

Considerations for Risk Associated with Zika Virus (ZIKV) Background Document

The following information will be used for a one-hour meeting on February 15, 2016 of AATB's Tissue Transmitted Diseases Advisory Group (TTDAG), a subgroup of the Physicians' Council.

Questions:

1. Should additional donor screening measures be taken and, if yes, what information should be collected?
2. Should donor criteria policy considerations be recommended or required for specific donor scenarios (i.e., for living donors, deceased donors, and/or specific tissue types)?

Donors included in AATB Standards & Accreditation:

1. Living donor (LD)
 - a. Reproductive (R) tissue donor (gametes: semen, oocyte) and "client depositor"
 - b. Delivery mother of birth tissue (BT) (this is a new tissue type and definition: birth tissue = gestational tissue donated at delivery of a living newborn. This includes placenta, Wharton's jelly, amniotic fluid, chorionic membrane, amniotic membrane, placental/chorionic disc, umbilical veins, and umbilical cord tissue)
 - c. Surgical Bone (SB) donors (e.g., femoral head; surgical bone for allogeneic use)
 - d. Autologous (A) tissue donors (e.g., bone skull flaps, parathyroid)
2. Deceased donor
 - a. Adult (>12 years old) – multiple tissue types (MS, OA, S, C, V, CT, DM)
 - b. Child (≤12 years old) – multiple tissue types (MS, OA, C)
 - c. Neonate [e.g., a donor of the heart for semilunar valves(C)]
 - i. Must screen the birth mother of a child donor who is ≤18 months of age or who was breast fed within the past 12 months
 - d. Non-transplant Anatomical Material (i.e., whole body or body parts; for use in education)

Tissue preservation methods (extent of processing varies; processing methods are not a consideration). Can this virus be preserved and be active?:

1. Fresh/refrigerated
2. Frozen
3. Cryopreserved
4. Lyophilized, dehydrated, or dessicated

Tissue recipient considerations:

1. Is it rare for a tissue recipient to be immune-compromised? It's not known whether the disease is more or less severe if transplanted to an immune-deficient person.
2. Is it rare for a tissue recipient to be pregnant? Microcephaly risk?
3. Adults, neonates and other children are recipients of cryopreserved (C) tissues. Virus preserved?

Depending on the outcome of discussion from this group, considerations for the Uniform Donor Risk Assessment Interview forms and/or flowcharts will be reviewed and discussed by the UDRAI Stakeholder Review Group comprised of representatives from organ, tissue and eye donation organizations/professionals as well as organ transplant societies and federal authorities. All 'recent' symptoms are covered in questioning except 'joint pain' and 'eye pain/conjunctivitis (pink eye).' The flowchart for travel hx can be updated.

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The following information has been collected but may not be all inclusive of available information to date:

- There are no commercial donor screening test kits; only a diagnostic test with limited availability through various health departments.
- Risk of ZIKV transmission via transplantation is not known.
 - After infection, ZIKV might be found in tissues and body fluids longer than in the bloodstream (i.e., semen/2-10 weeks)
- Risk of ZIKV transmission via breastfeeding is not known.
- Sexual transmission has been reported (semen; male to female)
 - Reproductive tissue donors of semen can be at risk for several weeks after ZIKV infection. Additionally, already approved semen donors who are actively donating require rescreening for communicable disease risks but the usual 6-month interval for screening donors may need to be shortened to every donation event.
 - From CDC Interim guidelines:
“Sexual transmission of Zika virus is possible, and is of particular concern during pregnancy. Current information about possible sexual transmission of Zika is based on reports of three cases. The first was probable sexual transmission of Zika virus from a man to a woman (6), in which sexual contact occurred a few days before the man’s symptom onset. The second is a case of sexual transmission currently under investigation (unpublished data, 2016, Dallas County Health and Human Services). The third is a single report of replication-competent Zika virus isolated from semen **at least 2 weeks and possibly up to 10 weeks** after illness onset; reverse transcriptase-polymerase chain reaction testing of blood plasma specimens collected at the same time as the semen specimens did not detect Zika virus (7). The man had no sexual contacts. Because no further testing was conducted, the duration of persistence of Zika virus in semen remains unknown.

