDA, there was an extremely low likelihood that the beef contained the BSE agent. The tissues of highest infectivity (brain, spinal cord, and distal ileum) all were removed from the infected cow at slaughter. “Therefore, the meat produced were cuts that would not be expected to be infected or have an adverse public health impact. The recall is being conducted out of an abundance of caution.”⁷ News reports indicate that some of the meat was purchased and consumed. The Centers for Disease Control and Prevention (CDC) comments, though, that “the risk for acquiring vCJD from consumption of BSE-contaminated product is low, presumably because of a ‘species barrier’ that provides substantial but incomplete protection against development of vCJD. In the UK, where an estimated one million or more cattle probably were infected with BSE, cases of vCJD continue to be reported; however, the number of cases of vCJD remains small.”⁸

The European Commission Food Safety Scientific Steering Committee reached a similar conclusion in its review of the safety of beef muscle meats, saying:

⁵ The species barrier is a concept in epidemiology derived from the finding that many infectious diseases confine themselves to single or related species, and infect unrelated species rarely or with difficulty, if at all.

⁶ For further information on Food Safety and Inspection Service AMR standards and testing, see the “Advanced Meat Recovery (AMR)” Web site at [<http://www.fsis.usda.gov/OA/topics/amr.htm>].

⁷ USDA, Food Safety and Inspection Service, *FSIS Update Of Recall Activities*, Jan. 5, 2004.

⁸ CDC, *Bovine Spongiform Encephalopathy in a Dairy Cow — Washington State, 2003*, MMWR, vol. 52, no. 53, Jan. 9, 2004, pp. 1280-1285.

Given the limited conditions of the research reported on and the consistent negative results of infectivity experiments with regard to the presence of TSE infectivity in muscles of cattle and sheep, there is currently no reason to revise (our) opinions with regard to the safety of bovine and sheep muscles. Also, should infectivity be present at very low levels below current detection limits, the risk of exposure to BSE infectivity is reduced to negligible levels by risk reduction measures in place and by the fact that exposure would be by the relatively inefficient oral route.⁹

However, Dr. Stanley Prusiner, the scientist who won the Nobel Prize for his pioneering work on the prion theory of TSEs, and whose subsequent work identified prions in the muscle of experimental mice, disagrees with the idea that muscle meats are safe. Prusiner, who now heads a company he founded to develop new rapid tests for TSEs, advocates testing of all cattle slaughtered for food in the U.S.¹⁰

Testing for CJD and other TSEs

A substantial hurdle in the management of BSE and human prion diseases is the lack of noninvasive test methods. Prions are not directly visible in a microscope, do not contain DNA, nor do they cause immune or inflammatory reactions, making typical test methods ineffective. Tests for accumulated prions in brain and spinal cord tissues serve as the “gold standard,” and are often the only reliable measures of infection.

Definitive diagnosis of CJD in humans requires the study of brain tissue, which can be obtained by biopsy in living patients, though this is considered highly invasive. Recently, scientists have found that vCJD differs from other forms of CJD in that abnormal prions accumulate in lymphoid tissues such as the tonsils and appendix. Tonsil biopsy has been used in the United Kingdom as one method of distinguishing vCJD from other neurologic disorders in living patients. TSEs that involve lymphoid tissue may offer pre-mortem testing options in animals as well. In sheep, testing of eyelid swabs has been used to diagnose scrapie. In cattle, though, the only BSE-affected lymphoid tissue is the lower small intestine, so as a practical matter, there is no test that can be used in live cattle.

Tests for BSE in cattle are performed postmortem on brain tissue. The Washington state cow was tested by immunohistochemistry (IHC), in which abnormal prions in slices of brain tissue bind to a special stain to make them apparent on microscopic examination, often before the characteristic spongiform lesions manifest. USDA considers the IHC test the “gold standard” for BSE, and uses it at the National Veterinary Services Laboratory (NVSL) in Ames, Iowa, in support of its BSE surveillance program. Upon finding a positive IHC test on the “index” cow on December 23, 2003, USDA sent samples to the Central Veterinary Laboratory in

⁹ European Commission Health and Consumer Protection Directorate, *Prions in Muscle, Statement Adopted by the Scientific Steering Committee at its Meeting of 4-5 April 2002*, at [http://europa.eu.int/comm/food/fs/sc/ssc/out254_en.pdf].

¹⁰ Rone Tempest, *Mad Cow Fears May Keep Labs Busy; The Use of New Rapid Screening Kits also Could Mean Income for UC*, Los Angeles Times, Jan. 12, 2004, p. B1.

Weybridge, U.K. for confirmation. The Weybridge laboratory is recognized as an international reference laboratory for BSE by the Office International des Epizooties (OIE), the international animal disease control organization comparable to the World Health Organization for human health.

The IHC test involves lengthy preparation and takes at least one week to run. Faster screening tests are used in BSE-affected countries. In the wake of the Washington state case, USDA announced a test-and-hold policy for all animals on which BSE tests are submitted, and has asked companies to submit applications for approval of rapid test kits.¹¹ The European Commission has approved several rapid tests for BSE.¹² The rapid tests still require the use of brain tissue.

