Representatives of the AATB, AOPO, and EBAA (the Associations) met for an hour by conference call on September 1st to discuss the Zika virus (ZIKV) with officials from FDA/CBER, the CDC, and HRSA. The meeting was also attended by members from the Office of the Assistant Secretary for Health (OASH) and the New York State Department of Health. Because ZIKV has now emerged in the contiguous United States in two counties in Florida, current and future challenges were discussed regarding screening organ, tissue and eye donors. This includes use of the CDC’s “Areas with Zika” website, the availability of appropriate tests when donor testing is desired, and research with a focus on transplantation and viral persistence in organs and tissues.

A few reference documents were reviewed briefly:

- FDA/CBER’s Immediate Implementation Guidance Document from early March that described “Donor Screening Recommendations to Reduce the Risk of Transmission of Zika Virus by Human Cells, Tissues, and Cellular and Tissue-Based Products”. This document addresses donor eligibility of living donors of HCT/Ps, including living donors of gestational tissues based on risk factors that include medical diagnosis of Zika virus infection, residence and travel to areas with ZIKV transmission, and sexual activity with partners with known ZIKV risks. For deceased donors of HCT/Ps, the donor eligibility is recommended to be determined based on a medical diagnosis of ZIKV infection in the past 6 months. Recommendations for organ donors are not covered in this document. There are no tests available for donor eligibility determination for HCT/P donors, and therefore there are no FDA recommendations in this area.

- OPTN’s “Guidance for organ donation and transplantation professionals regarding the Zika virus” published in early February and updated on July 28 with more CDC web links. The guidance describes to screen for recent travel history and epidemiologic risk factors, as well as recent donor symptoms.

(Note: Each guidance above refers to CDC webpages as references to use to establish “areas at risk” for vector-borne transmissions. Each guidance describes that testing these donors is not recommended at this time and that guidance can be updated as new knowledge is gained.)

- Donor screening questions, by way of ZIKV infection risk addenda to Donor Risk Assessment Interview (DRAI) forms and flowcharts, were issued in mid-March by the Associations for membership to use when screening deceased organ, tissue, and eye donors, and for screening living donors of gestational tissue (aka “birth tissue”).

**Viral Persistence**

In general, it is known that ZIKV can persist in some tissue types from living donors (e.g., gametes, gestational tissue) when it is no longer detectable in the bloodstream. Transplantable tissue from deceased donors can include viable cells (e.g., osteoarticular allografts, fresh skin, cellular tissues from adipose and bone marrow), and there are neonate deceased donors of
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cardiac tissue where screening for risk of transmissible disease is performed of the birth mother. Because active virus has been detected in gestational tissues and in human breast milk this could increase risk for a deceased neonate donor as well as for a pediatric donor who was breast-fed recently. More research is needed to understand tissue involvement in congenitally acquired ZIKV infections (e.g., retina) and persistence in fluid such as vitreous humor. The organ donation and transplantation community could also benefit from more data to describe ZIKV risk to potential recipients. Refer to the Research section further below for more discussion.

Donor Screening
When donation professionals have accessed the CDC’s “Areas with Zika” webpage, there has been some confusion regarding which links to use to get information specific to the organ, tissue and eye donation communities that is useful for screening donors for risk associated with travel or residency. Association members should follow this sequence of links below that are specific to “blood and tissue safety intervention”:


See this part of the page and click on “More >”:

![Blood and Tissue Collection Community](image)

The linked page is titled “Areas At Risk For Locally Acquired Vector-borne Zika Cases” and it has been created specifically for the purpose of blood and tissue safety intervention. The webpage further describes “Areas of Active Transmission in the United States” and also lists foreign countries and US territories with reported local transmission of ZIKV.

To establish travel or residency risk within the US for organ, tissue, and eye donors, the affected areas and their “as of” dates listed next to them on this page should be used to establish risk of ZIKV infection. It was also clarified in our meeting that, when a “county” within the state is listed, the risk for organ, tissue and eye donation is intended to include the entire county. Do not use neighborhood boundaries on other maps. Be aware that other information on the CDC’s Zika webpages can describe different dates and specific risk areas within counties but that information is directed at different public health interventions such as advisements involving pregnancy, residents and workers, travelers, mosquito control, state and local health departments, etc. On the date of the call (Sept. 1st), the following two counties and respective dates were listed for the US mainland:
This web page was updated the day before our call, with additional information for the screening process when a potential donor has travelled outside of the contiguous US. See “Travel notice posting dates for countries and territories with reported local mosquito transmission of Zika virus” which includes a table with dates travel notifications were posted to identify when the country or territory was officially identified as a ZIKV affected area at risk. **These places and dates are expected to be used to establish travel or residency risk for donors of organs, tissues, and/or eyes.**

We strongly encourage our members to bookmark this page (http://www.cdc.gov/zika/areasatrisk.html) and sign up to automatically receive email updates to the page. See:

Association members should monitor this site and look for further improvements.

