

# MEBTC

MIDWEST EYE-BANKS AND TRANSPLANTATION CENTER

December 19, 2002

Ms. Margaret M. Dotzel  
Associate Commissioner for Policy  
The Food and Drug Administration  
Dockets Management Branch (HFA-305)  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

Re: Docket No. 02D-0266

Dear Associate Commissioner Dotzel:

The Midwest Eye-Banks and Transplantation Center (MEBTC) appreciates the opportunity to comment on the Food and Drug Administration proposed guidance document: **Preventative 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)**. MEBTC is a 501(c)(3) not-for-profit organization whose mission is to recover and provide donated human eye tissue of the highest quality for sight restoring transplantation procedures. MEBTC is comprised of the Michigan Eye-Bank, the Illinois Eye-Bank and the Illinois Eye-Bank, Watson Gailey. These three eye banks provide over 2,500 corneas annually for transplant.

MEBTC eye banks are founding members of the Eye Bank Association of America (EBAA) and participate at all levels of the Association. We actively support the EBAA's programs in the establishment of Medical Standards and the accreditation of eye banks.

We strongly support the positions of the EBAA and the American Academy of Ophthalmology (AAO) on this issue. The MEBTC's comments on the proposed guidance document are attached.

Sincerely,



Florence M. Johnston  
President and Chief Executive Officer

02D-0266

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## MEBTC Comments

### FDA Draft Guidance:

#### **Preventative 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)**

MEBTC comments have been drafted in the following format: the FDA section will be identified, followed by MEBTC comments specific to that section. We have also included case history review statistics, as requested by the FDA, to illustrate the impact of the proposed recommendations on the donor pool.

### FDA Section IV, Recommendations for Donor Eligibility:

#### 1. Diagnosis of vCJD or other form of CJD

**MEBTC Comments:** EBAA Medical Standards contraindicate use of tissue from donors with CJD, with a family history of CJD or family at risk for CJD.

#### 2. Diagnosis of dementia or any degenerative or demyelinating disease of CNS or other neurological disease of unknown etiology (donors with dementia confirmed by gross and microscopic exam of brain to be caused by CVA, brain tumor, head trauma or toxic/metabolic induced dementia and who are confirmed not to have evidence of TSE on microscopic exam of the brain may be acceptable based on Medical Director review).

**MEBTC Comments:** Current EBAA Medical Standard D1.120, *Contraindications*, also contraindicates use of tissues from donors with the following:

- Death with neurologic disease of unestablished diagnosis
- Subacute sclerosing panencephalitis
- Progressive multifocal leukoencephalopathy
- Active viral encephalitis or encephalitis of unknown origin or progressive encephalopathy
- Rabies
- Reyes Syndrome
- Congenital rubella
- Recipients of human pituitary-derived growth hormone (pit-hGH) during the years 1963-1985
- Recipients of non-synthetic dura mater graft
- Those with dementia unless due to cerebrovascular disease, brain tumor or head trauma. Donors with toxic or metabolic-induced dementia may be acceptable pending documentation of consultation with Medical Director.

The proposed guideline would require proof through gross and microscopic exam of the brain or confirmation that there was no evidence of TSE for donors with dementia, and would still require Medical Director approval. The Transmissible Spongiform Encephalopathies (TSE) Advisory Committee (TSEAC) discussed the issue of brain biopsy/autopsy at their June, 2002 meeting. Dr. Nicholas Hogan, MD, PhD, UT, Southwestern presented the following information:

- Length of time for receipt of gross and microscopic results would go beyond time constraints for use of corneas
- Families would have to consent to the additional procedure
- Number of autopsies performed as a result of this requirement would dramatically increase
- The cost, ranging from \$750-\$2000, would not likely be paid by Medicare or insurance
- There would be a huge number of false positives

Based on these findings and further discussion, the Committee did not recommend mandating brain autopsy or biopsy at this time for corneal donors as an exclusion for CJD.

**MEBTC poses the following additional questions.** Who would perform the biopsy? If eye bank staff were expected to perform transorbital biopsies, what type of training would be required in order to perform the procedure to obtain the desired results? What are the potential risks involved in performing the procedure?

