BSE CONTINGENCY PLAN

U.S. FOOD AND DRUG ADMINISTRATION

Version 1.0 - February 15, 2001

I. PURPOSE

This Contingency Plan provides guidance outlining responsibilities and establishes procedures for FDA involving Bovine Spongiform Encephalopathy (BSE) emergency reports. These procedures cover FDA regulated products or ingredients that may have been introduced into the US market.

A. DEFINITIONS

Alert — any situation involving reports (confirmed or unconfirmed) of BSE/TSE in FDA regulated products including reports of contamination of feed, prohibited materials in imported products, reports of cases of Creutzfeldt-Jakob Disease (CJD)[1] or new-variant CJD (vCJD) cases in the U.S.

Emergency — an unforeseen combination of circumstances or the resulting state posing a serious risk to public health (both human and animal) that calls for immediate action.

BSE Emergency — any situation involving a presumptive or confirmed diagnosis of infection by the BSE agent in any bovine or product derived therefrom (domestic or imported) in the U.S.

II. BACKGROUND and HISTORY

Bovine Spongiform Encephalopathy (BSE), known as “mad cow disease,” is a transmissible, slowly progressive, fatal, degenerative disease affecting the central nervous system (CNS) of adult cattle. BSE is characterized by neurologic clinical signs and a long incubation period.

BSE belongs to a family of diseases known as the transmissible spongiform encephalopathies (TSEs). These diseases are caused by a transmissible agent, which is yet to be fully characterized. Specific types of TSE’s include scrapie, which affects sheep and goats; transmissible mink encephalopathy; feline spongiform encephalopathy; chronic wasting disease of deer and elk; and five rare diseases in humans, kuru, Creutzfeldt-Jacob disease (CJD), Gerstmann-Straussler-Scheinker syndrome, fatal familial insomnia (FFI), and new-variant Creutzfeldt-Jacob disease (vCJD) (Will et al. 1996.)

[1] Reporting of cases of CJD (while not associated with BSE per se) is necessary relating to verifying whether the case is vCJD and the history of the patient associated with donation of blood or tissue.

BSE was first recognized as a new distinct disease of cattle by researchers at the Central Veterinary Laboratory of the British Ministry of Agriculture, Fisheries and Foods (MAFF) at Weybridge, England, in November 1986 (Wells et al, 1987). However, there are indications that the first clinical case of the disease was observed as early as April 1985 (Wilesmith et al. 1988).

Regulatory controls taken in the United Kingdom to manage the BSE epidemic and prevent potential public health risks include an action to make the disease reportable (June 1998); a ban on the feeding of ruminant-derived protein supplements to other ruminants (July 1998); compulsory slaughter and incineration of suspect cattle (August 1998); a ban on the human consumption of specified offals, including brain, spinal cord, thymus, spleen, tonsils, and intestines (November 1989); a ban on the feeding of the specified offals or their products to all pet and farm animals (September 1990); a ban on the use of meat and bone meal in fertilizer (November 1991); redefinition of specified offal to include the intestines and thymus of calves less than 6 months old (November 1994); a ban on the feeding of all mammalian protein to all food-producing animals (April 1996); and a ban on the use of any cattle 30 months old or older in the human and animal food chain (April 1996).

In 1986 an outbreak of BSE was identified among cattle in the United Kingdom. Since then BSE has grown to epidemic proportions in the UK and has spread to other European countries, although with much fewer cases. Subsequently, over 90 human cases of vCJD were also identified. There is strong evidence suggesting that these cases were directly related to the BSE epidemic and possibly caused by the same agent. Because of this evidence of transmissibility to humans, infection with the BSE agent is considered a public health threat.

Reports of a case of vCJD in the U.S. may indicate the presence of BSE in the U.S. or a foreign exposure. In the rare event this were to occur, FDA would work closely with USDA, CDC and other public health agencies in their efforts to identify a source of exposure to the BSE agent.

USDA has taken measures to prevent the entry of BSE into the U.S. including banning cattle and cattle products from countries where BSE has been reported or where adequate surveillance programs are not in place; monitoring and testing for BSE in U.S. cattle; and educating producers and the public about the disease.

To prevent the establishment and amplification of BSE through feed in the United States, FDA implemented a final rule that prohibits the feeding of mammalian protein to ruminant animals in most cases. This rule, Title 21 Part 589.2000 of the Code of Federal

Regulations, became effective on August 4, 1997.

