AMERICAN
SOCIETY FOR
MICROBIOLOGY

Public and Scientific Affairs Board

January 17, 2003

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Docket No. 02D-0266 "FDA Draft Guidance Document for Industry: Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease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)

The American Society for Microbiology (ASM) is the largest educational, professional, and scientific society dedicated to the advancement of the microbiological sciences and their application for the common good. The Society represents more than 40,000 microbiologists, including scientists and science administrators in academic, industry and government institutions working in a variety of areas, including biomedical, environmental, and clinical microbiology. In response to the June 25, 2002 Federal Register notice announcing the availability of the draft document, "FDA Guidance Document 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), the ASM provides the following comments:

1. **Risk of transmission:**

   The guidance document identifies that there are greater risks for CJD/vCJD transmission through dura mater and cornea compared to blood and blood products; however, there is no comment/discussion pertaining to how to identify risks associated with donors that may be asymptomatic. For example, the transmission categories could be outlined as follows:

   A) Donors with no symptoms and no disease: no risk
   B) Donors with NO symptoms but who would have (if deceased donor) or do (if live donor) develop disease later: unknown risk
   C) Donors with symptoms and have current disease or could develop disease later: known risk of transmission.

   The donors in group B are the most difficult to identify and exclude from the donor pool. Although there is not a lot of data on transmissibility through transplanted tissue, the levels of prion for CJD (and vCJD) have been shown to be

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associated with cases of CJD transmission). This stratification of "high risk" tissues versus "moderate to low risk" tissues has not been incorporated in this draft, yet is part of the "CJD Disease: Recommendations for Disinfection and Sterilization" (Rutala WA, DJ Weber, CID 2001:32:1348-1356).

SUGGESTION: It would seem reasonable that a similar approach to stratifying tissue risk be included in the current guidance document. At the least, the Rutala reference should be quoted.

2. **General Approach:**

2.1 Acuity of organ survivability:

The current guidance document breaks down into two separate sections how to use clinical parameters to screen donors for potential CJD or vCJD infection. Recognizing that this is a very difficult task – it still has to be stated that the current format is almost impossibly complex and seems that it will be extremely difficult for companies to comply with. No consideration has been given for the acuity of the time-factor involved in the transplant. It appears that ALL HCT/P donors will require screening. Is it feasible to perform such screening for donors of hearts and lungs prior to transplant? It seems unlikely that an adequate screen (as described in this draft guidance document) could be accomplished in an adequate time-frame for such transplants.

SUGGESTION: It would be valuable to include a table summarizing what tissues/organs/cells are used for transplantation, including an indication of their acuity level (i.e. time limit while available for screening prior to implant). A possible stratification might include:

Tissue Risk category:	**Tissues**	**Donor Screening:**
1. High Risk	Brain(dura), eye(cornea), spinal tissue	Complete donor screening including brain biopsy prior to transplant
2. Mod-Low Risk	Kidney*, liver*, spleen*,	Require exclusion of confirmed and suspected CJD/vCJD donor
3. Low-No Risk	Heart*, lungs*, tendons	Require exclusion of confirmed and suspected CJD/vCJD

* Acquity issues: time constraints on time available for screening prior to implant
[Note: Table is by no means complete, but given to provide example]

3. **Screening for Deceased versus Living Donors:**

Some discussion should be included on how to handle CJD/vCJD in deceased versus living donors. The recommendation for brain biopsy from a deceased donor is possible, but not from a living donor.

SUGGESTION: Include some discussion (or recommendation) of screening for live versus deceased donors.

4. **Differentiating CJD from vCJD:**
   The current draft document recommendations for making the **diagnosis** of confirmed or suspected CJD are reasonable; however, the proposed algorithm for vCJD is exceedingly complex. The duration of illness requirement (> 6 months) seems excessive. Would donors with these symptoms for 4 months duration be acceptable for donation?

   SUGGESTION: Would it not be possible to assume that since vCJD has now transgressed the "species barrier," that the ability of vCJD to be transmitted to other humans through transplantation would be expected to be **no less** than that of CJD? Thus, manufacturers could treat the risk of vCJD and CJD as the same with respect to transmissibility? That is, there is some variability as to which tissues pose the highest risk (e.g. gut tissue). In this way the "minimum" time-frames for symptoms could be used. For example the diagnosis of "suspected" CJD or vCJD could be summarized as:

   Suspected prion-related illness (CJD or vCJD) in human donor:
   1. Progressive dementia
   2. At least two of the following: myoclonus, visual impairment or cerebellar signs, pyramidal or extrapyramidal signs, akinetic mutism, chorea, or dystonia
   3. May or may not have:
      EEG; may have typical EEG pattern for CJD (generalized triphasic periodic complexes at approximately one per second)

Recognizing that this summary of "suspected" cases would be broader than that proposed in the current guideline, it benefits from simplicity of interpretation.

5. **Range/volume of transplanted HCT/Ps:**
   Currently there is no indication in the draft document of the range of types of tissues etc used for transplant or the relative volumes.

   SUGGESTION: Include an appendix that outlines the types of HCT/Ps currently transplanted and the relative volumes of each that are used/year.

We appreciate the opportunity to comment and would be pleased to respond to any questions or requests for additional information.

Sincerely,

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