The Institute of Medicine has commented that existing tests (for TSEs) are several orders of magnitude less sensitive than is optimal, and has recommended that research efforts prioritize the development of tests with higher sensitivity, tests that can be performed using blood or other non-invasive samples, and tests that can use non-invasive brain imaging techniques to detect human prion diseases.¹³

Prevention of CJD in Healthcare Settings

As noted earlier, iatrogenic transmission of TSEs is the inadvertent transfer of infective material during medical procedures, such as tissue transplantation of corneas or *dura mater* (the protective covering on the brain or spinal cord), injections of growth hormone derived from cadavers, or transmission on neurosurgical equipment. A study published in 2000 stated that 267 cases of iatrogenic CJD have been reported worldwide. Of this total, seven were linked to the use of contaminated equipment: five from neurosurgical instruments and two from an invasive type of electroencephalogram (EEG) electrode.¹⁴ Removing prion infectivity from instruments and equipment has posed a particular challenge since prions (unlike viruses and other microbes) are resistant to heat, irradiation, gas sterilizing agents, and most disinfectants. All neurosurgical equipment-related cases occurred before current sterilization procedures were routinely implemented in health care facilities, and no cases have been reported since 1976.

¹¹ The USDA Animal and Plant Health Inspection Service, Center for Veterinary Biologics, is responsible for evaluating veterinary biologics, including test kits, for safety and efficacy.

¹² For more information on rapid tests, see European Commission, *The Evaluation of Tests for the Diagnosis of Transmissible Spongiform Encephalopathy in Bovines*, July 1999, at [http://europa.eu.int/comm/food/fs/bse/bse12_en.pdf].

¹³ Institute of Medicine, *Advancing Prion Science: Guidance for the National Prion Research Program* report, Nov. 17, 2003, at [<http://www.iom.edu/report.asp?id=16514>].

¹⁴ Other documented transmission cases of CJD include three cases due to corneal transplantation, 114 cases due to *dura mater* grafts, 139 cases from pituitary-derived hormones and four from gonadotropin hormone used in infertility treatment. Institute of Medicine. *Advancing Prion Science: Guidance for the National Prion Research Program*, prepublication copy, p. 102, at [<http://www.nap.edu/catalog/10598.html>].

Although destruction or disposal of surgical instruments may be the safest way to ensure that CJD is not transmitted in this way, it may not always be practical or cost effective. The World Health Organization (WHO) has developed CJD infection control guidelines for stringent chemical and autoclave sterilization of instruments that come in contact with high infectivity tissues (brain, spinal cord, and eyes) and low infectivity tissues (cerebrospinal fluid, kidneys, liver, lungs, lymph nodes, spleen and placenta) of patients with suspected or confirmed CJD.¹⁵ The WHO recommends that all disposable instruments and materials that come in contact with these tissues be incinerated, and that surfaces be decontaminated with specific chemical solutions for one hour and rinsed with water.

The WHO guidelines also address the prevention of transmission of TSEs between patients or to healthcare workers in hospital wards and laboratories. In general, TSEs are not transmitted through routine contacts in healthcare settings, and universal precautions against bloodborne exposure are considered adequate. Non-routine contacts for which special procedures are required are those involving nerve tissue, including “spinal taps” and certain other procedures. The guidelines also address hazards in the laboratory (where typical fixatives used for pathology specimens do not inactivate prions), and in morgues and funeral parlors, as well as proper procedures for handling medical waste suspected of containing TSE agents.

On December 17, 2003, the UK Department of Health announced the possible first case of vCJD acquired from blood transfusion. The donor gave blood in March 1996, and developed vCJD in 1999 and died. The recipient was transfused shortly after the donation and died of vCJD in the fall of 2003. While it cannot be proven that the recipient acquired vCJD from blood rather than from eating beef, the possibility that this case is transfusion-related cannot be ruled out. Both BSE and scrapie have been experimentally transmitted to sheep through blood transfusion, demonstrating that the BSE agent can be present in blood. Hence, the possibility of TSE transmission through blood was addressed in the United Kingdom prior to the announcement of the apparent first case. Faced with the largest number of vCJD cases, the United Kingdom has since the late 1990's applied a costly process called *leukoreduction* to all donated blood units, to remove white blood cells where prions are thought to reside. The United Kingdom also imports all its plasma and plasma products from the United States, and has not announced plans to alter this policy since the finding of a BSE-positive cow in Washington state.

¹⁵ WHO *Infection Control Guidelines for Transmissible Spongiform Encephalopathies.*, Report of a WHO Consultation, Geneva, Switzerland, Mar. 23-26 1999, at [<http://www.who.int/emc-documents/tse/whocdscsraph2003c.html>].

Treatment of Human Prion Diseases

Efforts to find effective treatments for human TSEs have thus far not borne fruit. The Creutzfeldt-Jakob Disease Foundation notes:

At the present time, there is no known effective treatment to arrest or cure CJD. The disease is inevitably fatal. The only treatments available for CJD patients focus on easing their symptoms and discomfort. Such measures may include drugs for controlling pain and myoclonus (muscle spasms), catheters to collect urine, intravenous fluids, feedings through tubes, and frequently repositioning the patient to avoid bedsores.¹⁶

Institutes of the National Institutes of Health (NIH) and several universities are screening compounds as potential treatments, though the first batch of compounds to undergo human clinical trials were not found to be helpful after the onset of clinical disease. Trials for potentially promising therapies are also underway in other countries. A search of the NIH database ClinicalTrials.gov did not yield any clinical trials for CJD or vCJD either planned or in recruitment at this time.