III. BSE EMERGENCY ORGANIZATION and OPERATING PROCEDURES

INITIAL NOTIFICATION

FDA's Emergency Operations Group in the Division of Emergency and Investigational Operations (DEIO), Office of Regional Operations, Office of Regulatory Affairs (ORA) serves as the agency's focal point for all emergency response activities on a seven-days-a-week, 24 hours a day basis and maintains the agency's Emergency Operations Center (EOC). The 24-hour FDA emergency contact number is **(301) 443-1240**, Fax (301) 443-3757, or e-mail to **emops1@ora.fda.gov**

Initial emergency alerts received by FDA headquarters units from USDA/APHIS, USDA/FSIS, FDA district offices, FDA Centers, other federal and state agencies, consumers and other sources outside FDA will be reported promptly by phone, fax or e-mail to DEIO.

Alerts may include reports of contamination relating to animal-derived or animal-containing product in any FDA regulated product, including foods with less than 3% meat, dietary supplements, cosmetics, biologics, drugs, devices, or veterinary products. Alerts may be reports of suspect CJD cases or cases of vCJD. [Report should include information related to the history of the individual relating to blood or tissue donation (or receipt) in the case of CJD cases, which will occur in the population. Any history related to foreign exposure for these cases would also be useful.] Other alerts may be reports related to cases of TSE in other animals which may be used for food or feed.

The alert should include:

- Description of the emergency situation and status (presumptive or confirmed).
- Description and number of animals affected/dead and their location.
- Description of product utilizing the affected bovine derived material (brand name, size, lot number, etc.)
- Responsible firm (manufacturer, supplier, distributor) and contact person at the firm (phone number)
- Press coverage if any or anticipated, or any other pertinent information
- Description of imported products in domestic commerce subject to BSE prohibitions.

- If available, traceback information on products to source to include domestic distribution chain, and where relevant, Customs entry data, responsible importer of record, and foreign shipper/manufacturer data.

After hours, or when the FDA's Emergency Operations Center is not in operation, the answering service will refer all BSE calls via pager to the DEIO Late Duty Officer.

See Figure 1 for a summary of the FDA Emergency Alert System.

A. DEIO RESPONSIBILITIES

FDA BSE emergency operations will be coordinated by The Division of Emergency and Investigational Operations (DEIO), working with the appropriate Center Emergency Coordination Unit. DEIO will have primary responsibility for ensuring that necessary investigations and actions are taken in response to emergency situations.

DEIO will immediately advise the appropriate field office(s), each Centers' BSE emergency coordination contact, the Commissioner's Office and the Office of Regulatory Affairs of emergency alerts, or when an investigation reaches presumptive status as described on page 7, Section IV, B. If the information did not come from USDA/APHIS, DEIO will immediately advise that agency.

The Office of Public Affairs (OPA) will be notified when press coverage is ongoing or imminent. Other offices at headquarters will be notified as appropriate.

DEIO will inform and forward to the Division of Federal-State Relations (DFSR) copies of all reports from field offices pertaining to state and local activities, actions, agreements and any press releases issued.

DEIO will notify the Division of Import Operations and Policy (DIOP) of BSE emergencies originating from foreign sources and provide DIOP with any traceback information derived from the initial report. [DIOP is part of a multi-agency work group with the U.S. Customs Service (USCS) and USDA for joint operations related to BSE preventative measures and emergencies originating from foreign sources.]

DEIO will coordinate information concerning emergencies with headquarters offices of other Federal agencies consistent with guidance in the Regulatory Procedures Manual (RPM). When international commerce is involved, DEIO will advise the Office of

International Programs (OIP) so that appropriate coordination may be initiated.

DEIO will prepare periodic updates or status reports on such alerts and investigations.

B. DFSR RESPONSIBILITIES

The Division of Federal-State Relations (DFSR), in cooperation with the regions or districts, will coordinate Agency interaction with state and local agencies in identified BSE emergency situations.

DFSR will maintain FDA's rapid communication system to state governments, major municipalities and poison control centers. DFSR will also continue the ORO/State Association efforts to develop uniform emergency operational guidelines.

In emergency situations, DFSR will:

Assure that the governors' offices have been notified of significant confirmed emergencies in their states.

