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Commissioner
Food and Drug Administration
5630 Fishers Lane
Rockville, MD 20852

Ref: Docket No. 97-N-484P
Proposed Rule: Current Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products; Inspection and Enforcement
21 CFR Part 1271, January 8, 2001

Dear Commissioner:

The American Academy of Ophthalmology appreciates the opportunity to comment on the proposed "current good tissue practice" rule that aims to safeguard public health through increased regulation of human cellular and tissue-based products. The Academy is the world's largest ophthalmic educational and scientific non-profit organization, with more than 27,000 eye physician and surgeon members. Our mission is to ensure that the public can obtain the best possible eye care.

The Academy agrees with the FDA's intent to protect public health by ensuring that 'cells and tissues be handled according to procedures designed to prevent contamination and to preserve tissue function and integrity.' However, we believe there is a fundamental flaw in FDA's rationale for viewing primary graft failure rates as evidence that the function and integrity of donor corneas are impaired through improper handling by eye banks. We believe this is an assumption that cannot be substantiated.

Eye banks are 501 (c) (3) charitable organizations that acquire, process, store and distribute corneal tissue. Eye banks perform a service to the human community and are not manufacturers of tissue. The Eye Bank Association of America (EBAA), representing 96 U.S.

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eye banks, has adopted and implemented strict accreditation programs and stringent medical standards to ensure the high quality of all banked human eyes and eye tissue. Adherence to these standards has resulted in no transmission of systemic infectious disease over the last 14 years. 97 percent of all corneal tissue provided for transplant originates from members of the EBAA. U.S. member eye banks do not import any eyes or eye tissue.

The proposed rule cites one published paper on the rates of primary corneal graft failure as evidence that the function and integrity of donor corneas are significantly impaired, thereby creating the need for additional transplant procedures and increasing the risk of introduction, transmission, and spread of communicable disease.

We believe that the FDA has misinterpreted the Wilhelmus study on primary corneal graft failure rates. Often, factors other than handling, preservation and storage of corneas result in failure of a corneal graft. During the three-year study period (January 1, 1991 to December 31, 1993), an estimated 111,000 corneal transplants were performed with a primary graft failure rate of 0.1 percent. The Wilhelmus study of 147 patients concludes that no clearly defined donor or eye banking factor accounted for most cases of primary graft failure. Noting the limitations of the study, Wilhelmus et al. states that the control group may have been screened, handled, and transplanted differently from the study cases reported. Also of importance is the fact that in only seven percent of the voluntarily reported cases of primary corneal graft failure were corneas preserved and stored for more than one week, compared with three percent in the control group. As Wilhelmus suggests, the data do not allow a determination of the point of storage time at which graft failure becomes a definite risk. Importantly, the data indicate that other factors, not storage time, contribute to primary graft failure in most cases.

Another, perhaps more definitive study of graft failure, was conducted by the Collaborative Corneal Transplantation Studies Research Group. The group reviewed records of 457 high-risk transplant recipients. A high-risk patient was defined as having at least two quadrants of stromal vascularization and/or a history of

previous graft rejection. The strongest risk factors for corneal graft failure and rejection were young recipient age, the number of previous grafts, history of previous anterior segment surgery, preoperative glaucoma, quadrants of anterior synechiae, quadrants of stromal vessels, a primary diagnosis of chemical burn, and blood group ABO incompatibility. This group concluded that donor and corneal preservation characteristics had little influence on graft outcome. (Ophthalmology 1994 Sep;101(9):1536-47). It is important to note that this research was derived from a randomized, controlled clinical trial involving multicenter studies, sponsored by the National Eye Institute.

In the most recent case control study published in 1994, Mead et al. found that improper tissue preparation was not associated with primary graft failure (Cornea 1994;13(4):310-316). From July 1, 1986 to June 30, 1988, the Massachusetts Eye and Ear Infirmary reviewed 778 corneal transplant cases performed by 9 surgeons, and found 22 cases of primary corneal graft failure. Mead found that surgical factors, especially the identity of the surgeon, were the most statistically significant risk factors associated with primary graft failure. The quality of donor tissue preparation was not found to be a statistically significant cause of primary corneal graft failure.

The Academy urges you to reassess the potential causes of primary corneal graft failure. Corneal transplantation is a safe and efficacious procedure with a distinguished 50-year history. Eye banks have a success rate to be proud of. As you promulgate regulations, the Academy hopes you will consider the current eye banking medical safety standards and procedures already in place in eye banks that provide transplant recipients with safe, sight-restoring surgery.

Thank you for your time and consideration.

Sincerely,

William L. Rich III, MD
Secretary for Federal Affairs

Mark J. Mannis, MD
Chair
Committee on Eye Banks