U.S. Federal Government: Roles and Responsibilities

Lacking measures to detect or remove abnormal prions in beef, or to treat people who have been infected, the bulk of public health protections against BSE occur in the agricultural sector, where programs are designed to keep the agent out of livestock feed, cattle, and the beef supply. Numerous activities in the USDA prevent the introduction and spread of BSE and assure the safety of beef. FDA plays a role in protecting animal and public health through its regulation of livestock feed. For a discussion of BSE prevention efforts in the agricultural sector (including FDA measures to assure the safety of animal feed, and USDA measures to assure the safety of beef), refer to CRS Issue Brief IB10127, *Mad Cow Disease: Agricultural Issues for Congress*, and CRS Report RL32199, *Bovine Spongiform Encephalopathy (BSE, or 'Mad Cow Disease'): Current and Proposed Safeguards*.

Additional public health protections against BSE and other TSEs involve the traditional federal public health agencies within the Department of Health and Human Services (HHS), the Environmental Protection Agency (EPA), and the Department of Defense (DoD). The activities of these agencies (including FDA efforts to protect the human foods, drugs, biologics and cosmetics it regulates) are discussed here.

Department of Health and Human Services. HHS conducts numerous activities to prevent human prion diseases such as CJD. The National Institutes of Health (NIH) support basic biomedical research on prion diseases, including studies of disease transmission and progression, and development of candidate test methods and treatments. The Centers for Disease Control and Prevention (CDC) conducts surveillance for CJD and other neurologic illnesses, to determine disease prevalence

¹⁶ Creutzfeldt-Jakob Disease Foundation, Inc., *CJD Info*, at [<http://cjd.foundation.org/CJDInfo.html>].

and detect trends. CDC also develops recommendations on infection control to protect patients and health care workers from potential transmission of TSEs in healthcare facilities. FDA is responsible for the safety of certain foods and all drugs, vaccines, cosmetics and nutritional supplements containing beef products, as well as the safety of the blood supply and donated organs and tissues.

In 2001, HHS released the *Bovine Spongiform Encephalopathy/Transmissible Spongiform Encephalopathy (BSE/TSE) Action Plan*. The plan outlined a number of steps to improve scientific understanding of BSE and related diseases and strengthen public health safeguards in four areas of responsibility — surveillance (CDC), protection (FDA), research (NIH), and oversight (Office of the Secretary).¹⁷ HHS has also established an Interdepartmental Steering Committee for BSE/TSE Affairs.¹⁸ The role of the committee is to provide ongoing coordination between agencies, identification of and response to potential vulnerabilities in the United States to BSE and vCJD, and coordination of risk communication plans by the various agencies.

Current efforts of specific HHS agencies on TSE research, surveillance and prevention are discussed below.

National Institutes of Health. In FY2003, NIH spent \$29.4 million for basic research on TSEs, an increase of \$2.1 million over FY2002; the estimate for FY2004 is \$30.5 million. Basic research on TSEs is supported by four NIH institutes. A fifth institute is conducting a long-term follow-up study of patients who developed CJD after receiving pituitary-derived human growth hormone (hGH) therapy. The work of these five institutes is briefly described below.

National Institute of Neurological Disorders and Stroke (NINDS). NINDS has funded research to develop improved test methods for human prion diseases. The institute is also funding research on “whether the transmissible agent is, in fact, a prion and trying to discover factors that influence prion infectivity and how the disorder damages the brain. Using rodent models of the disease and brain tissue from autopsies, they are also trying to identify factors that influence the susceptibility to the disease and that govern when in life the disease appears.”¹⁹

¹⁷ The HHS BSE Action Plan is announced in an HHS Fact Sheet, “Federal Agencies Take Special Precautions to Keep “Mad Cow Disease” out of the United States,” Aug. 23, 2001, at [<http://www.hhs.gov/news/press/2001pres/01fsbse.html>]. The Action Plan itself is appended to a Notice of Meeting, HHS, “Bovine Spongiform Encephalopathy/Transmissible Spongiform Encephalopathy (BSE/TSE) Action Plan,” 66 *Federal Register* 44146, Aug. 22, 2001.

¹⁸ The committee is chaired by the Commissioner of FDA and includes representatives of CDC, FDA, NIH, USDA, the United States Trade Representative, the Office of Management and Budget, the Customs Service, the Department of State, the Department of Defense, the State Association of Feed Control Officials, the National Association of State Departments of Agriculture, and the White House Office of Science and Technology Policy.

¹⁹ NIH, NINDS Creutzfeldt-Jakob Disease Information Page, at [http://www.ninds.nih.gov/health_and_medical/disorders/cjd.htm].