Notify all states of confirmed emergencies involving more than one state. Indicate potential or problem products entering commerce.

Prepare (or distribute) information requested by states for their emergency roles, and assure that states are fully advised as to what action the Agency can recommend to them under the circumstances of the specific emergency.

As routine functions, DFSR will:

Maintain a directory showing the responsibilities of major state organizations, names, telephone numbers, and addresses of key state personnel, and other information needed to quickly enlist nation-wide state and local assistance to FDA's emergency operations.

C. CENTER RESPONSIBILITIES

1. Emergency Coordination Unit

All Centers currently maintain an "Emergency Coordination Unit", which serves as the focal point for emergency response with DEIO. Centers are responsible for scientific evaluations and for policy decisions, in cooperation with DEIO and the Associate Commissioner for Regulatory Affairs (ACRA), in their respective program areas. Each Center has a BSE committee for serving that scientific, compliance and policy decision function for the Center's emergency response consistent with Chapter 7-10, RPM.

2. Center BSE Coordinator

Each Center has a designated BSE coordinator that serves as initial contact point between DEIO and the Center.

The Center BSE Coordinator will contact DEIO, if DEIO is not already notified of the BSE incident, the Center BSE Committee and all other appropriate FDA staff as listed on the Center BSE emergency coordinators' contact List. If notification comes from ORA/DEIO, the Center BSE emergency coordinator will contact all appropriate Center staff. If notified by any other source, the Center BSE coordinators will also notify DEIO.

The Center BSE Coordinators are responsible for maintaining:

- Daily contact with DEIO staff on status of situation
- Daily updates to BSE Committee chair and other members as necessary until status is confirmed.
- Current BSE file that will include:
  - Center BSE Coordinators Contact List (Attachment A).
  - Lists of all products known to contain bovine derived active ingredients and associated FDA product codes.
  - Health hazard evaluations.
  - Other literature related to human risk associated with BSE.
  - Current scientific research concerning transmissibility and effective inactivation processes.
  - Names of Committee members, updated and provided to DEIO as needed.

The Center BSE Coordinator is responsible for updating the BSE contact lists on a quarterly basis and sending the updates to DEIO.

The Center BSE coordinators are identified below:

CBER: The Chief of Program Surveillance Branch, Division of Inspections and Surveillance, Office of Compliance and Biologics Quality coordinates CBER's emergency response. Each CBER division director will designate the contact and alternate contact for his/her division.

CDER: The Recall Coordinator/Drug Shortage Manager, Office of Compliance, coordinates CDER's emergency response. Each CDER division director and deputy director will act as the contact and alternate contact for their division or will designate persons to act in this capacity.

CDRH: The Issue Manager, Issues Management Staff, Office of Surveillance and Biometrics will be coordinating CDRH's emergency response. Each CDRH division director and deputy director will act as the contact and alternate contact for their division or will designate persons to act in this capacity.

CVM: The Director, Division of Compliance coordinates CVM's emergency operations, with scientific support from the Division of Animal Feeds.

CFSAN: The Director, Office of Field Programs coordinates CFSAN's emergency operations, with scientific support from the appropriate divisions.

IV. EMERGENCY CASE PROCEDURES

The following cases represent anticipated potential BSE emergencies. In most cases, the TSE/BSE causative agent is likely to be of foreign origin since no BSE infected bovine have been identified in product of U.S. origin. Consequently, all emergency procedures must incorporate both domestic and import/international operations. With the exception of Case A below, DEIO will be notified of all other defined cases.

A. Central Nervous System (CNS) Suspect Bovine

1. Definitions

A Central Nervous System (CNS) Suspect designated by USDA/APHIS is any bovine that has CNS signs (such as lack of coordination, aggression, seizures, fine head tremors, etc). According the USDA BSE Response Plan, USDA inspection procedures include identifying animals with central nervous system conditions. Animals with such conditions are considered suspect for BSE, prohibited from slaughter, and referred to APHIS for examination.

2. Actions

USDA will not notify FDA in suspect bovine cases, however if FDA receives a report of such an animal, FDA will notify USDA/APHIS.

Pathologists at APHIS' National Veterinary Services Laboratories (NVSL) histopathologically examine the brains from these condemned animals. In addition, samples are tested using a technique called immunohistochemistry, which tests for the presence of the protease-resistant prion protein (a marker for BSE). If the examination or testing show no evidence of BSE, no further action is taken by USDA.

