DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

December 17, 1993

TO: Manufacturers of FDA-regulated Products

The Food and Drug Administration (FDA, the Agency) is issuing this letter to request that bovine-derived materials from cattle which have resided in or originated from countries where Bovine Spongiform Encephalopathy (BSE) has been diagnosed not be used in the manufacture of FDA-regulated products intended for administration to humans. We are advising you of our current recommendations pertaining to the use of such bovine-derived products.

FDA is providing the following information to explain why the Agency thinks that an animal disease (such as BSE) may potentially be a concern in the manufacture of FDA-regulated products intended for administration to humans. BSE has been reported for more than 109,000 cattle in the United Kingdom [Fall, 1993 quarterly report of the Ministry of Agriculture, Fisheries, and Food (MAFF)], and to a much lesser extent in other European countries. This neurological disease is a transmissible spongiform encephalopathy (TSE), and is similar to other TSEs such as scrapie in sheep and Creutzfeldt-Jakob Disease (CJD) in humans. The spongiform encephalopathies are uniformly fatal, and no rapid diagnostic test for infection in living animals (or humans) is currently available. Iatrogenic transmissions of CJD from both pituitary-derived human growth hormone (somatotropin) and dura mater[1] have been reported. Research projects into the exact nature of both the BSE agent and other spongiform encephalopathy agents, host range, patterns of pathogenicity, and development of rapid antemortem diagnostic tests are ongoing. Available scientific information indicates that these agents are extremely resistant to inactivation by normal disinfection or sterilization procedures. The list of countries where BSE is known to exist (BSE-countries) is maintained by the United States Department of Agriculture (USDA). Countries listed in the Federal Register on December 6, 1991 (56 FR 63865 - 63870) include France, Great Britain (includes the Falkland Islands), Northern Ireland, the Republic of Ireland, Oman, and Switzerland.

While transmission of the causative agent of BSE to humans has not been reported to date, FDA considers the recommendations below to be prudent at this time to further reduce any potential risk of exposure or transmission of a BSE-agent to humans by FDA-regulated products.

The Agency notes that regulated products intended for administration to humans and manufactured with bovine-derived materials derived from cattle that have at any time been in BSE-countries may be adulterated under Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act), for drugs and biological drug products; or Section 501(h) of the Act, for medical devices and biological device products. The Agency is considering rulemaking to restrict the use of bovine-derived materials from BSE-countries. At this time, FDA recommends that bovine-derived materials from BSE-countries not be used in the manufacture of FDA-regulated products.

The Agency is providing the following suggestions to prevent the use of bovine-derived materials from cattle which have resided in or originated from BSE-countries. FDA recommends that manufacturers:

a. identify bovine-derived materials used in the regulated product and identify all countries where the animals used for the material have lived. This information may be provided to the regulated-product manufacturer by the supplier of the bovine product. The supplier may also provide the manufacturer with appropriate veterinary regulatory inspection certification of slaughter, as required by the country of origin of live animals.

b. maintain traceable records for each lot of bovine material and each lot of FDA-regulated product using these materials. These records should be part of the batch records, and available for FDA inspection.

c. document the country of origin of the live animal source of any bovine-derived materials used in the manufacture of the regulated product. Documentation should be maintained for any new or in-process lots of licensed, cleared, or approved products; products pending clearance or approval; and investigational products intended to be administered to humans. Such documentation should be a part of the traceable records maintained in conjunction with batch production records, and such information should be available for review during FDA inspections.

d. maintain copies of the records identified above for FDA-regulated products that are manufactured with bovine-derived materials at foreign sites, or by the foreign manufacturers. The U.S. firms responsible for marketing these products should be responsible for these records. Manufacturers of products subject to licensure should maintain records at the site of manufacture.

The Agency recommends that the information identified above be obtained for all currently approved, cleared, or licensed products, pending or approvable products, and investigational products.

Some manufacturers of FDA-regulated products may have already provided some of this information in applications to the USDA for permits to import certain animal products into the United States. In some instances, copies of these applications and permits may contain some of the information that the FDA is requesting. FDA suggests that this information be documented, recorded, and maintained for all bovine-derived products currently manufactured or marketed in the U.S. This information should be available for FDA inspection.

If you have any questions regarding the above items please contact the appropriate center as follows:

Center for Devices and Radiological Health: 301-594-4692 ext. 158

Center for Drug Evaluation and Research: 301-594-0054

Center for Biologics Evaluation and Research--
Contact the Application Division in the CBER Office responsible for the regulation of your product. These Offices are:

Office of Vaccines Research and Review	301-594-2090
Office of Therapeutics Research and Review	301-594-5109
Office of Blood Research and Review	301-594-2012

Regulated-product manufacturers are referred to the USDA for current information and countries on the "BSE-list". Additional information and regulations concerning bovine spongiform encephalopathy (BSE) and affected animals may be obtained from the open veterinary literature and the United States Department of Agriculture (see 9 CFR 94.18).

Sincerely yours,

Jane E. Henney, M.D.
Deputy Commissioner for Operations

1. Brown P, Preece MA, Will RG. "Friendly fire in medicine: hormones, homografts, and Creutzfeldt-Jakob disease". Lancet 1992:340:24-27.