National Institute of Allergy and Infectious Diseases (NIAID). NIAID conducts TSE research in its Rocky Mountain Laboratories (RML) in Hamilton, MT, and funds similar research in university labs. Studies look at how TSEs cross the “species barrier” and ways to predict whether a given TSE is likely to do so. The RML is developing new prion test methods and creating new and useful strains of mice for research. The RML emphasizes research in two areas; Chronic Wasting Disease (CWD), and therapeutic approaches. Primate and other studies are ongoing to determine if CWD could be transmitted to humans and on other aspects of CWD control such as a vaccine for deer and elk. In addition, the RML uses cell cultures and other tools to screen compounds that might inhibit the formation of abnormal prions and prevent or slow the progression of TSEs.²⁰

National Heart, Lung and Blood Institute (NHLBI). NHLBI research related to TSEs has focused on ensuring the safety and adequacy of the blood supply. NHLBI has supported research to devise a test to screen blood and tissue donors and to determine whether or not CJD is transmissible by blood and blood products. Such research may also lead to the development of a diagnostic tool to detect preclinical disease. In addition to blood safety research, the NHLBI Web site states that:

... in FY2001, NHLBI-supported investigators reported that mouse skeletal muscle can propagate prions and accumulate substantial titers of them. Because significant dietary exposure to prions might occur through the consumption of meat, even if it is largely free of neural and lymphatic tissue, a comprehensive effort to map the distribution of prions in the muscle of infected livestock is needed. Furthermore, muscle may provide a readily biopsied tissue that can be used to diagnose prion disease in asymptomatic animals and even humans.²¹

National Institute on Aging (NIA). NIA is supporting research on the treatment and prevention of prion diseases such as CJD. According to the NIA website, “investigators have used a number of approaches to identify compounds that are effective in clearing prions from cells in tissue culture. Two drugs, quinacrine (an anti-malarial drug) and chlorpromazine (an anti-psychotic drug), are known to enter the brain and are among the compounds that cause the clearance of prions in tissue culture. These compounds were effective at non-toxic concentrations and have been used for many years in humans, making them likely subjects for clinical trials to test their efficacy in treating people with CJD who otherwise face certain death.”²²

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). NIDDK is conducting a follow-up study of patients who developed CJD after receiving human growth hormone (hGH) therapy. The hGH was made by the National Hormone and Pituitary Program (NHPP) funded by the U.S. Public Health Service. Between 1963 and 1985, about 7,700 people received hGH derived from

²⁰ NIH, “NIAID Research on Prion Diseases,” Web page, Jan. 2004, at [<http://www.niaid.nih.gov/factsheets/priondis.htm>].

²¹ NIH, *National Heart, Lung, and Blood Institute Rare Diseases Report, FY 2001*, undated document, available at [<http://www.nhlbi.nih.gov/resources/docs/raredisrpt01.htm>].

²² NIH, National Institute on Aging, *FY2003 Justification of Estimates for Appropriations Committees*, at [<http://www.nia.nih.gov/fy2003%5Fcongress/justification.html>].

the brain tissue of cadavers; 26 have developed CJD. All 26 began hGH treatment before 1977 when a new purification step was added to hormone production. The new step may have eliminated the risk of CJD (prions), but since the disease takes years to develop, it is unknown if those who started treatment after 1977 are also at risk. Of those treated before 1977, about 1% developed CJD, 10,000 times higher than the general population rate of one case per million. Most had received many different preparations of hGH over long periods of time. While the average treatment time with hGH was three years, people who developed CJD were treated with hGH for about nine years. The longest reported time from the start of hGH treatment to first signs of CJD is 33 years in U.S. patients. In Holland, one patient has developed CJD 38 years after a very brief use of hGH, the longest incubation period to date.²³

Centers for Disease Control and Prevention. In FY2003, CDC spent \$3.5 million on activities related to TSEs; funding in FY2004 is \$4.5 million and the request level for FY2005 is also \$4.5 million. Of the CDC total, \$2 million supports the National Prion Disease Pathology Surveillance Center (NPDPS) at Case Western Reserve University in Cleveland, Ohio. CDC established the NPDPS in 1997 in collaboration with the American Association of Neuropathologists. NPDPS conducts testing on suspected cases of human prion disease in the United States, refines methods for discriminating the different disease forms, studies potential markers of prion diseases in blood and urine samples, and maintains information on human cases. Since 1997, the NPDPS has evaluated 1221 patients and identified 732 cases of prion disease, most of them sporadic CJD.

CDC uses a number of methods to conduct surveillance for CJD and vCJD in the United States; these efforts began in 1996. Human TSEs are a reportable disease in 12 states. National cause-of-death data are reviewed to monitor CJD epidemiology. CJD cases in individuals under 55 are investigated to identify possible cases of vCJD. CDC assists in the investigation of possible vCJD cases reported by health care providers. Following the finding of BSE in the United States, CDC recommended that physicians heighten their awareness of potential symptoms of CJD and vCJD, and avail themselves and their patients of the free services of NPDPS in evaluating cases.²⁴ Nonetheless, the rate of autopsies is low in the United States, raising concern that cases of human prion disease may be missed, or be misdiagnosed as other ailments such as Alzheimer's disease. Some argue that human surveillance is inadequate to rule out the presence of domestic cases of vCJD.²⁵

²³ Other countries are also monitoring the development of CJD in patients who received hGH: France, 1,700 were treated with hGH, 89 have CJD; England, 1,848 were treated, 38 have CJD; New Zealand, 5 have CJD after hGH treatment; Holland, 2 have CJD; and Brazil and Australia each have one CJD case. The New Zealand patients and the patient from Brazil received hGH made in the United States, but it was not identical to hormone distributed by NHPP. France, Britain, Holland, and Australia produced their own hGH.