B. Presumptive Positive BSE Case

1. Definitions

A BSE Presumptive Positive is a bovine that APHIS has designated as laboratory test positive for BSE with:

- Presence of histopathological lesions of BSE in the brain,
- Positive for immunohistochemical staining for BSE agent.

In the USDA/APHIS BSE Response Plan, a pathologist from USDA/NVSL will hand carry the sample to the United Kingdom for confirmation. The international animal health community has recognized the United Kingdom's Central Veterinary Laboratory (CVL) as the world's reference laboratory for diagnosing BSE.

2. Actions

USDA/APHIS will notify FDA (DEIO 24 hour number) in the case of a presumptive positive BSE in an animal.

Once FDA is notified, DEIO and CVM will work with USDA/APHIS to determine the remains of the animal.

The following scenarios may be a rare occurrence however they are listed as possible scenarios:

a) Animal-derived material used in any FDA-regulated product or its manufacture.

- Determine feed history and origin of presumptive positive bovine for source of potentially BSE contaminated feed and animals.
- Determine feed history and origin of herd mates of presumptive bovine positive for source of potentially BSE contaminated feed.
- Determine feed history and origin of geographically close herds to presumptive positive premises for source of potentially BSE contaminated feed, animals, and bovine-derived material.
- Prepare draft press releases in coordination with USDA/APHIS in anticipation of positive confirmation of BSE case.
- If case is determined to be negative for BSE, case is closed.

b) Animal rendered to animal feed:

- FDA will identify renderer and trace meat and bone meal forward.
- State resources may be used in the investigation.
- FDA will work with the involved state to isolate and secure animals consuming contaminated feed.

c) Animal isolated without processing to feed (frozen, refrigerated, and incinerated)

- Arrange for secure disposal.

C. Confirmed Positive BSE Case Diagnosis

1. Definitions

A BSE presumptive positive case that has been confirmed by the United Kingdom's Central Veterinary Laboratory.

2. Actions

- Continue FDA investigation, data collection, feed history and controls, and information on disposition of derived materials.
- Continue communicating with USDA and other agencies regarding case activities.
- Finalize and distribute press releases.

a. BSE animal(s) originating within the U.S.

- FDA Centers involved will provide immediate and long-term health hazard assessment and action recommendations to Center Directors and DEIO.

b. BSE animal(s) originating outside of the U.S.

Determine whether bovine ingredients from the case may have entered into the U.S. manufacturing processes for regulated products. If not, case will be closed.

If ingredients have been determined to be in the U.S. the appropriate FDA Center will provide an immediate health hazard assessment and action recommendations to the Center Directors and DEIO.

FDA working with USDA/APHIS will attempt to determine the origin of the animal including whether it was from a known BSE country.

D. Imported product (containing meat or animal by-product) originating from a BSE affected country that is identified as not being refused by USDA/APHIS or FDA.

Actions

1. The appropriate FDA Center(s) will decide on the health hazard and if an immediate health hazard exists, DEIO will notify DIOP to add the product, country, and firm to the import alert for detention without physical examination of future entries. Any distribution of product will be evaluated to determine need for further FDA action, such as recall.

2. If there is no immediate health hazard, DEIO will notify DIOP for further appropriate action.

V. Recalls

If management of the BSE event includes product recalls, the recall procedures in Chapter 7 of the RPM will be followed.

VI. FINAL ASSESSMENT

DEIO and the participating Centers will carry out a final assessment of the emergency event to evaluate the FDA emergency response and identify any deficiencies.

VII. IMPLEMENTATION

The agency policy is effective immediately.

