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December 22, 1999

Jane Henney, M.D.
Commissioner
The Food and Drug Administration
5630 Fishers Lane
Rockville, MD 20852

Ref: Docket No. 97N-484S; Suitability Determination for Donors of Cellular and Tissue-Based Products; 64 Federal Register 189; September 30, 1999.

Dear Commissioner Henney:

On behalf of our more than 100 U.S. member eye bank organizations, the Eye Bank Association of America (EBAA) appreciates the opportunity to comment on the Food and Drug Administration's (FDA) proposed rule: **Suitability Determination for Donors of Human Cellular and Tissue-Based Products**. Our membership represents a participation rate of 99% of the entire U.S. eye banking community and provides 97% of all corneal tissue for transplantation. All eye banks are 501(c) (3) organizations whose mission is to procure and provide donated human eye tissue for sight restoring transplantation procedures. The Association strives to ensure the superior quality of banked human eyes through the adoption and implementation of stringent medical standards.

Introduction:

The eye banking community is proud of its history. The first corneal transplant was performed in 1905 and the first eye bank opened in New York in 1944; this bank marked the first organized attempt to facilitate the transfer of tissue from donor to patient. The eye banking model was successfully replicated in other communities across the United States. Following the development of the eye banking system, the EBAA was founded in 1961 by the American Academy of Ophthalmology. The Association was the first transplant association and the first to establish medical standards. The Association also established and administers a comprehensive education and certification program for technicians and other eye bank professionals, continuing education programs for ophthalmologists and researchers, and an institutionalized program of accreditation for eye banks. EBAA's Medical Standards and certification program are used as models for other programs.

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Page two, EBAA Comments

[The FDA has been provided copies of EBAA's Medical Standards and supporting documents.]

The EBAA's Medical Standards are specific to banked human eye tissue, scientifically-based and developed to ensure safe transplantation. EBAA's Medical Standards are twice-yearly peer-reviewed and revised when necessary to ensure the practice of state-of-the-art safety procedures. Such standards and procedures are also reviewed annually by the American Academy of Ophthalmology. It should be noted that the EBAA was the first transplant organization to institute mandatory testing of transplant donors for the presence of HIV. The Association was among the first transplant organizations to institute mandatory testing and screening procedures for hepatitis B and C as testing became available.

FDA's Proposal:

FDA proposes to broadly regulate human tissue and requires most establishments to test for syphilis and screen for transmissible spongiform encephalopathies (TSE), including Creutzfeldt-Jakob disease (CJD); exceptions are made in certain limited situations. The proposal ignores the agency's statement on page 52713 of the Federal Register, which states that the risks of disease transmission vary by cellular and tissue-based product.

EBAA's Position:

The American corneal tissue supply is safe. No public health threat exists; there has been zero transmission of systemic-infectious disease in over 560,000 corneal transplants, for the last 13 consecutive years. The present regulatory system, consisting of current FDA regulation under Part 1270, the eye bank communities adherence to stringent community-specific and self-imposed standards, and protections afforded by the legal system in this country, is effective as noted by the community's safety history.

The proposed regulation places corneal transplant tissue under a generic and all inclusive regulatory framework not warranted by experience or scientific evidence. This proposed rulemaking, inclusive of all tissue, mimics the practice of defensive medicine -- "defensive rulemaking" -- where tests are ordered beyond the scope of practice parameters, are costly, and add no determined medical benefit. Generic and broad-based safety standards will undermine specific requirements that are peer-reviewed for the eye banking community. The adoption of FDA's broad regulatory approach may actually foster problems in a community that has experienced no transmission of systemic-infectious disease for over 13 years. These issues are specifically addressed later in this response.

The economic impact of the proposed rule is significantly understated. The requirements under the proposed rule would produce a cost with no related increase in safety. The burden of potentially paying a user fee in the future for this type of unnecessary oversight will further add to acquisition costs. Cost increases are not easily absorbed by the not-for-profit eye bank community. At some point, access will be impaired for no justifiable reason.

