Quick Summary
Transmissible Spongiform Encephalopathies Advisory Committee Meeting
June 26 & 27, 2002

Topic #1
Validation of Procedures to Prevent Contamination and Cross-Contamination with TSE Agents of Human Tissue Intended for Transplantation

FDA asked the TSEAC to advise them on appropriate measures to prevent contamination and cross-contamination by TSE agents of human cells and tissues intended for transplantation. Since FDA is in the process of finalizing its proposed tissue regulations, and of issuing draft guidance, the agency thought that this was an appropriate time to discuss this issue. Speakers presented information on the three approaches that could be taken to reduce the risk of TSE transmission—careful screening of the donor for TSE and risk factors for TSE, control of the recovery and processing of cells and tissues to prevent contamination and cross-contamination, and the use of steps during manufacturing of cells and tissues to remove or inactivate any TSE agents that may be present. The committee heard talks about possible additional screening measures, risk assessment models, the potential value of post-mortem brain autopsy or biopsy, previous transmissions of CJD by dura mater, cornea and human pituitary-derived growth hormone, effects of batch size on risk of infectious agent contamination, experiments on transmission of CJD through various tissues and body fluids, single donor aseptic recovery and processing of ocular and bone tissue, equipment and instrument disinfection methods, process validation, and TSE agent clearance studies in experimental models.

Committee Discussion and Votes on Questions

1. **Which of the following measures and controls is (are) appropriate to prevent TSE agent transmission to the recipient of human cells and tissues?**

A. Recommend additional donor eligibility/exclusion criteria

?? **Upper age limit**

YES-0; NO-14; ABSTAIN-0; INDUSTRY REP-No

?? **Head trauma exclusion**

YES-0; NO-14; ABSTAIN-0; INDUSTRY REP-No

?? **Negative brain autopsy or biopsy for all donors**

YES-0; NO-14; ABSTAIN-0; INDUSTRY REP-NO

?? **Negative brain autopsy or biopsy <u>only</u> for dura mater**

YES-14; NO-0; ABSTAIN-0; INDUSTRY REP-Yes

B. Recommend specified methods for HCT/P recovery and/or processing to prevent contamination and cross-contamination by TSE agents:

?? **Decontamination of instruments and surfaces**

?? **Methods for removal and/or inactivation of TSE agents during manufacturing**

The committee members did not vote on the questions as stated. The Chairman posed a revised question, as follows:

"Do the Committee members recommend that FDA should define validated inactivation procedures for TSE decontamination of instruments and surfaces, and propose methods for removal and/or inactivation of TSE agents from HCT/Ps that may be contaminated by TSEs, differentiating high risk from low risk tissues?"

The vote on this recommendation was:

YES-14; NO-0; ABSTAIN-0; INDUSTRY REP-Yes

?? **Single-donor aseptic processing or permit pooled processing under certain circumstances with adequate controls**

Recommended that FDA should consider single-donor aseptic processing as the gold standard, and that FDA should permit pooled processing under certain circumstances with adequate controls.

The vote on this recommendation was:

YES-14; NO-0; ABSTAIN-0; INDUSTRY REP-Yes

C. Other

2. Please comment on the design of a satisfactory TSE agent clearance study for HCT/Ps, in terms of the following criteria:

A. Suitable TSE agent strain and animal model

B. Accept measurement of abnormal forms of prion protein alone, or require infectivity assays

C. Accept substantial reduction (how much?) or require complete elimination of detectable prion protein and/or infectivity

D. Accept a single validated method or require that more than one validated method for eliminating TSE agents be included in the study

E. Other

Recommended that the TSE strain and animal model used could vary, depending upon the study.
Recommended to require infectivity assays, and commented that in order to show validity and reproducibility, measurement of abnormal prion protein would also be needed.
The committee did not comment on the amount of log reduction that would be acceptable, or on the need for more than one validated method.

Topic # 2

FDA Draft Guidance on 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)

FDA published draft guidance, entitled "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)" in June 2002. This draft guidance was based upon recommendations made by the TSEAC in the January 2001 meeting. At that meeting the TSEAC members unanimously agreed that there is a significant risk of transmission of vCJD through transplantation of HCT/Ps, compared to the risk of transmission of vCJD by blood transfusion. The recommendations for tissue donor deferral in this draft guidance were similar to the recommendations for blood donor deferral recently published in January 2002. The contents of the draft guidance (specifically detailing the deferral criteria and highlighting the differences between the tissue draft guidance and the blood guidance) were presented. Potential strategies for assessing the impact of this guidance on the tissue supply in the United States were discussed.

FDA asked the TSEAC to comment on the recommendations made in the draft guidance, and to consider how information can be obtained about the effect of implementing these tissue donor deferral criteria on the tissue supply in the United States.

The committee discussed the difficulty of obtaining reliable information from the person being interviewed, rather than the donor himself. The committee could not recommend what to do with an "I don't know" answer and suggested that the eye bank community and/or EBAA conduct a pilot study to assess the potential impact that these draft recommendations could have on the tissue supply and/or how frequently family members would answer "I don't know." The committee distinguished between those tissues that have transmitted classic CJD (dura mater and cornea) from other types of tissues.

The committee felt that survey questionnaires may not be an effective way to assess the impact of these criteria on the tissue supply because of differences in between blood and tissue donors, since tissue donors are largely a cadaveric population. The committee is

interested in being updated on information obtained about the effect of these deferral criteria on the tissue supply.

June 27, 2002
Committee Updates

The committee was presented with a review of FDA's revised guidance on blood donor deferrals for risk of CJD and vCJD. The committee then heard a presentation from the Department of Health and Human Services on its new tracking procedure to monitor the blood supply. The committee also listened to presentations from blood centers and related organizations on the effect of implementing geographic donor deferrals for risk of vCJD. The current decrease in blood supplies was felt to be due to several factors, including initiation of new donor deferrals, typical summertime decrease in donations, and donor disenchantment since 9-11. Blood organizations have anticipated and responded to the new deferrals with increased donor recruitment efforts, and development of blood supply monitoring systems.

The committee expressed concerns about the diminishing blood inventories and the effect that the annual decrease in blood donations in the summer months could have on the country's blood supply. They asked that this situation continue to be monitored, and suggested that if needed, FDA should review their guidance on donor requirements as they relate to CJD issues, and should continue to address other strategies to augment the blood supply.

This quick summary is written as an overview of the committee discussion until transcripts are available. Please refer to the committee transcripts for a detailed account of the meeting.