²⁴ CDC, "Bovine Spongiform Encephalopathy in a Dairy Cow – Washington State, 2003," *MMWR*, vol. 52, no. 53, Jan. 9, 2004, pp. 1280-1285.

²⁵ A discussion of this possibility is presented by Todd Hartman, "Mad Cow's Untold Story; Studies Quietly Raise Questions About Threat to Humans," *Rocky Mountain News*, Jan. 12, 2004, p. 5A.

Food and Drug Administration. The FY2005 budget request for FDA provides \$30 million, an \$8 million increase over FY2004, for BSE prevention efforts at the agency.²⁶ These include measures to prevent the spread of BSE in the animal feed supply, discussed in CRS Report RL32199, *Bovine Spongiform Encephalopathy (BSE, or 'Mad Cow Disease'): Current and Proposed Safeguards*. Other public health protections at FDA are discussed below.

A Transmissible Spongiform Encephalopathy (TSE) Advisory Committee was formed in 1998 to advise the FDA Commissioner on matters regarding the safety of FDA-regulated products. The committee, which meets at least semi-annually, includes representatives of government, such as BSE experts at the USDA, and experts from academia and the private sector.²⁷

The FDA Center for Biologics Evaluation and Research (CBER) is responsible for the safety of the U.S. blood supply. Protecting recipients of blood and blood products from CJD and TSEs is difficult, because there are no tests of any kind for TSEs in blood. FDA states that, "the main way to lower the theoretical risk of vCJD in blood is through deferral of donors who might have eaten contaminated beef products."²⁸ FDA has recommended that persons having resided in the United Kingdom during specified time periods (and certain other groups) be barred from blood donation in the United States, to eliminate the potential for transmission of disease from blood donors infected but not yet showing symptoms of vCJD.²⁹ Adding new threats like vCJD to the list of deferrable conditions has obvious implications for adequacy of the blood supply. FDA reported that it is undertaking an assessment of the BSE exposure risk to blood donors in the United States and Canada in light of the single BSE case that has been reported in Canada (presumably FDA will consider the U.S. case as well), and notes that:

Although it is premature for the FDA to present any results of this ongoing assessment, we believe that the likelihood of exposure to the BSE agent for both Canada and the U.S. is and has been very small. ... FDA does not believe that there are sufficient data at this time to warrant changing our blood donor deferral

²⁶ The request includes funding for the Animal Drugs and Feeds program, for inspections of livestock feed facilities, as well as for other FDA programs to implement new standards developed after the discovery of the BSE-positive cow in Washington state. U.S. Department of Health and Human Services, *Budget in Brief FY2005*, p. 5, and *Fiscal 2005 Budget: Health and Human Services*, Feb. 2, 2004.

²⁷ Home Page of the FDA TSE Advisory Committee, at [<http://www.fda.gov/cber/advisory/tse/tsemain.htm>].

²⁸ FDA, *Questions and Answers on FDA Guidance Entitled "Revised Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob (CJD) Disease and Variant Creutzfeldt-Jakob Disease (vCJD) by Blood and Blood Products,"* Apr. 16, 2002, at [<http://www.fda.gov/cber/gdlns/cjdvcjdq&a.htm>].

²⁹ FDA, *Guidance for Industry: Revised Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Blood and Blood Products*, Jan. 2002, at [<http://www.fda.gov/cber/gdlns/cjdvcjd.htm>].

guidance. We will continue to study this issue and take further action as appropriate.³⁰

FDA is also responsible for the safety of human drugs, vaccines, dietary supplements, cosmetics, and certain foods that may contain beef by-products, such as broths and gelatin. Since 1993 FDA has issued guidances and warning letters for manufacturers of drugs and vaccines (which are stringently regulated through a pre-market approval process and oversight of required good manufacturing practices), prohibiting the use of certain bovine-derived products from countries in which BSE had been found. In addition, FDA alerted manufacturers of gelatin products and dietary supplements of the need to avoid using bovine-derived products from those countries.³¹

On January 26, 2004, FDA announced the forthcoming publication of an interim final rule that would expand protections in the wake of the finding of BSE in the United States. These expanded protections are intended to harmonize with prohibitions implemented by USDA on December 30, 2003, to protect the beef supply. The rule will prohibit a number of domestic bovine-derived material from FDA-regulated human food, dietary supplements and cosmetics.³² As of late February 2004, the rule has not been published.

