ISSUE SUMMARY—TOPIC #4.E

TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES ADVISORY COMMITTEE MEETING
February 13, 2004

CDRH current recommendations on measures to minimize risk of TSE agents in medical devices.

ISSUE

Staff from the Center for Devices and Radiological Health (CDRH) will update the Transmissible Spongiform Encephalopathies Advisory Committee (TSEAC) on procedures currently in place to minimize the risk of CJD transmission for: 1) implantable medical devices prepared from bovine and human material, 2) medical devices used in patients after reprocessing and 3) *in vitro* diagnostic test kits for CJD detection.

BACKGROUND AND DISCUSSION

CDRH oversees a broad spectrum of medical products ranging from implantable devices prepared with bovine and human material to sterilizers and reprocessing equipment and *in vitro* diagnostic test kits. For this reason CDRH's approach to minimize risk of TSE transmission from medical devices is both comprehensive and flexible by including: premarket application review, postmarket surveillance of product performance and safety, laboratory research, expert guidance from FDA Advisory Committees, and communication with industry, the medical community, and the general public through meetings, letters, general and specific product guidance, and *Federal Register* notices.

Regarding implantable medical devices derived from human and bovine sources, a few examples of this approach are:

?? In 1997, 1998, and 2001 CDRH met with TSEAC to assess methods for improving the donor selection, tissue procurement, and processing for human dura mater. The information provided at these meetings was communicated to industry through letters to individual device suppliers and subsequently a guidance document.

?? In 1998, CDRH published, "Guidance for Industry - Medical Devices Containing Materials Derived from Animal Sources (Except for In Vitro Diagnostic Devices)" http://www.fda.gov/cdrh/ode/88.html which provides recommendations for information to be included in IDE, PMA, and 510(k) submissions for medical devices that either contain or were exposed to animal-derived materials during manufacture. These recommendations include maintaining traceable records for each lot of bovine material used in device production and submitting a detailed description of the manufacturing processes in any premarket review application.

?? In 2000, CDRH published, "Guidance Document for Dura Substitute Devices; "Guidance for Industry," http://www.fda.gov/cdrh/ode/guidance/1152.html, which provides a summary of the information to be included in a pre-market notification application (510(k)). Such information includes a request for information about the species and tissue used in the medical device as well as how the health of the herd is maintained and monitored.

?? In 2003, CDRH issued letters to over 25,000 manufacturers, contract sterilizers, importers, and repackagers in the medical device industry. This letter reminded manufacturers of the 1998 Guidance (http://www.fda.gov/cdrh/ode/88.html) and stated that FDA investigators may evaluate the adequacy of these procedures and the effectiveness of their implementation during manufacturing facility inspections. This letter also reminded manufacturers that they could obtain the most current information on BSE and related diseases through the U.S. Department of Agriculture (USDA) website at www.aphis.usda.gov/oa/bse.

?? In 2003, FDA completed classification of human dura mater as a Class II medical device and published the "Class II Special Controls Guidance Document: Human Dura Mater; Guidance for Industry and FDA Staff" http://www.fda.gov/cdrh/ode/guidance/054.html.

?? In addition to premarket review, CDRH works with individual product manufacturers on a product-by-product basis concerning issues such as device manufacturing facilities and reagent/component sourcing.

To reduce the potential for CJD transmission in human tissue-derived medical devices, premarket review includes a determination that product manufacture methods include the same types of safeguards described in the CBER proposed rules on suitability determination for donors of human cellular and tissue-based products published by CBER in 1999.

Regarding devices used to inactivate TSE agents and the reprocessing of medical devices:

CDRH regulates medical devices that may be used to inactivate TSE agents (e.g., sterilizers) as well as surgical instruments that may be exposed to TSE intraoperatively. Currently, no medical product has been cleared/approved for removal of TSE agents from medical devices. A few examples of how CDRH is minimizing the risk of TSE transmission in this area are:

?? CDRH has and continues to work with the CDC in identifying procedures for removing TSE agents from medical devices.

?? In 2003 CDRH met with the TSEAC to evaluate the adequacy of scientific data for removing TSE agents from medical devices. Based on the information received at this meeting, CDRH continues to work with individual product manufacturers to develop data (based on the WHO guidelines) to validate the ability of an instrument or processes to remove TSE agents from medical devices.

?? CDRH in collaboration with the Center for Biologics Evaluation and Research (CBER) is performing laboratory research examining the effectiveness of methods for removing TSEs

from the biomaterial surfaces used in medical devices. Preliminary results of these studies were presented to TSEAC in 2003.

Regarding in vitro diagnostic devices

Although testing for the BSE causative agent is a common procedure in animals, to date FDA has not cleared or approved a test for prions to be used in human specimens. Two important laboratory tests are possible. The first would be a test to screen blood and tissue products to ensure that patients receiving these products are not exposed to prions, which are implicated in new variant CJD. Review for this type of product would be performed in the Office of Blood in CBER. The second would be a test to aid in the diagnosis of a patient with variant CJD or infected and at risk for developing CJD. Review of this product would be performed in the Office of In Vitro Diagnostics in CDRH. Both centers have mechanisms for meeting with companies early in the development of new tests to help establish "least burdensome" pathways to market. Both centers also have procedures for expediting the review of new and breakthrough diagnostics with significant public health impact. Sponsors are urged to contact regulatory staff in the appropriate Center if working in this area to obtain advice on types of submissions and study design to ensure rapid transfer of technology into the laboratory marketplace.