244 East Main Street
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October 6, 2000

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

8893 '00 OCT 23 A10:03

Reference: Docket No. 00N – 1463 (Labeling requirements for systemic antibacterial drug products intended for human use)

Dear Sirs:

The following comments are made in reference to the above document.

1. Eliminate the redundancy of the statement ("inappropriate use ... caused by susceptible microorganisms") that is proposed to appear under the product name and "Precautions" by having it appear only under the product name.
2. Add to the label a "Clinical Microbiology" section following the "Clinical Pharmacology" section under which the statement ("appropriate use ... of its susceptibility profile") that is proposed to appear under "Clinical Pharmacology" would appear. The statement, which is important, is more correctly a "Clinical Microbiology" statement rather than a "Clinical Pharmacology" statement. By creating a "Clinical Microbiology" section the label user will be able to easily recognize the statement.
3. Add to all labels dealing with antiinfectives a "Clinical Microbiology" section. The addition of a "Clinical Microbiology" section to all labels dealing with antiinfectives would more clearly identify to the user important information about the drugs use in the treatment of infections and the reasons why if not used correctly it could cause harm to the patient. Physicians and nurses are used to seeing clinical microbiology information under "Clinical Microbiology" rather than "Clinical Pharmacology". They refer to the "Clinical Pharmacology" to obtain information about the behavior of the drug in the patient (ex. absorption, excretion).

Sincerely,

Frederic Marsik, Ph.D.
Diplomat, American Board of Medical Microbiology

00N-1463

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**EYE BANK ASSOCIATION of AMERICA**

*Dedicated to the Restoration of Sight since 1961*

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October 5, 2000

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

Ref: Docket No. 00N-1425; Agency Information Collection Activities; Proposed Collection; Comment Request; Human Tissue Intended for Transplantation; 65 Federal Register 152; August 7, 2000.

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 agency's information collection activities for human tissue intended for transplantation. 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 eye tissue through the adoption and implementation of stringent medical standards.

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 the tissue are reimbursable. 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 the donor family interview. 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 such tissue, in some cases there is a 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, which provides such tissue.

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EBAA Annual Meeting, Washington, DC, June 21-24, 2000
EBAA Education Conference, Orlando, FL, October 20-23, 1999
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Eye banks have complied with FDA regulatory requirements to prevent the transmission of human immunodeficiency virus (HIV) hepatitis B, and hepatitis C, as outlined in Part 1270 (21 CFR Part 1270). It should, however, be noted that the there has been no report of transmission of systemic-infectious disease since 1987 -- years before the FDA published its Interim Rule (December 14, 1993). The EBAA was the first transplant organization to institute mandatory testing of donors for the presence of HIV; and was among the first to institute mandatory testing and screening procedures for hepatitis B and C as testing became available.

The notice of comment states (Federal Register; August 7, 2000; p. 48245) that the "FDA assumed that any record keeping burden would continue as customary and usual business practice of an establishment that are members of those organizations and therefore no additional burden is calculated ... and that the requirement for written procedures is a one-time burden." The EBAA believes this statement is flawed. It is true that the data required for collection by the FDA is the same, as the data required of EBAA eye bank members for certification as an eye bank; it is flawed in the assumption that no additional cost is incurred to follow FDA requirements for data collection.

There is a cost in preparing data for two different entities (the EBAA and the FDA) in two different formats. Labor costs are involved in reviewing FDA requirements and guidance documents and overseeing compliance thereof. FDA's statement that this is only a one-time cost is also not accurate. FDA standards, guidance documents, and inspection procedures continue to evolve adding to the costs of compliance. Record keeping requirements are increased whenever FDA adjusts its guidance documents and may be increased by individual FDA inspector interpretations stemming from an eye bank inspection.

Comparing FDA regulations to an eye bank facility's operating procedures is just the first step. EBAA standards require that management and an eye bank's Medical Director provide oversight, direction, and approval of any substantive change in procedures; and, that on at least an annual basis all procedures and staff competency evaluations are reviewed and retested. Corrective action is then promulgated. Changes in the eye bank facility's standard operating procedures must be made and implemented. Most likely forms and/or logs are 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. One eye bank, that has the ability to collect cost data on a broad scale, estimates, that at a minimum, the annual cost impact of complying with present FDA regulation is $10,000.00. Such costs increase the cost of corneal acquisition fees by $25.00 per cornea.

There is also a significant cost associated with an FDA inspection. Part of the inspection process, involves a review of record keeping and written procedures. FDA inspections require that resources and personnel be made available from other areas of an establishment to comply with the inspector's requests. Such shifts in resources cost establishments overtime pay, lost work, and delays in time schedules. The cost for a one to two day FDA inspection is estimated by some eye banks to be $1,000.00 or more dollars; a three to four day FDA inspection is estimated to be $2,000.00 or more dollars. As noted above, all eye banks are not-for-profit entities. New costs are not easily absorbed and should not be unnecessarily incurred. The Association will begin to formally collect cost data associated with an FDA inspection.