Page three, EBAA Comments

Corneal tissue destined for human transplant is not a manufactured device or drug, but is a living tissue with a very limited period of viability. The cornea must be recovered, evaluated, medically screened including serological testing for viral markers and provided for transplantation as soon as possible. Ideally, this occurs in one to two days after tissue recovery. Beyond five days, a cornea is unlikely to be acceptable to a U.S. surgeon. Unlike other human tissue, time is of the essence in screening and releasing corneal tissue in the effort to achieve the optimal surgical outcome for the patient/recipient. The FDA's proposed requirements under this rule will increase testing time with no proven benefit, thus pushing the acceptable time limit for transplantation, posing quality problems.

The American Corneal Tissue Supply is Safe:

Since the adoption of EBAA's Medical Standards in 1980, there have been only two reported cases of systemic disease transmission by corneal transplantation in over 850,000 corneal transplants in the United States. Both, cases of hepatitis B, occurred in the early 1980s prior to the development of hepatitis testing. As noted above, the EBAA was among the first transplant organizations to institute mandatory screening and testing procedures for hepatitis B. **With the advent of hepatitis B testing, there have been no cases of any systemic infectious disease transmission in over 560,000 U.S. corneal transplants. This record is testimony that the present self-regulatory approach is working. A 100% safety record cannot be improved.**

On the rare occasion when transmission of systemic infectious disease has occurred, the community has immediately responded, risen to the challenge, reviewed the case vis-à-vis relevant standards and available scientific knowledge, and adopted changes to prevent future occurrence. In sum, in emerging situations there is a mechanism to institute new eye bank community standards to safeguard the donor cornea pool.

EBAA medical standards require routine screening of donors for the following: active viral hepatitis, human immunodeficiency virus (HIV), or HIV seropositive donor, active viral encephalitis or encephalitis of unknown origin, Cruetzfeldt-Jacob Disease (CJD), and rabies. EBAA requires screening of donors for symptoms of transmissible spongiform encephalopathies (TSE) or CJD despite the fact that no known corneal recipients have contracted TSE or CJD in the last twenty-five years in the U.S. This fall, the EBAA convened a group of medical experts to further evaluate standards and procedures for safety relative to TSE and CJD concerns presented outside the United States. We believe this data is critical to determining appropriate eye banking practice. This model, a peer-reviewed scientific approach to public health concerns, is necessary to protect public health and ensure the integrity of the eye banking system.

In the Case of Corneal Tissue, No Public Health Threat Exists:

The FDA fails to demonstrate any compelling public health threat or need to justify the imposition of a broad regulatory approach for all tissue to include human corneal/eye tissue. **Zero transmission of systemic infectious disease in over 560,000 consecutive corneal transplants does not constitute a public health threat.**

Page four, EBAA Comment

The Present Regulatory System Provides Sufficient and Effective Oversight:

- 1) All U.S. eye banks are subject to present FDA regulation pursuant to part 1270 relative to HIV and hepatitis screening and testing procedures. It is misleading to allow the public to believe there are not universal standards in place, when clearly there are for HIV and hepatitis.
- 2) The FDA currently inspects eye banks for compliance with part 1270.
- 3) Should public health problems be generated from a certain eye bank, the FDA has other enforcement powers to call upon.
- 4) In the private sector, the EBAA provides a self regulated accreditation program for member banks. There is one eye bank operating outside the EBAA system in the State of Florida. This Florida eye bank is inspected and monitored for quality compliance under Florida State law, which has incorporated the EBAA's standards by reference.
- 5) The U.S. has a well defined tort system in place through its courts. Scientifically-based standards adopted by accrediting bodies would be used to define the standard of medical practice. If a bank were to significantly deviate from a community adopted standard, this standard would be referenced in a malpractice proceeding.

The EBAA believes there is sufficient oversight of the present eye banking system. Adding new broad-based regulatory requirements will not improve a 100% safety record. In fact, generic and broad-based safety requirements, inclusive of almost all types of human tissue used in transplantation, will replace the value of tissue specific safety requirements already developed and peer reviewed by specific tissue communities. This creates a situation where safety is diminished in certain communities leaving the transplant population more vulnerable to disease transmission or other quality problems.

