TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES ADVISORY COMMITTEE MEETING

February 12 & 13, 2004

Issue Summary Topic 4.B

Minimizing Risks of TSE Agents in Human Tissues

ISSUE

FDA will update the committee about the methods used to minimize risks of TSE agents in FDA-regulated medicinal products. The talk "Minimizing Risks of TSE agents in Human Tissues" specifically addresses human tissues used for transplantation.

DISCUSSION

CBER's regulatory approach to protecting the supply of human tissues from TSE agents is implemented through a combination of current regulations (rules), current recommendations (guidance), proposed regulations (draft rules), and proposed recommendations (draft guidance).

Relevant documents include:

Current Regulation

- 21 CFR part 1270—Human Tissues Intended for Transplantation (1997)[1]

Interim Regulation

- Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing (1/27/2004)[2]

Current Recommendations

- Guidance for Industry: Screening and Testing of Donors of Human Tissue Intended for Transplantation (1997)[3]
- Guidance for Industry: Validation of Procedures for Processing of Human Tissues Intended for Transplantation (3/2002)[4]
- Guidance for Industry and FDA Staff—Class II Special Controls Guidance Document: Human Dura Mater (12/2003)—Center for Devices and Radiological Health (CDRH)[5]

Proposed Regulations

- Suitability Determination for Donors of Human Cellular and Tissue-Based Products; Proposed Rule (9/30/99)[6]

?? Current Good Tissue Practice for Manufacturers of HCT/Ps; Inspection and Enforcement; Proposed Rule (1/8/01)[7]

Proposed Recommendations

?? Draft Guidance for Industry: Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) (6/02)[8]

?? Current thinking: draft recommendations to explain how human tissue establishments may comply with the requirements in the donor suitability rule, when finalized

21 CFR 1270[1] does not directly address the prevention of TSE transmission through donor screening and testing. However, 1270.31(d) requires that firms have validated procedures to prevent infectious disease contamination or cross-contamination by tissue during processing. The requirement in 1270.31(d) has been clarified in guidance[4]. The Donor Suitability Proposed Rule would specifically require screening and testing (when available) of human tissue donors for human TSEs including CJD. A draft guidance that would clarify our current thinking about appropriate measures to meet screening and testing requirements would accompany the rule, when finalized.

FDA published a draft guidance document[8] in January 2002 entitled "Draft Guidance for Industry: Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)," to make tissue establishments aware of our concern about preventing the transmission of the TSE agent in human tissue products, and to ask for comment on the draft guidance.

Recommendations for donor screening made in this draft guidance:

A potential HCT/P donor should be determined ineligible if the donor:

1) has been diagnosed with vCJD or any other form of CJD;

2) has been diagnosed with dementia or any degenerative or demyelinating disease of the central nervous system (CNS) or other neurological disease of unknown etiology; (HCT/Ps from donors with dementia confirmed by gross and microscopic examination of the brain to be caused by cerebrovascular accident, brain tumor, head trauma, or toxic/metabolic dementia and who are confirmed not to have evidence of TSE on microscopic examination of the brain may be acceptable based on an evaluation by the Medical Director.)

3) is at increased risk for CJD; (Donors are considered to have an increased risk for CJD if they have received a human dura mater transplant, human pituitary-derived growth hormone, or have one or more blood relatives diagnosed with CJD.)

4) spent three months or more cumulatively in the U.K. (defined in Appendix of draft guidance) from the beginning of 1980 through the end of 1996;

5) is a current or former U.S. military member, civilian military employee, or dependent of a military member or civilian employee who resided at U.S. military bases in Northern Europe (Germany, U.K., Belgium, and the Netherlands) for 6 months or more from 1980 through 1990, or elsewhere in Europe (Greece, Turkey, Spain, Portugal, and Italy) for 6 months or more from 1980 through 1996;

6) lived cumulatively for 5 years or more in Europe from 1980 until the present (note this criterion includes time spent in the U.K. from 1980 through 1996);

7) received any transfusion of blood or blood components in the U.K. between 1980 and the present; or

8) has injected bovine insulin since 1980, unless you can confirm that the product was not manufactured after 1980 from cattle in the U.K.

HLA-matched hematopoietic stem cells (HSC) may be collected from a donor who would otherwise be determined to be ineligible by one or more of recommendations 3-8 above. Such HSCs could be used if necessary to achieve an appropriate HLA match with a recipient and if the benefits of such use outweigh the risks. Under the appropriate circumstances, we may consider such use to be an urgent medical need.

There are currently no recommendations for testing donors for CJD or vCJD because there are no FDA-approved screening tests.

Our current thinking is to publish one guidance containing recommendations for determining human tissue donor suitability, and that may include the draft recommendations for CJD and vCJD mentioned above.

REFERENCES:

1. Food and Drug Administration. Human Tissue Intended for Transplantation; Final Rule. Federal Register 1997; 62:40429-40447. http://www.fda.gov/cber/tissue/docs.htm
2. Food and Drug Administration. Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing; Interim Final Rule. Federal Register 2004; 69:3823-3826. http://www.fda.gov/cber/tissue/docs.htm
3. Food and Drug Administration. Guidance for Industry: Screening and Testing of Donors of Human Tissue Intended for Transplantation. 1997. http://www.fda.gov/cber/tissue/docs.htm
4. Food and Drug Administration. Guidance for Industry: Validation of Procedures for Processing of Human Tissues Intended for Transplantation. 2002. http://www.fda.gov/cber/tissue/docs.htm
5. Food and Drug Administration. Class II Special Controls Guidance Document: Human Dura Mater; Guidance for Industry and FDA. 2003. http://www.fda.gov/cdrh/ode/guidance/054.html
6. Food and Drug Administration. Suitability Determination for Donors of Human Cellular and Tissue-Based Products; Proposed Rule. Federal Register 1999; 64:52696-52723. http://www.fda.gov/cber/tissue/docs.htm
7. Food and Drug Administration. Current Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products; Inspection and Enforcement; Proposed Rule. Federal Register 2001; 66. http://www.fda.gov/cber/tissue/docs.htm
8. Food and Drug Administration. Draft Guidance for Industry: Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps). Federal Register 2002; 67:42789. http://www.fda.gov/cber/tissue/docs.htm