It was recommended that the date a living donor is screened for ZIKV risk should occur as close as possible to the date of donation.

**Testing**
There are no tests available for donor eligibility determination for HCT/P donors, and therefore there are no FDA recommendations in this area. Concerns from the Associations include the lack of availability of testing when testing a donor is desired, and the inability to use any ZIKV test results for living donors of cells/tissues who meet risk associated with residency or travel. The Associations described there are generally two types of ZIKV test kits, molecular tests such as rt-PCR and NAT, and serological tests for detecting IgM and IgG antibodies. The Associations
voiced these tests are “diagnostic” tests under authorization for Emergency Use and some are test kits submitted under an IND (Investigational New Drug) application. To monitor Emergency Use Authorizations (EUAs) for ZIKV test kits, see either FDA website:

http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCLegalRegulatoryandPolicyFramework/ucm182568.htm#zika

http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika

To date, there has been a lot of information provided to the public regarding ZIKV testing available for blood donation and for use by health departments but there seems to be little movement for test kits specifically designed and developed for testing of living or deceased donors of HCT/Ps. It was also described that availability of ZIKV testing is very limited, commercial testing labs are having difficulty with access to these test kits, and testing is not readily accessible nationwide to organ procurement organizations, tissue banks, or eye banks.

There was discussion of the regulatory pathway for development of ZIKV donor assays to receive a labeling claim for testing organ or tissue donors. It is possible for the manufacturers of some ZIKV diagnostic tests, or those currently under IND for testing blood donors, to move towards an IND application that includes screening donors of organs, tissues, or eyes. Test kits currently under IND are used for blood donor testing and they are molecular tests (rt-PCR or NAT), but these manufacturers’ interest in claims for use with specimens from donors other than blood donors has not been confirmed. The donation communities could lobby for their desire to pursue this interest by directly contacting the manufacturers of these test kits. Commercial testing laboratories could also be involved in this discussion.

For test kit manufacturers seeking a claim for their infectious disease test to use blood samples collected from deceased donors, refer to the relevant FDA/CBER guidance: Guidance for Industry: Recommendations for Obtaining a Labeling Claim for Communicable Disease Donor Screening Tests Using Cadaveric Blood Specimens from Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) 11/12/2004.

To promote test kit validation, some eye banks and tissue banks have expressed interest to provide blood samples from donors whose tissues are recovered only for research, and it is possible to also provide tissue from at-risk donors.

Testing tissue itself (i.e., examination using histology and immunohistochemical staining) can also be useful for inclusion in study protocols related to evaluating persistence in certain tissues.

If ZIKV testing of an organ, eye or tissue donor is pursued, determining how the test results will be used and shared is clearly important to establish. During the call, concern was also expressed by an end user of tissue that more discussion should occur regarding labeling tissue
allografts, e.g. with a warning to describe that risks associated with ZIKV remain unknown for tissue from a deceased donor.

**Research**
There is much interest in further research to establish relevance of ZIKV to organ, tissue and eye donation and transplantation. Collection of data is very important to organize. The FDA/CBER and CDC are very interested to know what research and data collection activities are occurring that originate outside of those which they have involvement. For example, a UT Southwestern study was described where 350 paired blood and vitreous samples have been collected and tested for ZIKV using a PCR test (all results have been nonreactive to date). Donor samples for this study are being collected from (mostly) the Dallas area, followed by New York, and from Puerto Rico.

It would be helpful if the Associations could coordinate efforts and engage with their members in this research. For example, perhaps donation organizations located in at-risk areas (i.e., Puerto Rico, the two counties in Florida) could be contacted to develop protocols that could be used to obtain blood samples and tissue samples for use in test kit validation and viral persistence studies for what are perceived to be at-risk tissues. The AATB, EBAA, and AOPO could coordinate such a project with membership and with test kit manufacturers. Funding for Zika research is being discussed in congress now. Further discussions with the FDA, CDC and others could help provide some funding to reduce the financial burden of these research efforts of our members.

**Commitment**
Ongoing communication among all stakeholders is important. We would like to thank all those who participated on this call. AOPO, EBAA and AATB will continue to work together and communicate with government agencies and members with updates. Recommendations are welcome.