Environmental Protection Agency. EPA recently announced the agency's intention to regulate, under federal pesticide law, products that claim to inactivate prions. EPA plans to issue a final rule to include prions in a list of microbial pests that the agency regulates under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). EPA is also developing recommendations on disposal methods of animal carcasses that are infected with prions. These EPA efforts are a result of the agency's participation "in a federal agency working group, which includes FDA, CDC and USDA, that was formed to examine the risks that prions pose to humans, animals, and the food supply."³³

Department of Defense. In the FY2002 DoD appropriations act (P.L. 107-117, Senate Report 107-109), Congress provided \$42.5 million for the National Prion Research Program (NPRP). The new program is administered by the Army's

³⁰ FDA, Minutes of the Transmissible Spongiform Encephalopathies Advisory Committee, July 17-18, 2003, at [<http://www.fda.gov/cber/advisory/tse/tsemain.htm>].

³¹ A summary of FDA protections prior to the U.S. finding of BSE is in the statement of Stephen Sundlof, Director of the FDA Center for Veterinary Medicine, before the Senate Committee on Commerce, Science and Transportation, *Mad Cow Disease: Are Our Precautions Adequate?*, hearing, 106th Congress, 2nd sess., Apr. 4, 2001, (Washington: GPO, 2001).

³² FDA, "Expanded 'Mad Cow' Safeguards Announced To Strengthen Existing Firewalls Against BSE Transmission," press release, Jan. 26, 2004.

³³ "EPA to Regulate Mad Cow Proteins as Pests Under Federal Law," *InsideHealthPolicy.com*, Feb. 10, 2004.

Medical Research and Materiel Command (MRMC).³⁴ About \$6.5 million of the total will be used for overhead costs by MRMC, leaving \$36 million for research, of which \$20 million is to be targeted at rapidly developing a diagnostic test to detect the presence of prion disease and to study the prevention, transmission, inactivation or pathogenesis of TSEs, including chronic wasting disease (CWD).

The Institute of Medicine (IOM) was asked by MRMC to assess present scientific knowledge about TSEs and to make recommendations on funding the highest priority research. An interim report, released by IOM in January 2003, provided guidance (focusing specifically on prion detection and disease diagnosis) to one of the review panels that assessed the submitted research proposals. The final IOM report, *Advancing Prion Science*, released in November 2003, updated material in the interim report and made recommendations on the highest priority research in TSE surveillance, prevention, and treatment.³⁵

Outstanding Research Needs

Prion research has been advanced by the development of numerous strains of genetically-altered mice. Each strain responds to infection with a TSE in a fairly predictable fashion. Some strains, called “proxies,” mimic TSEs in natural hosts, yielding valuable insights such as the role of genetics in susceptibility and disease progression. Incubation periods in mice, while still lengthy at one-two years, are much shorter than incubation periods in natural hosts. But despite the advantages of mouse research models, they represent enough of a departure from natural conditions that findings may not always be applicable to natural prion diseases. Experts often debate the relevance of specific findings from these studies.

The Institute of Medicine report, *Advancing Prion Science*, noted the many barriers to understanding of prion diseases and their control. IOM recommendations for research priorities included: basic research; improving diagnostics; testing blood for evidence of TSEs; improving surveillance for TSEs in the United States; assessment of strategies for prevention and treatment; strengthening the national prion research infrastructure; and examining specific risks to the U.S. military. Barriers to prion research and some specific findings highlighting the uncertainties of this work are discussed below.

³⁴ MRMC manages biomedical research programs that are part of the DoD and Army budget submission. It also manages congressionally targeted biomedical research programs, such as the NPRP, through the Office of the Congressionally Directed Medical Research Programs (CDMRP). A request for proposals under the NPRP was published on Aug. 2, 2002; the submission deadline was Oct. 30, 2002. Two different panels reviewed the proposals in Dec. 2002 and Feb. 2003. NPRP funded 38 of the 136 proposals that were received. For more information, see DOD, *Congressionally Directed Medical Research Programs*, at [<http://cdmrp.army.mil/nprp/>].

³⁵ Institute of Medicine, *Advancing Prion Science: Guidance for the National Prion Research Program*, Nov. 17, 2003, at [<http://www.nap.edu/catalog/10598.html>]. (Hereafter cited as Institute of Medicine, *Advancing Prion Science*.)

The Slow Pace of Prion Research. Prion research is hampered by the nature of the disease and the protections required for its study. To protect researchers, prions must be handled in laboratories with Biosafety Level 2 or 3 protections (depending on specific prions and studies).³⁶ All prion diseases are characterized by long incubation periods; experimental transmission studies take years to yield results. Seventy-five percent of NIH funds awarded for TSE research go to only two laboratories. The size of the prion research community is relatively small.

Poorly Understood TSE Disease Process. Scientists do not have a complete understanding of which tissues are affected (and therefore, are infectious) at each point of the TSE disease process. Also unclear are the mechanisms by which the agent enters the body, how it disseminates within the body, and the routes used to reach the brain and cause the cellular damage that leads to clinical symptoms. Depending on the TSE, it is unclear how the agent spreads from host to host and what features of the host determine susceptibility or resistance.