Attachment A

BSE EMERGENCY PHONE NUMBERS

	OFFICE
USDA (APHIS)	
APHIS Emergency Program Staff	**301-734-8073**
Dr. Linda Detwiler	609-259-5826
Allen Jenny	515-663-7927
CDC	
Dr. Lawrence Schonberger	404-639-3091
NIH	
Dr. Paul Brown	301-496-5292
FDA	
ORA 24-hour Emergency Number	**301-443-1240**
Ellen Morrison	301-443-1240
Joy Dawson	301-827-1144
Press Office	301-827-6250

BSE COORDINATORS AND CONTACTS LIST

	OFFICE
CVM BSE Contacts	
Gloria Dunnavan	301-594-1726
Dr. Burt Pirchett	301-827-0177
Dr. George (Bert) Mitchell	301-827-5587
CFSAN BSE Contacts	
1. Joe Baca	202-205-4187
2. Dr. John Kvenberg	202-205-4187
3. Dr. John Sanders	202-205-4608
Dr. Robert Brackett (alt)	202-205-8139

CDER BSE Committee Members

	OFFICE
BSE Coordinator, Recall Coordinator/Drug Shortage	

Michael Verdi	301-594-2456
BSE Working Group	
Dr. Yuan-Yuan Chiu	301-827-5918 x2
Carol Vincent (alternate)	301-827-7510
Medical Officer	
Dr. Russell G. Katz	301-594-2850
Chemistry, Manufacturing, and Controls Expert	
Dr. Yuan-Yuan Chiu	301-827-5918 x2
Frank Holcombe, Jr. (alt)	301-827-5849

Executive Secretary

June Cory	301-594-5608

CBER Committee Members

	OFFICE
BSE Coordinator, Recall Coordinator/Drug Shortage	
Jerome Davis	301-827-6220
Beatrice Greenberg	301-827-6220
BSE Working Group	
Dr. David Asher	301-594-6432
Dr. Andrew Lewis	301-827-0650
Medical Officer	
Dr. Andrew Lewis	301-827-0650
Dr. David Asher (alternate)	301-594-6432
Product Quality Expert	
Rolf E. Taffs	301-827-4554
Gerald Feldman (alternate)	301-827-1720
Executive Secretary	
Karen Orchard	301-827-0637

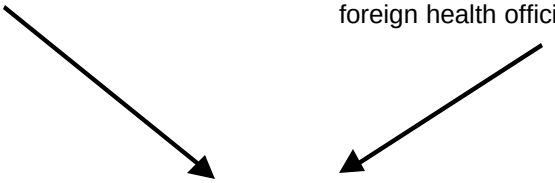
CDRH BSE Committee Members

	OFFICE
BSE Coordinator, Issue Manager	
Nancy Pressley	301-594-3060
BSE Working Group	
Dr. Kiki Hellman	301-443-7158
Medical Officer	
Dale Travis	301-594-0606
Product Expert	
Karen Warburton	301-594-1744 x122
Executive Secretary	
David Berkowitz	301-594-3090 x152
Lisa Kennell (alternate)	301-443-8262 x166

Figure 1
FDA EMERGENCY ALERT SYSTEM

Information provided from FDA internal sources

Information provided from outside sources (other Federal/state agencies, foreign health officials, industry, press



DEIO
(Command Center-agency wide and interagency focal point for 24 hour, 7 day communications)

- Primary responsibility for monitoring emergency alert information and coordinating investigations and scientific evaluations
- Serves as focal point for communications and as catalyst to prompt action
- Advises appropriate field office, Center emergency coordination unit and ORA of significant emergency alerts or when investigation reaches stage II, presumptive status
- Coordinates information concerning emergencies with headquarters offices of other Federal agencies; and in cooperation with the Office of International Programs when other foreign governments involved

Each Region/district
Has designated contact

During emergency, district may take lead or DEIO may assume lead

Centers' Staffs
Emergency Coordination Units:

CBER/Office of Compliance & Biologics Quality
CDER/Office of Compliance
CFSAN/Office of Field Programs
CDRH/Office Compliance
CVM/Office of Surveillance & Compliance

Office of Regulatory Affairs
Serves as focal point within Office of the Commissioner

Div. Federal/State Relations
Coordinates Agency interaction with state and local agencies in cooperation with region, district, DEIO

References

Wilesmith, J.W.; Ryan, J.B.M.; Hasten, W.D., et al. 1992. Bovine spongiform encephalopathy: epidemiologic features 1985 to 1990. Veterinary Record 130:90-94.

Will, R.G.; Ironside, J.W.; Zeidler, M.; Cousens, S.N.; Estibeiro, K.; Alperovitch, A.; Poser, S.; Pocchiari, M.; Hoffman, A.; Smith, P.G. 1996. A new variant of Creutzfeldt-Jacob disease in the UK. Lancet 347:921-925.

USDA BSE Response Plan, October 1998.