FDA's Economic Impact Estimates Are Significantly Understated:

Human corneal tissue is a donated human gift. Under Public Health statute (P.L. 98-504; 42 USC 273 et seq., the National Organ Transplant Act of 1984) corneal tissue cannot be purchased or sold. Only the costs of acquiring tissue are reimbursable. As noted earlier, all eye banks are 501 (c)(3) organizations.

A great deal of tissue is necessarily lost throughout the medical screening process due to test results indicating contraindication to transplant or risk factors identified during construction of a donor profile. Eye banks only invoice an acquisition fee for a cornea that is transplanted. In some instances, tissue is provided by an eye bank as a charitable service for indigent care, or for furthering the advancement of the science of sight. The donating eye bank incurs all the costs associated with the procurement and distribution of the eye tissue. While there is generally no acquisition reimbursement for this tissue, in some cases the eye bank receives nominal payment for a portion of the direct costs associated with the procurement, testing, and/or transporting the tissue. In all cases, there is a financial loss to the eye bank.

Page five, EBAA Comments

Today, we are fortunate to meet the demand for corneal tissue. Tissue shortages could result in the near future given the number of new procedures which alter the cornea to improve sight (e.g. LASIK, PRK). Such individuals cannot be donors. We must be careful not to discard viable tissue for non-scientific based concerns. Cost and access problems will result.

The EBAA has reviewed the FDA's estimated economic impact of the proposed regulations and believes them to be significantly understated. The agency states the areas likely to be affected are donor screening, donor testing, record keeping, quarantine, donor suitability determinations, donor documentation, allograft documentation, and labeling.

The FDA only estimated the time needed for one person to "compare the proposed regulations against the facility's current standards". As communicated elsewhere in our response, the EBAA takes issue with the overall necessity of the proposed regulations as well as certain specific provisions. However, if implemented in their current form, the proposed regulations would necessitate changes for every one of the operational functions identified by the FDA (listed above) and others not identified for every eye bank in the United States. The time and resources necessary to comply would not be limited to "comparing" or identifying items for compliance.

For example, any identified area for change after comparing the FDA regulations to an eye bank facility's operating standards is just the first step. Typically, management and an eye bank's Medical Director must provide oversight, direction and approval of any change. Corrective action must be promulgated. Changes in the eye bank facility's standard operating procedures must be made and implemented. Most likely forms and/or logs must be changed. The most significant amount of time and resources is related to the retraining of all affected staff and subsequent quality assurance to insure compliance.

The EBAA has not performed a cost impact study but plans to do so. The economic impact is certainly more than the FDA's estimate of \$45 to \$229. Unfortunately, the comment period did not provide sufficient time for a thorough cost assessment of the provisions discussed therein. One authority on eye bank costs estimated the annual impact at \$10,000 to \$20,000 per average eye bank.

The EBAA is particularly sensitive to cost issues since the United States Health Care Financing Administration recently sought to significantly reduce Medicare reimbursement for the cost of eye banks providing a corneal tissue for transplantation. Eye Banking, as a non-profit community, inherently provides a subsidized service. An inaccurately low estimate of the impact of any additional regulation will severely harm our community's endeavors to provide our sight restoring service to the corneal blind.

The EBAA urges the FDA to correct the economic impact of the regulation. We will be happy to assist with this effort.

EBAA Proposal to the FDA:

The EBAA respectfully requests relief from the imposition of additional broad regulatory requirements established under this proposed rule for human eye tissue until a public health threat is founded. Specifically, the EBAA asks that banked human eye tissue be characterized as "Allogeneic banked human eye tissue" and that banked human eye tissue be subject to no "new" systemic-infectious disease requirements until a public health threat and need is demonstrated. Instead of being subject to unnecessary, broad-based regulatory requirements that diminish peer-reviewed tissue specific standards, the EBAA would support a mandatory reporting requirement for the transmission of systemic infectious disease through corneal transplantation.

Page six, EBAA Comments

The EBAA supported the registration provisions proposed in the Federal Register, May 14, 1998, the "Establishment, Registering, and Listing for Manufacturers of Human Cellular and Tissue-Based Products." As noted above, we would also support mandatory reporting of systemic infectious disease transmission. This requirement, coupled with mandatory registration, would provide a data collection vehicle to assess the need for additional government oversight. At this juncture, the Association believes this would be a prudent approach.