Origin of Sporadic CJD. Experimental findings in mice raise concern about the spectrum of human disease that could result from exposure to BSE. Researchers used mice genetically engineered with the human version of prion instead of the mouse version, to simulate human disease. When the mice were infected with the BSE agent, some developed signs of vCJD and others developed signs consistent with sporadic CJD. The scientists believe it is possible that some human patients with sporadic CJD may have a disease arising from BSE exposure. This finding highlights the difficulties in extrapolating the results of rodent studies to natural conditions, and the need for rigorous surveillance and characterization of human prion diseases.

Spread of CWD in the United States. The lack of understanding of CWD transmission and whether it can cause disease in humans or cattle is of concern. The Institute of Medicine report *Advancing Prion Science* concluded that while there is no evidence that CWD is transmissible to humans, “the theoretical risk of infection led the committee to advise people to avoid exposure to CWD-contaminated meat and meat products. The wide range of practices for processing venison, the paucity of regulation or oversight in this area, and the many opportunities for spreading the CWD agent influenced the committee’s conclusion in this regard.”³⁷

Persistence of BSE in the United Kingdom. In August 1996 the United Kingdom tightened a ban on the recycling of livestock into feed used for farm animals, because cases of BSE continued to occur despite an initial ban instituted in mid-1988. A total of 77 cases of BSE in animals born after the 1996 ban have been

³⁶ Biosafety levels 1-4 were developed by CDC and NIH to classify pathogens according to risk in the laboratory, and define conditions and practices that assure the safety of workers and the community. Level 4 pathogens pose the greatest risk and require the most stringent practices. Current biosafety requirements are found in *CDC/NIH, Biosafety in Microbiological and Biomedical Laboratories*, 4th ed., 1999, at [<http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4toc.htm>].

³⁷ Institute of Medicine, *Advancing Prion Science*, p. 3.

reported; 49 cases were reported in 2003. Although contaminated feed, imported prior to a 2001 restriction, is suspected to be the cause, it remains to be seen whether cases will soon decline as predicted by this theory, or whether other explanations should be considered.

Stability of TSE disease agent. Prions are one of the most stable organic substances known. Even when prion infectious tissue is incinerated at 600 degrees Centigrade, there is still some infectious activity remaining in the ash sample. Many physical, chemical and irradiation methods have been tried in order to inactivate prions with very little success. Some combinations reduce the amount of infectivity without totally eliminating prions on a reliable and consistent basis. Glass and steel surfaces seem to be particularly difficult, a major concern because hospitals, laboratories, and industry (slaughter houses, rendering plants, animal feed companies) use instruments and equipment composed of these materials.

Asymptomatic carriers. Experiments in mice and hamsters demonstrated a “silent carrier” state for BSE. Tissues from experimentally-infected animals that never became ill nonetheless caused illness when used to infect a second species. The relevance of these findings, and possible implications for the safety of cattle feeds containing by-products from other mammalian species, are under discussion.

Low autopsy rate. According to estimates in the IOM report *Advancing Prion Science*, at least half of human victims of TSEs in the United States do not receive autopsies, and therefore are not identified as having TSEs. This is a major obstacle to reaching an understanding of the level of human TSE disease in this country.

Risk Communication – Talking About Rare But Serious Risks

Risk communication has risen in importance since the terror attacks of 2001. It is one of the required activities for state health departments receiving federal funds for bioterrorism preparedness. (It should be noted that there is no evidence that the finding of BSE resulted from an intentional act.) Risk communication is considered essential for success in controlling infectious diseases such as SARS or influenza, when officials may ask the public to cooperate with disease screening at airports, home isolation, vaccination programs, or other control measures. The finding of BSE in the United States presented another of many recent challenges in health risk communication for government officials.

CDC, which provides training and curricula in risk communication for public health personnel, describes crisis and emergency risk communication as:

... the attempt by science or public health professionals to provide information that allows an individual, stakeholders or an entire community, to make the best possible decisions about their well-being, under nearly impossible time

constraints, and to communicate those decisions, while accepting the imperfect nature of their choices.³⁸

CDC recommends having risk communication plans and designated spokespersons in place pre-event. Both USDA and HHS had done so as part of their BSE response plans, and may also have benefitted from the experience of their Canadian counterparts, who had run the public relations gauntlet on BSE just months earlier.

Several specific risk communication challenges are at play for BSE. The human form of BSE, vCJD, as well as CJD, are *dread diseases*. While rare, they are debilitating, painful, uniformly fatal diseases for which there is no treatment. Communicating to the public about what is today believed to be a *negligible risk* is a challenge; the audience may not appreciate quantitative information that is meaningful to experts. Also, there can be an intuitive conflict between assertions of minimal risk and announcement of new actions in response to an event. The newness of BSE and related diseases leaves gaps in scientific understanding, and considerable *uncertainty* in some areas. And, even where there is scientific consensus, the facts are nonetheless quite complex. The finding of BSE in a cow in Washington state was followed by a barrage of information, mostly from government officials and the media, not all of it relaying the same messages.

USDA officials have served as the principal spokespersons for the U.S. government since BSE was discovered here. With the exception of a few public statements made by Secretary of Agriculture Ann Veneman, spokespersons were technical experts. These officials have had two key audiences — American consumers, who account for 90% of the market for U.S. beef, and importing countries, responsible for the other 10%, which was valued at \$3.3 billion in 2003.³⁹ Officials have stated that the U.S. beef supply is safe, and that persons who may have eaten recalled beef from the affected animal are not at risk. They have not recommended any changes in consumer behavior.

