April 6, 2016

Division of Dockets Management (HFA–305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852


Submitted electronically at www.regulations.gov

Dear Dockets Manager:

On behalf of the 85 U.S. member eye bank organizations, the Eye Bank Association of America [hereinafter referred to as the “EBAA” or the "Association"] submits these comments to the guidance document entitled Use of Nucleic Acid Tests to Reduce the Risk of Transmission of Hepatitis B Virus from Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products, dated January 2016. The draft guidance document is intended to provide establishments that make donor eligibility determinations for donors of human cells, tissues, and cellular and tissue-based products (HCT/Ps) with recommendations concerning the use of FDA-licensed nucleic acid tests (NAT) in donor testing for hepatitis B virus (HBV) DNA.

I. EBAA Background

Our U.S. member organizations provide close to 100% of all corneal tissue used for transplantation in the U.S. All EBAA eye bank members 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, which are scientifically based, and specific to ocular tissue.

The EBAA is the world’s oldest transplantation association, established in 1961 by the American Academy of Ophthalmology (AAO). The EBAA first established medical standards and an accreditation program for inspection of eye banking organizations in 1980, and certification of technicians followed in the late 1980s. The Association’s standards and procedures have been used as a model for adaptation by other organizations in the United States, and other countries. They are reviewed and revised twice a year by a board of renowned corneal surgeons and certified technicians with expertise and extensive experience in eye banking and then formally considered by the AAO, which has endorsed them each year since 1981. The EBAA standards representing "best practices" in eye banking, are based on science specific to ocular tissue, and enjoy widespread recognition and acceptance. The Medical Advisory Board is responsible for promulgating EBAA Medical Standards and a U.S. Food and Drug Administration (FDA) representative sits on the board.

The EBAA Accreditation Board, also established in 1980, conducts inspections of eye bank members on a regular three-year cycle or more often, as necessary. Eye banks which are accredited by the
EBAA, follow EBAA medical standards, and employ EBAA procedures which closely parallel and often exceed those of the FDA Good Tissue Practice regulations.

The EBAA appreciates this opportunity to provide public comments on this draft guidance document. On behalf of our member banks, we would like to offer these comments for consideration.

II. **Comments to the Recommendations in the Guidance Document**

In order to adequately and appropriately reduce the risk of relevant communicable disease agent or disease transmission (21 CFR 1271.85(a)(3)), we recommend that you test HCT/P donors for HBsAg and for total anti-HBc (IgG and IgM).

In addition, FDA recommends that you test HCT/P donors for HBV using an FDA-licensed NAT donor screening test in accordance with the manufacturer’s instructions.

- Any HCT/P donor whose specimen tests negative (or non-reactive) in all three assays (i.e., HBsAg, total anti-HBc (IgG and IgM), and HBV NAT) may be considered to be negative (or non-reactive) for purposes of making a donor eligibility determination.
- Any HCT/P donor whose specimen tests positive (or reactive) using any of the assays (i.e., HBsAg, total anti-HBc (IgG and IgM), or HBV NAT) is considered ineligible (21 CFR 1271.80(d)(1)).

**Recommendation:**
The EBAA supports the requirement that HCT/P donors be tested for HBV using an FDA-licensed NAT donor screening test, in addition to testing for HBsAg and for total anti-HBc (IgM and IgG). We concur that NAT testing is necessary to detect viral infection during the infectious window period or breakthrough infections in previously vaccinated individuals.

**Rationale:**
Hepatitis B virus has been transmitted by corneal transplantation as described by Hoft et al. The two cases occurred before hepatitis testing was mandated by the Medical Standards of the EBAA in 1986. Both donors would clearly be excluded by present eye-bank standards and FDA regulations, because both were HBsAg positive.

The study by Khalil et al confirms the presence of hepatitis B virus in human corneas and demonstrates that preservation in corneal storage media for up to 6 days could not eliminate the virus from the cornea.

The Zou study estimates that implementing individual HBV NAT testing for tissue donors could reduce the probability of donor HBV viremia at the time of donation from 1 in 34,000 to 1 in 100,000 (Ref 10).

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In 2014, the EBAA Statistical Committee approved adding HBV NAT to the data collected on serological reasons tissue intended for surgery was not suitable for transplant. HBV NAT was responsible for 347 U.S. corneas not being released in 2014 and 287 in 2015.

Data from the 2015 Eye Banking Statistical Report is summarized below:

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<thead>
<tr>
<th>Not Released - Serology</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
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<tr>
<td>HIV</td>
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<td>258</td>
<td>253</td>
<td>255</td>
<td>300</td>
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<tr>
<td>HIV I/H Ab</td>
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<td>173</td>
<td>169</td>
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<tr>
<td>HIV NAT</td>
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<td>70</td>
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<tr>
<td>HBV</td>
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<td>5425</td>
<td>6366</td>
<td>5810</td>
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<tr>
<td>HBsAg</td>
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<td>876</td>
<td>786</td>
<td>1130</td>
<td>1070</td>
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<tr>
<td>HBCab</td>
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<td>4392</td>
<td>4639</td>
<td>4889</td>
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<td>4</td>
<td>10</td>
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<td>538</td>
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<td>342</td>
<td>466</td>
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</tr>
</tbody>
</table>

The addition of nucleic acid testing to the screening of tissue donors should reduce the risk of these infections among recipients of donated tissue. Eye banks are currently utilizing the FDA-licensed multiplex assays that can simultaneously detect HIV, HCV, and HBV in a single blood specimen.

III. CONCLUSION

The EBAA thanks the FDA for the opportunity to comment on the draft guidance document. The Association appreciates the FDA's efforts to help ensure the safety of human tissues for transplant and prevent the transmission of communicable disease by HCT/Ps.

The EBAA stands ready and willing to assist the FDA and our other transplant partners to develop appropriate regulatory scheme to ensure the safety of human tissues offered for transplant.

Sincerely,

Kevin P. Corcoran, CAE
President & CEO