Specific Issues Contained in the Proposed Rule:

The attached pages (Attachment I, pages 1-9) address certain subject matter contained in the proposed rule. As you will note, the EBAA believes the most important issues raised in the proposed rule are not appropriate to the eye banking model. The provisions required in the proposed rule will add significant costs without the benefit of additional safety, and diminish quality standards developed by the community for tissue used in corneal transplantation procedures. In sum, the FDA could foster quality problems in a community where none have existed for over 13 years.

We appreciate the opportunity to comment on this proposed rule and hope that you find our arguments compelling. Please know that the EBAA is available to respond to any additional questions.

Sincerely,



Patricia Aiken O'Neill, Esq.
President/CEO

Enclosures

Attachment I:
Specific Issues in the Rule
Pages
(1-9)

EBAA Attachment I

- **“Manufacturer”, “Product”, and “Marketing”**

*These terms are found throughout the proposed rule and preamble
To describe eye banks corneal tissue, and donor matching.*

Under the definition, the organizations that recover, screen, test, process, store, label, package, or distribute human cellular, or tissue based products are referred to as “manufacturers”. Webster defines this term as “one that manufactures” or “makes into a product suitable for use; to make from raw materials by hand or machinery.” This term demeans the human aspect of what eye banks do which is to utilize, not manufacture, graciously and compassionately donated human tissue for the benefit of mankind. It would be more respectful of the thousands of donors and donor families to use a less offensive term.

“Marketing,” suggests a business model of competition and profitability. Corneas are neither sold nor bought under present law. There are no plans to alter corneas for other health care uses. This term is inappropriate for the community, and could potentially destroy a charitable education and donation network if the general public is led to believe banked human eyes are “marketed”.

In fact, using such terms puts regulation in conflict with several state statutes which declare “the procurement, processing, testing, storing, or providing of human tissue for human transplant” to be “a service” and that such “service does not constitute the sale of goods or products to which implied warranties of merchantability and fitness for a particular purpose are not applicable.” Designating eye banks as “manufacturers” (and tissue as a “product”) is false and misleading and raises potential legal issues, as well. It would establish expectations and standards different from the services an eye bank delivers; human eye tissue cannot be manufactured. It could subject eye banks to inappropriate product liability litigation.

EBAA Comment:

The EBAA recommends that the agency carefully evaluate such business terms for its impact on the donation system. The Association believes these terms are inappropriate to describe human anatomical donation and the provision of tissue for transplantation.

- **“Relevant Disease Risk”**

Section 1271.3-(y) (2)

Section 1271.3 (y) (2) defines “relevant” communicable disease agent or disease that warrants screening and testing of all donors. This definition and requirement thereto is overly broad. Such definition would subject all tissue entities to unfair malpractice claims, leaving the system vulnerable and subject to unnecessary costs.

EBAA Attachment I

If FDA's "relevant disease risk" for eye banks is represented by the Agency's tolerance for CJD and Treponema pallidum, one case and zero cases respectfully, it appears that the mere hypothetical threat of a disease or agent will make it eligible for required screening and testing.

The FDA does not identify a specific mechanism for community input, no advisory committee review, etc. This requirement would leave the tissue community vulnerable to the imposition of requirements not scientifically reviewed.

EBAA Comment:

The EBAA recommends deletion of this broad requirement. Appropriate rulemaking procedures and a demonstrated public health need must apply.

Syphilis

Section 1271.85-(a) (5)

Section 1271.85 (a) (5) requires screening for Treponema pallidum (syphilis). This disease has been repeatedly and intensively addressed by the eye banking community and, after a great deal of consideration, has been found to be not relevant to eye banking. As stated in the Federal Register page 52701, a communicable disease agent must be relevant. "First, for a communicable disease agent or disease to be "relevant," its prevalence among donors would have to be sufficient to warrant screening or testing of all donors. Second, "there will need to be a risk of transmission of disease agent or disease by human cellular or tissue based product...."