A primer on risk communication from the Canadian Food Inspection Agency, written prior to the finding of BSE in Canada, opines about communicating risk in the face of uncertainty:

... the public has tired of false reassurances of safety and of decisions presented as though they are relatively conclusive when fundamental uncertainties still remain. (One expert) states that the public is quite capable of understanding the concept of uncertainty and thus should be provided with clear information about the uncertainties around risk. This in turn will increase perceptions of trust in information sources and better acceptance of emerging technologies.⁴⁰

³⁸ CDC, *Emergency and Risk Communication*, Web page, at [http://www.cdc.gov/communication/emergency/erc_overview.htm].

³⁹ For more information on trade in U.S. beef products, see CRS Report RS21709, *Mad Cow Disease and U.S. Beef Trade*, by Charles E. Hanrahan and Geoffrey S. Becker.

⁴⁰ Canadian Food Inspection Agency, *Risk Communication and Government, Theory and Application for the Canadian Food Inspection Agency*, Spring 2001, at [<http://www.inspection.gc.ca/english/corpaffr/publications/riscomm/riscommme.shtml>].

Some experts in health risk communication have been critical of USDA's handling of the situation and at least one felt that spokespersons overstated the level of certainty, saying they were 'being vastly more reassuring about the safety of U.S. beef than (they) should be.'⁴¹ In contrast, various Members of Congress, in hearings of both the House and Senate Agriculture Committees, generally praised the Secretary of Agriculture and her staff for their handling of the situation.⁴² USDA officials have provided dozens of press briefings, often on a daily basis, since the finding of the BSE-positive cow was announced on December 23, 2003, and have at times made officials from USDA's Food Safety and Inspection Service (FSIS) and from FDA available at these briefings. FSIS expanded the available hours for its toll-free consumer hotline during the first few weeks after the finding, and staff at USDA's Animal and Plant Health Inspection Service also maintained expanded hours for its toll-free information hotline as well.

It is too soon to know the effect of official risk communication efforts. A Wall Street Journal Online-Harris Interactive Health-Care poll of U.S. consumers on January 6-8, 2004, found that:

(Twenty) percent of Americans ... say fear of mad cow disease will change their eating habits; 16 percent of those who say they will change their eating habits ... will do so by eliminating beef from their diets.; and, 88 percent ... are confident that the government will take the proper steps to stop the spread of mad cow disease in the United States.

One news report noted similar findings from another poll and the finding that initial stock market reactions quickly stabilized, and suggested that public familiarity with "Mad Cow disease" following events in the United Kingdom and Canada allayed consumer fears here.⁴³ Thus far, none of the countries that banned imports of U.S. beef following the announcement has fully resumed trade, though there are likely a number of factors other than risk communication that affect these decisions.

⁴¹ Antonio Regalado, "Scientific Data Offer No Proof Of Beef Safety," *Wall Street Journal*, Dec. 29, 2003.

⁴² See statements and transcripts from hearings of the U.S. House of Representatives, Committee on Agriculture, *Review of the USDA's Bovine Spongiform Encephalopathy (BSE) Response*, Jan. 21, 2004, and the U.S. Senate, Committee on Agriculture, Nutrition and Forestry, *Full Committee Hearing to Examine the Current Situation Regarding the Discovery of a Case of Bovine Spongiform Encephalopathy in a Dairy Cow in Washington State as it Relates to Food Safety, Livestock Marketing and International Trade*, Jan. 27, 2004.

⁴³ Michael Fumento, "Not Having a Cow Over Mad Cow. What Gives?" *Washington Post*, Jan. 18, 2004, p. B1.

Legislation

In the 108th Congress, legislation related to TSEs up to this point has largely focused on food safety and agricultural practices. These proposals, relating to animal identification systems, the safety of animal feeds, testing of cattle for BSE, and other measures, are listed in CRS Issue Brief IB10127, *Mad Cow Disease: Agricultural Issues for Congress*. Two bills include provisions pertaining more directly to human health. S. 2007 (Durbin) and H.R. 3714 (DeLauro) would require annual reports to Congress regarding U.S. programs for surveillance of human prion diseases.

Conclusion

The finding of BSE in an American cow in December 2003 has had a marked impact on U.S. beef export markets, but an apparently modest impact on domestic beef consumption. Most experts believe the threat to public health from this finding is minimal. Nonetheless, numerous programs in place to prevent BSE, or control its spread, were enhanced once the BSE case was reported. Whether these actions were sufficient is a matter of debate.

Crafting the appropriate public policy response to this finding requires attention to the experiences of other affected nations, and respect for the breadth of scientific uncertainty posed by prion diseases. Congress may wish to consider the TSE protections put in place by the FDA, the CDC surveillance program for human prion diseases, and the prion research activities proposed by these agencies, the NIH and DoD, along with activities in the agricultural sector, to determine the appropriate commitment of resources needed to prevent these rare but devastating diseases.