MEBTC reviewed 2,373 donor case records from July 1, 2001 to June 30, 2002. Of these donors, 14 had a history of CVA with dementia or other mental status changes noted. Four donors were diagnosed with brain tumors with mental status changes noted.

#### **FDA Section IV, Recommendations for Donor Eligibility:**

4. **Donors who have spent 3 or more cumulative months in UK from 1980-1996**
5. **Current or former US military member, civilian military employees or dependent of either who have lived at US military base in Northern Europe (Germany, UK, Belgium, Netherlands) for 6 or more months from 1980-1990, or other parts of Europe (Greece, Italy, Turkey, Spain, Portugal) for 6 or more months form 1980-1996**
6. **Donors who lived cumulatively for 5 years or more in Europe from 1980-present (includes time spent in UK from 1980-1996)**

#### **MEBTC Comments:**

MEBTC currently does not obtain this information as part of our screening process, but believes it will be extremely difficult, if not impossible, to consistently obtain accurate information. This is due to the fact that medical and social history is obtained from someone other than the donor. This individual may be able to answer relevant medical/social history questions, but have limited knowledge of the detail required by the questions suggested in this section, e.g., a spouse who has known the donor for five

years may not be aware of the dates and lengths of stay for travel in Europe and whether it amounted to 3 cumulative months.

In addition, the FDA currently states that the medical/social history interview can be completed by an individual who is knowledgeable of the donor's relevant medical history and social behavior and who can provide competent information (e.g., nearest available relative, member of the household, other individual with a close relationship to the donor or the donor's primary treating physician). Would this requirement eliminate the donor's primary treating physician as a candidate for completing the medical/social history interview since he/she would not necessarily be aware of the donor's travel history, military history or whether they were living on a military base in those years?

**7. Donors who received any blood or blood product transfusion in the UK from 1980-present.**

**MEBTC Comments:**

MEBTC currently does not obtain this information, but believes that it would be extremely difficult, if not impossible, to obtain accurate information regarding blood or blood product transfusion received in the UK in the specified time period. Since cornea donors are cadaveric, eye banks must rely on the donor's next-of-kin or other person with a close relationship to provide medical and social history information. Considering that the person has just experienced the death of a loved one, it is unlikely that the individual would be able to recall detailed medical history from 20 years prior. In addition, it is very possible that the individual may not even have knowledge of this information if they didn't know the donor then. In light of the fact that there have been no known cases of vCJD transmission to humans via blood transfusion, we feel that this proposal should be deleted.

**8. Donors who have injected bovine insulin since 1980 unless you can confirm that the product was not manufactured after 1980 from cattle in UK.**

**MEBTC Comments:** MEBTC reviewed 2,373 donor cases from July 1, 2001 to June 30, 2002. Of those, 385 donors (16%) noted a history of diabetes. Of those, 224 donors (9%) were known to receive insulin. As a result, 448 corneas would not be suitable for transplantation unless we could confirm the type of insulin that the donor had taken. This constitutes approximately 16% of the tissue supplied by MEBTC for that one-year period.

As noted in prior sections, the fact that the medical/social history is being provided by a family member or significant other, would make it extremely difficult, if not impossible, to obtain the information required by this section. The individual may not have knowledge of this detail of their loved one's life.

Furthermore, this is the only section in the Guidance Document that specifically requires confirmation of the information or the donor must be deferred. Since there have been

no cases of transmission of vCJD in recipients of bovine insulin manufactured in BSE countries, this seems to be an unreasonable requirement.

**Section V. Nonclinical Scientific or Educational Use:**

**If tissue isn't destroyed, you should label an ineligible donor as follows:**

- 1. With a Biohazard legend;**
- 2. "For nonclinical use only"; and**
- 3. "Collected from donor diagnosed with CJD"; "Collected from donor determined to be at risk of CJD" or "Collected from a donor with a potential risk of vCJD", whichever is applicable.**

**MEBTC Comments:** Would all tissue determined to be not suitable for transplantation based on the FDA criteria require this type of labeling regardless of whether the risk was theoretical or not? If this is the case, this requirement could lead to a drastic decrease in human eye tissue used for critical ophthalmological research, because researchers would be hesitant to use tissue labeled in this manner.

CM FDA CJD guidance document comments