There has been no confirmed evidence, nor reported suspicion of transmission of Treponema pallidum (syphilis) by corneal transplantation. Respected studies have demonstrated no evidence of viability of Treponema pallidum under corneal storage conditions used by eye banks in the United States (Macasai, Norris, *Cornea*, 1995; 14:595-600). It has also been demonstrated (Goldberg, Laycock, Kinard, Wang, Pepose, *AMJ Ophthalmol*, 1995:119:1-6) that serologic testing for syphilis does not serve as a surrogate marker for HIV testing. In addition, the low incidence of new reported cases (less than 7,000 cases in the United States in 1998) makes this a poor screen to recommend.

Positive serologic tests for syphilis in pre-screened eye bank donors are almost always false positive tests and even if they were true positive tests, there has been no reported case of transmission of syphilis through transplantation of corneal tissue. Thus, requiring Treponema pallidum testing would reduce the number of available corneal donors, increase costs, and provide no additional protection for recipients.

EBAA Attachment I

EBAA Comment:

The EBAA recommends deletion of this requirement for screening and testing for treponema pallidum for those involved in eye banking.

- **Leukocyte – Rich Cells or Tissue**

Section 1271.85 (b)

Section 1271.85 (b), requires additional testing for donors of viable, leukocyte-rich cells or tissue. Page 52705 of the Federal Register lists “stem cells” as “examples of leukocyte-rich cells or tissue.” This term should be better defined as “hemotologic” stem cells since, in eye banking, corneal epithelial stem cells are being more frequently used in transplantation and these cells are not leukocyte-rich and should not be included under the rubric “stem cells.” This problem could be eliminated if stem cells were better defined in the proposed rule.

EBAA Comment:

The EBAA believes this example is one among many that identify problems of appropriate applicability in the rule.

- **Transmissible Spongiform Encephalopathies (TSE)
And Cruetzfeldt-Jakob Disease (CJD)**

On page 52706 of the Federal Register, “the agency requests comment on the feasibility of testing for TSE/CJD in donors of corneal tissue.” In over 55 years of U.S. eye banking, only one reported case of CJD transmission has been documented. That particular tissue was recovered from a patient who died in a neurological institute. The donor tissue was never evaluated nor screened by the local eye bank. Zero cases have been reported since the EBAA implemented its medical standards in 1980. One case in over 55 years indicates a negligible prevalence in the donor pool. According to the FDA, “its prevalence among donors would have to be sufficient to warrant screening and testing of all donors.”

Due to reports of recent transmission outside the United States, the EBAA, concerned that “no future transmission occurs”, convened a group of internationally renown scientific experts in CJD, eye banking and epidemiology* to provide appropriate guidelines and parameters for TSE and CJD. The EBAA expects a report and scientific data on this subject soon and will forward it to the agency. It should be noted that the countries where recent transmission occurred do not adhere to standards as stringent as those adopted by EBAA member banks. Further, under current EBAA standards, the tissue would not meet EBAA donor criteria and would not have been transplanted.

EBAA Attachment I

At the present time, a brain biopsy is not a realistic way of screening donors for TSE, because of the time requirement involved. A brain biopsy would require consent for a brain autopsy to be performed. Brain autopsy results in donor disfigurement and delays in funeral arrangements, which would impact families and, we believe, would drastically reduce the number of people willing to donate. It would also add significant costs to eye banks. The length of time necessary to complete the microscopic study of brain tissue would result in expiration of the corneal tissue, i.e., aging of the cornea beyond the 7-10 days when a tissue could be placed for transplantation. In the absence of a serologic rapid test, the eye banking community is looking at possible historical screens for TSE as noted above.

EBAA Comment:

The EBAA recommends that the agency take no action in this area at this time. The EBAA will shortly receive recommendations from an Ad Hoc group of experts convened to examine CJD/TSE concerns. The group's findings will also be shared with the agency.

*Ad Hoc Committee for CJD:

(Advisory to EBAA Medical Advisory Board)

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EBAA Attachment I

Paul Brown, MD
Senior Scientist

National Institute of Neurology and Stroke, National Institutes of Health, Bethesda, Maryland

- ### **Legislative Consent**

Sections 1271.3 (o) and 1271.75 (d)

The Section 1271.3 (o) and Section 1271.75 (d) require a donor medical history interview. There is no evidence that there has been any increased risk of transmission of disease through corneas obtained under legislative consent absent a medical history interview. In the absence of such evidence, and given the lack of confirmation of the validity of such interviews, mandating such a requirement does not appear to have adequate scientific substantiation.

