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Transplant Services Center

Ellen L. Heck, M.T., M.A.
Director

Medical Directors
Charles, R. Baxter, M.D.
Paul R. Bergstresser, M.D.
H. Dwight Cavanagh, M.D., Ph.D.
Charles S. Petty, M.D.

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Ruth Solomon M.D.
Center for Biologics
Dept. of Health and Human Services
Food and Drug Administration
1401 Rockville Pike Ste. #200N
Rockville, MD 20852-1448

Dear Dr. Solomon:

In its continued effort to increase safety of all transplantable tissues, the FDA in 21CFR parts 210-11820 and 127 have once again addressed important issues of testing and donor screening perimeters as they relate to communicable disease and the possible transmission of such diseases. While this concern on the part of the FDA may be commendable, there are within this document a few small areas which might warrant clarification.

These areas are as follows:

Donor screening section 1271.80 (b) collection of the donor's specimen for testing, for living donors a specimen may be collected up to seven days prior to recovery. It would appear the FDA's intent here is to address specimens for reproductive and cellular transfers of individuals who are living and continue to be living after the time of testing. However, it might be interpreted to mean an individual who was living at the time the blood sample was drawn.

For a hospitalized patient this may cause confusion in determining an acceptable pre-transfusion/infusion sample. Therefore, it is suggested that for cadaveric donors a statement be made to clarify this point. A statement to the effect that a pre-mortem and/or pre-transfusion sample which meets FDA guidelines regarding fluid/blood administration is suitable for testing from any sample which has been drawn and appropriately stored during the current period of hospitalization. Current hospitalization would be defined as inclusive of consecutive periods where a patient may be transferred from one hospital to a second facility to receive treatment related to the same occurrence. It would be an

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extreme disadvantage to transplant programs to be unable to retrieve transplantable tissue due to a misinterpretation of this testing period. Further, it would be reasonable to assume that such hospitalized sample was still representative of the donor's serum antigen and/or antibody level.

Second, in the area of donor testing the FDA makes reference to relevant communicable disease agents and although Syphilis would certainly be described as a relevant communicable disease in certain circumstances, its transmission through a corneal transplant is highly unlikely, and therefore, I wish to refer the FDA to the paper by Dr. Marion Macsai, from the Journal of Cornea (Macsai et al, Cornea, 1995; 14:595-600) and ask that the agency give careful consideration as to whether or not this is indeed a relevant testing criteria for cornea tissue transplant.

Next, I would like to comment on what is perhaps the most controversial area of this document, the area of donor screening by medical history review. Although the program at the University of Texas Southwestern Medical Center engages in family interview for medical/social history on all donors and although I understand the FDA's former and ongoing sensitivities to legislative consents, I would point out the following difficulty. While the FDA has recognized an interview with a primary treating physician as adequate to obtain medical/social history, such an interview without the permission of the deceased and/or the deceased's family would be difficult if not impossible to obtain given the privacy considerations around medical information. Nevertheless, I agree with the FDA when it says requiring a donor medical history interview for corneas obtained under legislative consent is necessary to ensure that the risk of communicable disease transmission is appropriately addressed. However, I am concerned the FDA may not have used the appropriate example to emphasize the history screening value. Tissue safety may not be positively impacted by screening for the TSE since the number of symptomatic donors in the population is very limited and the asymptomatic donors will not be picked up through this methodology. Virtually all eye bankers would join the FDA in aggressively looking for an appropriate testing modality which would further ensure the safety of transplantable tissue from the possibility of TSE/Creutzfeldt-Jakob disease transfer. However, adding a history screening requirement may not be as enthusiastically embraced. If required, FDA may expect a strong division among members of the transplant community. Nevertheless, since interview does impact detection of high risk behavior for other diseases such as Hepatitis and HIV the medical history requirements of this regulation section 1271.3(o) may indeed be entirely appropriate. If FDA does impose an interview requirement and if this has direction toward TSE, it is to be hoped FDA will carefully consider the questions and the evaluation of these questions and receive input from transplant practitioners and other experts concerned with this disease entity.

Finally, I would like to express concern over the wording of this regulation in the summary where the language speaks about the requirements for manufacturers of human cell and tissue based products. It is our contention as providers of allograft tissue and corneal to humans for a variety of medical conditions that we are indeed not manufacturers, as we do not generate a new product or create it's properties. We are rather the provider of or the conduit through which transplant allografts are made available from the donor to the recipient via the request from and under the total medical oversight of the transplanting physician. Therefore I strongly urge the FDA to amend this document to clarify and/or remove the term manufacturers.

Thank you for this opportunity to comment and for the ongoing effort FDA has demonstrated in involving the community in the rule making process. Also we recognize the difficulties which face FDA in its effort to make human tissue transplants an effective and safe treatment modality while balancing the availability and cost effectiveness of such measures.

Sincerely

A handwritten signature in cursive script, appearing to read "Ellen Heck".

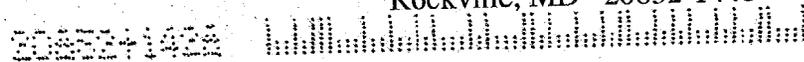
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5323 Harry Hines Blvd.
Dallas, Texas 75235-9074



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