



APR 19 2000

Food and Drug Administration
1401 Rockville Pike
Rockville, MD 20852-1448

TO: Manufacturers of Biological Products

The Food and Drug Administration (FDA) has issued letters (May 3, 1991, December 17, 1993, and May 9, 1996) and a guidance document (September 1997) requesting that materials derived from ruminants 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. The United States Department of Agriculture (USDA) also issued an interim rule on January 6, 1998, restricting the importation of ruminants, meat and meat products from ruminants, and certain ruminant products and byproducts from all countries of Europe. Because of the serious nature of this issue, the Center for Biologics Evaluation and Research (CBER) believes it critical to update the current recommendations.

CBER strongly recommends that manufacturers take whatever steps are necessary to assure that materials derived from all species of ruminant animals born, raised or slaughtered in countries where BSE is known to exist, or countries where the USDA has been unable to assure FDA that BSE does not exist, are not used in the manufacture of FDA-regulated products intended for administration to humans. The Agency has previously recommended that manufacturers take the following steps to prevent this occurrence:

1. Identify all ruminant-derived materials (e.g., culture medium, transferrin, albumin, enzymes, lipids) used in the manufacture of regulated products. FDA considers the manufacture of biological products to include the preparation of master (including the original cell line) and working cell banks, as well as materials used in fermentation, harvesting, purification and formulation of the products.
2. Document the country of origin and all countries where the live animal source has resided for each ruminant-derived material used in the manufacture of the regulated product. The regulated-product manufacturer should obtain this information from the supplier of the ruminant-derived product. The regulated-product manufacturer should also obtain the appropriate veterinary regulatory inspection certification of slaughter, as required by the country of origin of live animals, from the supplier. 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.
3. Maintain traceable records for each lot of ruminant material and each lot of FDA-regulated product manufactured using these materials. These records should be part of the product batch records and available for FDA inspection. Such records should be maintained for products manufactured at foreign as well as domestic facilities.

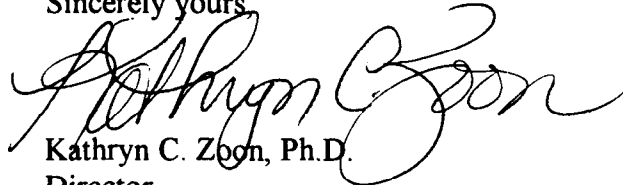
It is the responsibility of the manufacturer to obtain up-to-date information regarding countries where BSE is known to exist, or countries where the USDA has been unable to assure FDA that BSE does not exist. This information is available from the USDA's Animal and Plant Health Inspection Service (APHIS) at telephone number 301-734-8364, website address <http://www.aphis.usda.gov/ncie>, and codified at 9 CFR 94.18 (see attached).

Specific product-related questions should be directed to the appropriate application division within CBER's product offices. The phone numbers are:

Dr. David Asher, Office of Blood Research and Review	301-827-3524
Dr. Paul Richman, Office of Vaccines Research and Review	301-827-3070
James Crim, Office of Therapeutics Research and Review	301-827-5101

Thank you for your attention to this matter.

Sincerely yours,



Kathryn C. Zoon, Ph.D.
Director
Center for Biologics Evaluation
And Research

Attachment