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

Re: Docket No: 02D-0266; Draft Guidance for Industry: Preventative Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD)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)

Dear Sir or Madam:

We respectfully submit the following comments on the above-referenced draft guidance document. We apologize for making them after the deadline, but we did ask that the comment period be extended.

In the draft guidance, FDA proposes that U.S. HCT/P manufacturers should consider certain HCT/P donors ineligible based upon certain factors, including the donor's country of origin. Specifically, FDA proposes that the following donors be considered ineligible from HCT/P donation: 1) donors who spent three months or more cumulatively in the U.K. from the beginning of 1980 through the end of 1996; and 2) donors who have lived cumulatively for 5 years or more in Europe from 1980 until the present. *See* Proposed Draft Guidance at 15 (identifying 2 of the 8 proposed recommendations for donor eligibility).

These proposed donor deferral recommendations would effectively preclude the importation of any HCT/Ps donations from most European countries[1].
While we acknowledge that it is important to reduce the risk of transmission of CJD and vCJD from any source, the proposed guidance document's deferral criteria for HCT/Ps does not further

[1] The following countries were identified as the affected European countries for donor deferral: Albania, Austria, Belgium, Bosnia-Herzegovina, Bulgaria, Channel Islands, Croatia, Czech Republic, Denmark, England, Falkland Islands, Finland, France, Germany, Gibraltar, Greece, Hungary, Ireland, Isle of Man, Italy, Liechtenstein, Luxembourg, Macedonia, Netherlands, Northern Ireland, Norway, Poland, Portugal, Romania, Scotland, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, Wales and Yugoslavia. *See* Proposed Draft Guidance, Appendix.

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this goal. Specifically, there are three major reasons why the proposed donor deferral proposal should not be applied to all HCT/P donors:

- **FDA Should Establish Policies Based on Incident Reporting**

FDA notes that there are no published studies regarding the transmissibility of vCJD by HCT/Ps and that transmission of vCJD by most HCT/Ps is considered a "theoretical possibility." *Id.* The deferral criteria makes a blanket exclusion based upon the donor's geography without factoring in whether an individual donor was potentially exposed to Bovine Spongiform Encephalopathy ("BSE") agents. Given the dramatic increase in reported cases of BSE in the United Kingdom, it is agreed that donations from the United Kingdom or persons who have lived/visited the United Kingdom for the periods proposed should be excluded for donation. However, a blanket exclusion of the remainder of Europe is inappropriate given the small number of reported native and imported cases of BSE in these countries (Brown, P, et. al. "Bovine Spongiform Encephalopathy and Variant Creutzfeldt-Jakob Disease: Background, Evolution, and Current Concerns" Emerging Infectious Diseases, 7(1), 2001).

- **All of Europe is not alike**

We would like to point out to the FDA that the incidence of vCJD varies considerably from one country to another. We wish to point out the table attached taken from a 2001 Center for Disease Control paper which shows that most of the vCJD cases are in the United Kingdom. Because of that the FDA may wish to reconsider its proposed regulation to just limit it to United Kingdom, rather than Europe. To add Italy, for
example, where no reports of vCJD have occurred, seems to be excessive. Excluding the United Kingdom does make sense.

- **All Tissues are Not Alike in Regard to Infectivity. Bone Has No Known Risk of Disease Transmission**

The attached table taken from the 1997 World Health Organization report on transmissible spongiform encephalopathies categorizes the infectivity of various tissues. Category I (High Infectivity) applies to brain, spinal cord, and eyes. Category II (Medium Infectivity) tissues are listed as spleen, tonsils, etc. Category III (Low Infectivity) examples are nerves, bone marrow, liver, etc. And Category IV (No Detectible Infectivity) tissues are as listed, with bone and cartilaginous tissue being in this category. While geographic donor deferrals may be appropriate for some tissue products because of increased risk of disease transmission, the geographic donor exclusion criteria should not be applied to <u>all</u> HCT/Ps equally, especially where the risk of disease transmission is lower for certain HCT/Ps, such as bone. We have searched the medical literature and cannot find one documented case in humans or animals where transplanted bone was the cause of the spread of CJD or vCJD. Until such a known risk is identified, restricting the donor pools as proposed seems overly cautious and unnecessary.

The FDA has set a precedent for excluding only certain types of tissues and not all tissues from a donor. For example, FDA has recognized certain exceptions to the geographic donor exclusion criteria for homatopoietic stems cells based on medical need (*See* Proposed Draft Guidance at 15-16) and for source plasma. Guidance for Industry, Revised Preventative Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Blood and Blood Products, at 13 (# 8) (January 2002).

- **Denying the Proposed European Donors Will Only Further Reduce the Availability of Critically Needed, Medically Necessary HCT/Ps.**

FDA's proposal for donor deferral would exclude every potential HCT/P donor from approximately 38 countries in the world (as well as many other exclusions for U.S. military stationed in Northern Europe and travelers of more than 3 months cumulatively in the U.K.). See Proposed Draft Guidance at 15. Reducing the pool of HCT/P donors in this manner will adversely affect the availability of HCT/Ps, such as human bone, which are medically needed for transplantation. This proposal, if implemented, will only increase the shortage of these critical unique materials.

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We appreciate the opportunity to comment on the proposed guidance document. Please do not hesitate to contact me with any questions.

Sincerely

Edward M Basile

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Enclosure