EBAA Medical Standards document that legislative consent cases can be screened for risk factors and an adequate donor profile can be constructed through the use of the investigator's reports, autopsy results, and other sources of donor history.

EBAA Comment:

The EBAA recommends no change in policy from present federal regulation. A 1998 report presented before EBAA's Medical Advisory Board by the EBAA Policy and Position Research Committee, specifically summarizes the EBAA position (see Attachment II).

- ### **Storage**

Section 1271.65

Section 1271.65 requires separation of suitable tissue from "quarantine" tissue. Physical separation would require additional refrigerator storage units for quarantined tissues, and would present an unnecessary cost and space burden.

EBAA Comment:

No "storage" problems have resulted in the transmission of systemic-infectious disease. EBAA recommends that the agency permit eye banks to follow community standards for storage.

EBAA Attachment I

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FDA - Licensed Tests

Section 1270.80 (c)

Section 1270.80 (c) requires the use of FDA-approved tests. Tests specifically labeled for cadaveric specimens shall be used instead of a more generally labeled test when applicable and when available.

No currently FDA-approved serological tests exist for cadaveric samples. Due to the nature of eye recovery, the majority of samples collected are cadaveric.

EBAA Comment:

Current EBAA's Medical Standards for labeling and testing requirements meet or exceed this proposed requirement. We encourage the FDA to work with laboratories and manufacturers of diagnostic tests to approve tests for cadaveric specimens.

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Collection of Blood Samples

Section 1271.80 (b)

Section 1271.80 (b) of the proposed rule "...requires that the donor specimen be collected at the time of recovery of cells or tissue from the donor or within 48 hours after recovery; except that the specimen from a living donor may be collected up to 7 days prior to recovery...."

There are several problems with this proposal for eye banking:

- (1) The best sample is one that is obtained from the donor pre-mortem. A FDA-approved blood test kit would actually test the blood within the guidelines of the kit, since such kits are only approved for blood from living patients. Frequently, post-mortem samples are hemolyzed and this leads to false-positive tests.
- (2) Not permitting pre-mortem samples negates all blood samples taken pre-infusion and pre-transfusion in cases of blood loss (adults) and infusion of fluids and blood (adults with blood loss and all children under 12 years.) This whole proposal grossly contradicts FDA's final rule that requires pre-infusion and pre-transfusion samples in such cases. This requirement also conflicts with another section in the Proposed Rule, 1271.80 (d) (2) (i): "A specimen taken from the donor after blood loss but before the transfusion or infusion is available for relevant communicable disease testing."
- (3) Setting a standard of blood sample collection up to 48 hours after recovery establishes dangerous outer-testing limits for banked human eyes. The later the specimen collection, the more hemolyzed the blood, and the greater chance for testing errors.

EBAA Attachment I

EBAA Comment:

Allowing a donor specimen to be collected up to 48 hours after recovery is not recommended for purposes of eye donation. This requirement would foster quality problems for eye banks. This is one example of where the proposed rule is overly broad and actually relaxes community standards. This proposed standard could lead to dangerous quality problems not currently exhibited. The EBAA recommends deletion of these standards. Tissue specific community standards for eye banking must be allowed.

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Plasma Dilution Algorithm

Section 1271.80 (d)(2) and (d)(2)(i)

Section 1271.80 (d)(2) and 1271.80 (d)(2)(i) of the proposed rule and previous FDA guidance documents provide direction for the final determination of serology test results. Nevertheless, direction under the proposed rule remains either vague or unsupported by scientific logic. For example, “blood loss” needs clarification. In addition, dilution algorithms are required if infusions and transfusions exceed 2000 mL over specific time periods. This becomes a practical issue of performance. How can you determine if the algorithm needs to be implemented due to the 2000 mL limit without actually performing the tabulation?

Most facilities have complied with this regulation by merely performing a dilution algorithm on all donor cases destined for transplant use. Finally, the inclusion of whole blood cell total volume in calculations does not meet scientific principles. The volume of the red blood cells does not contribute to plasma dilution, only the actual plasma volume of the whole blood or the components used to produce reconstituted whole blood prior to transfusion contribute to dilution of the plasma.