It should be noted that record keeping requirements prescribed by the FDA are more onerous to

eye banks since the vast majority of donations occurring each year involve eye donors. During 1999, more than 48,000 eye donors were procured by EBAA member banks. Each donor generated at least two donor tissues resulting in, at a minimum, more than 96,000 tissues for which individual records must be maintained and followed for ten years beyond the date of transplantation, distribution, disposition, or expiration of the tissue, whichever is latest. Eye bank record keeping requirements are especially voluminous when compared with the record keeping requirements involved with the total number of organ donors, 5,843, for 1999 (United Network for Organ Sharing website).

FDA requires eye banks to have written procedures in place that follow "all Significant steps in the infectious disease testing process under S 1270.1, which shall conform to the manufacturers' instructions for use contained in the package inserts for the required tests. These procedures shall be readily available to the personnel in the area where the procedures are performed unless impractical. Any deviation from the written procedures shall be recorded and justified." This requirement extends to testing on specimens performed by independent laboratories. Eye banks cannot be expected to watch and supervise the performance of every single test performed by CLIA certified independent laboratories and record deviations made by such laboratories. Expectations that FDA may have for eye banks to actively participate in determining a laboratory's technical competency is unreasonable. Does this FDA standard set a precedent that all medical tests be directly observed to see that package inserts for tests are followed? The EBAA believes this requirement is overly burdensome, unreasonable, and enormously expensive to track.

Record keeping requirement and procedures will again be impacted during January 2001. This is when FDA has mandated the use of FDA approved test kits for use with cadaveric blood specimens to meet regulation testing requirements. Infectious disease test kits validated for use with cadaveric blood are not widely available. At this time, the EBAA is aware of only one manufacturer whose test kits are approved for testing of cadaveric blood. The testing equipment required to employ the use of such cadaveric kits will require many laboratories to purchase new equipment to make the use of these kits possible. Many laboratories are hesitant to purchase new equipment to implement the use of one manufacturer's test kit. Some laboratories will not have access to the new test kits for financial reasons, and some will continue to utilize current testing procedures. Eye banks will be responsible for finding laboratories that employ the use of the new cadaveric kits, and banks will have to accordingly adopt new written procedures. Identifying and organizing relationships with laboratories capable of cadaveric testing is an expensive and time-consuming undertaking. The regulation does not contemplate such costs.

The FDA should consider the negative impact upon the corneal tissue supply and tissue viability that results from requirements (not demonstrated as necessary for health and safety) that effectively mandate eye banks to utilize laboratories located far away from their local service area. Testing schedules between eye banks and laboratories must be carefully orchestrated to insure the timely reporting of results. Delays in obtaining infectious disease test results increase the time between the donor's death and transplant surgery. Cornea tissue is time sensitive and will lose its viability within a short period of time; the tissue is customarily used within 5-6 days. An extra day could likely cost the community up to 20 percent of its tissue. The adjusted mean for the average gross cost per tissue is $1719.00; loss of transplantable tissue means loss in charitable donation and revenue to support the ongoing operation of the eye bank.

**Closing Remarks:**

The EBAA and its members have willingly complied with the FDA standards (21 CFR parts 16 and 1270). Accordingly, the Association has not spent the resources needed to calculate the exact cost of the provisions of this regulation. The Association, on behalf of its membership, can tell the FDA that there is an additional financial burden placed on banks resulting from this rule and that the requirements for written procedures represent on going, not one-time, costs as discussed above.

The Association will begin to collect cost data from its members relative to the costs of an FDA inspection. EBAA will also begin to carefully document each proposed change in step required by the FDA to meet the requirements of this rule.

The FDA has proposed two new rules impacting organizations involved with human tissue: 1) Proposed Rule; Establishment Registration and Listing for Manufacturers of Human Cellular and Tissue-based Products; 63 Federal Register, 93, May 14, 1998; and, 2) Proposed Rule; Suitability Determination for Donors of Cellular and Tissue-Based Products; 64 Federal Register 189; September 30, 1999. The cumulative impact of the adoption and implementation of the aforementioned proposed rules will undoubtedly alter the operation of an eye bank, and add cost.

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 and PRK, etc.). Such individuals cannot be eye tissue donors. Again, a 100% safety record is in tact and demand is being met. Unnecessary changes add cost without demonstrable benefit. At some point the agency has to assume the burden of its actions on the donation community.

Sincerely,

Patricia Aiken O'Neill

Patricia Aiken O'Neill
President/CEO