EBAA Comment:

The EBAA recommends no change from FDA’s present policy on plasma dilution.

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Screening and Confirmatory Testing

Section 1270.80 (d) (1)

Section 1270.80 (d) (1) of the Notice of Proposed Rulemaking (NPRM), declares a donor who tests “repeatedly reactive or positive for a particular agent unsuitable, thus the cells and tissues from that donor could not be used.”

EBAA Comment:

Current clinical practice suggests that confirmatory tests be used when available to verify positive screening tests. In order to avoid discarding transplantable tissue, we urge the

EBAA Attachment I

FDA to follow current clinical practice and reconsider its position because of the lack of scientific information that negates current clinical practice. The FDA does accept confirmatory testing for Treponemal disease. Policy should be consistent with medical practice, allowing confirmatory tests (where available) to prevail in all cases.

- **Recordkeeping Requirement**

Section 1271.55 (1) (i)

Section 1271.55 (1) (i) requires manufacturers to include a copy of the donor's relevant medical records in documentation to accompany the tissue.

Under FDA's proposed rule an eye bank would have to obtain permission to release the medical records of the donor. Any identification of the donor would have to be redacted. This requirement is cumbersome, costly, and would ultimately provide confusing and conflicting data to transplant physicians. It appears that eye banks would need to send copies of the donor's full hospital chart to the surgeon and hospital Operating Room. This would require a donor's medical chart be included with the recipient's hospital chart. This could create a confusing situation and lead to error. Identifying cause of death and including a brief summary of medical condition to be delivered with the tissue is more appropriate. This would shield sensitive materials. In the rule a definition of

Summary of Medical Records is given, however, the proposed rule does not appear to simply permit a summary to be sent with the donor.

EBAA Comment:

The EBAA recommends deletion of this requirement as excessively burdensome. EBAA practice, per Medical Standards, has effectively guarded against transmission of systemic-infectious disease.

- **Privacy**

Section 1271.55 (d)

Section 1271.55 (d) requires deleting the donor's name from documentation accompanying the tissue.

The Department of Health and Human Services proposed rule addressing "Standards for Privacy of Individually Identifiable Health Information, Federal Register Vol. 64 No. 212 45 CFR Parts 160 through 164 RIN 0991-AB08," would require deletion of much more data than the "donor name" as required in this standard.

EBAA Attachment I

EBAA Comment:

The Association is currently providing comment to the Department of Health and Human Services, on the proposed rule regarding (Federal Register Vol. 64 No. 212 CFR Parts 160 through 164 RIN 0991-AB08) Standards for Privacy of Individually Identifiable Health Information. We believe the proposed HHS regulation would adversely impact the transplant community. The regulation would severely burden the transplant process because of mandatory preauthorization requiring consent to review medical records. The proposed regulation will also restrict the research community's access to corneal tissue. The Association will request an exemption from this proposed rule so that the transplant community can continue to have access to essential donor information, in a timely fashion, that is necessary to facilitate the transplant process.

Attachment II
(Pages 1-4)

MEDICAL EXAMINERS LAWS AND THE ISSUE OF TISSUE SAFETY

Increasing concern about disease transmission has led to increasing scrutiny of organ and tissue procurement practices. The recent proposed and final rulings by the Food and Drug Administration (21CFR1270) highlight this concern. Contained in these rulings is the requirement that information be obtained concerning donors through "a documented dialogue with an individual or individuals who would be knowledgeable of the donor's relevant medical history and social behavior..." but "for corneal tissue procured under legislative consent where a donor medical history screening interview has not occurred, a physical assessment of the donor is required and other available information shall be reviewed." This legislation appears to respect the importance of a medical history while at the same time allowing states which procure tissue under medical examiner laws to continue to do so, even without a direct interview. These rulings and the concerns of some members of the eye banking community have led to a request for re-appraisal of the issue of tissue obtained through medical examiner laws. At least two basic issues present themselves: one is the issue of the safety of medical examiner tissue; another is the ethical concern inherent in obtaining tissue without specific consent from the donor or donor family. This paper will attempt to deal only with the issue of safety. The issues related to ethics will be left to other arenas for debate.

Prior to discussing safety issues it would be appropriate to assess the impact of medical examiner legislation on the supply of corneas in the United States. The Lions Eye Bank of Texas at Baylor College of Medicine, through its executive director M.B.

Danneffel, surveyed United States eye banks and found that while 33 states have medical examiner laws only nine used them in 1996. Of the 43,711 usable corneas procured in the United States that year, 4,752 or 11% were procured under medical examiner legislation. Thus the impact is not great although in some areas it is substantial.

To evaluate the safety of medical examiner tissue we will first attempt to review the relevant literature. Direct comparisons between hospital and medical examiner tissue were sought. Very few such comparisons exist. Danneffel and A. Sugar¹ found almost an identical seropositivity for human immunodeficiency virus (HIV) in medical examiner cases (0.87%) and hospital cases (0.83%) screened from 1986 to mid 1988. Heck et al² found 5 of 205 prospective donors, already screened to attempt to eliminate high risk groups, positive by ELISA and Western blot for HIV. All prospective donors were medical examiner cases and no comparison group with non-medical examiner cases was evaluated. Hwang et al³ reviewed 4,451 consecutive potential donors from the Los Angeles County Medical Examiner and excluded 1,680 (37.7%) on the basis of history or physical examination. Of the remaining 2,771 potential donors 27, (0.97%) were repeatedly positive on ELISA screening for HIV. Again a non medical examiner group was not provided for comparison.

Another way of looking at the issue of safety is to assess adverse reactions reported. Through the EBAA adverse reaction reporting system, Kirk Wilhelmus found for adverse reactions reported from 1993 to 1997, 10 endophthalmitis cases were from medical examiner cases, 54 from hospital patients and in 16 the source was unknown. This makes medical examiner cases account for 15.6% of endophthalmitis cases where the tissue source was known. For primary donor failures, 1995 to Feb., 1998, 24 of 144

reported cases where the source was known were from medical examiner cases or 16.6%. The exact proportion of all grafts from medical examiner sources during this time period is uncertain but probably is somewhere between 11 and 25%. In a more limited but better controlled study Danneffel, Scardino, Wilhelmus, and Woodbury (written communication December 18, 1997 submitted as ARVO abstract) retrospectively reviewed all adverse reactions reported from 8,211 corneal tissues distributed by their eye bank from 1993 through 1996. 13 adverse reactions were from 5,580 medical examiner obtained tissues (0.24%) and 6 were from 2,631 next-of-kin consented sources (0.23%).

Specific cases of systemic disease transmission have been reported including 2 cases of Hepatitis B and 4 cases of Creutzfeldt-Jakob disease as well as cases of rabies. None of these were from medical examiner cases and all appeared to have histories available although in all United States cases transplantation took place prior to institution of the present medical standards. Nonetheless, the risk of transmission of systemic viral disease persists, even in the presence of a family history interview. The risk of prion-associated diseases such as Creutzfeldt-Jakob is low but certainly not zero. Hogan and Cavanagh⁴ and in revised figures Hogan, Heck, and Cavanagh (written communication January 9, 1998, submitted as ARVO abstract) suggest that approximately one donor per year would be expected in the United States donor pool to have Creutzfeldt-Jakob disease. They felt that historical exclusionary criteria, those already in place, would exclude such a donor. Whether medical examiner screening of tissue would exclude such a donor is unknown. The question persists as to the adequacy of medical examiner determination of causes of death but questions also exist as to the accuracy of family interviews as well.

In summary no data are presented here which demonstrate evidence of increased disease transmission risk from donor tissue derived from medical examiner sources. Whether such tissue, when lacking historical data, will present increased risks in the future is unknown. This review is limited by the scarcity of well designed studies of the predictive value of clinical and interview data collection in both medical examiner and hospital settings. Until data from appropriate studies are available, it is suggested that reasonable efforts be made to obtain historical information on all corneal donors. The Medical Advisory Board of the EBAA will need to continue to monitor and assess this issue. A scientific basis for altering present policies does not yet exist.

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