In all three cases, the men developed symptomatic illness. **Whether infected men who never develop symptoms can transmit Zika virus to their sex partners is unknown.** Sexual transmission of Zika virus from infected women to their sex partners has not been reported.”
- Probable transmission via transfusion has been reported (Brazil); pathogen reduction technologies are available for platelets and plasma and, if used, can reduce risk.
- Viremia/Clinical symptoms (<http://www.cdc.gov/zika/symptoms/>)
 - The incubation period appears to be a few days to a week, and symptoms typically resolve within a week (viremia ≈ 14 days?). Zika virus usually remains in the blood of an infected person for about a week but it can be found longer in some people. Maximum length of viremia believed to be < 28 days. Serious illness and/or death appear to be very rare.
 - Zika infection typically causes a mild dengue-like illness with most common to include: fever (>100°F), a rash, and eye pain including conjunctivitis (pink eye). Myalgia (muscle or joint aches) and headache can also occur. People usually don’t get sick enough to go to the hospital, and they very rarely die of Zika.

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- Asymptomatic infection occurs in approximately 80% of Zika- (and dengue-) infected individuals. The opposite is true for chikungunya infection where the majority of infected individuals exhibit symptoms, including prolonged arthralgia or joint pain.
- Asymptomatic, viremic donors may be referred for tissue donation and can be screened and tissue recovered, processed, distributed, and transplanted
- There have been cases of Guillain-Barré syndrome reported in patients following suspected Zika virus infection. The relationship between Zika virus infection and Guillain-Barré syndrome is not known. Consider that this syndrome would develop at a point after the infection and the person may not be infectious.
- There remains a possible association between maternal Zika virus infection and adverse fetal outcomes, such as congenital microcephaly.
- US tissue banks distribute finished tissue allografts for transplant to other countries. International expectations for screening donors for risk associated with ZIKV should be honored or stricter policies by US tissue banks can be established.

Applicability to ??

- Eye Banks,
- Tissue Banks,
- Organ Procurement Organizations,
- Reproductive Tissue Banks,
- *In vitro* Fertilization Clinics,
- Non-transplant Anatomical Donation Organizations,
- Bioskills Laboratories, and
- Biospecimen Repositories.

Table of ZIKV Guidance/Recommendations for Donation (to date)

Date	Entity	Issued	Asymptomatic Donor	Symptomatic Donor	Other
2-1-16	AABB (for blood and blood component donors)	Recommendations via Bulletin	Travel; Self-deferral; 28 days to country currently reported as having endemic areas: Mexico, the Caribbean, or Central or South America	Use of the current donor history questionnaire will identify and disqualify symptomatic donors; donor call back to blood center encouraged if demonstrate at least 2 related symptoms post donation	Screening for malaria risk overlaps in some areas
2-4-	HRSA (for	Guidance via	Travel hx is a focus;	Symptomatic	Risk:

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16	organ donation and transplant professional s)	website & other announcements to stakeholders	use -- http://www.cdc.gov/zika/geo/	donors are a focus (although only 20% exhibit Sxs); a living donor with ZIKV should be deferred	benefit evaluation; post transplant recipient travel advisory
2-5-16	CDC	Interim Guidelines for Prevention of Sexual Transmission of Zika Virus — United States, 2016	Travel hx is focus	Recommend to abstain	Differs slightly for men with pregnant sexual partner versus men with non-pregnant sexual partner
2-9-16	Health Canada	Via email Notice to regulated stakeholders; provides guidance, recommendations	Travel hx focus; communicate if organ donor traveled to Zika affected area in past 21 days (living donor postponement for 21 days); living donor of HPCs postponement if past 21 days; Cord blood donors should not be undertaken if travel occurred in past 21 days; recommended that tissue banks not undertake donation from donors that have returned from Zika affected area in past 21 days; Semen donor deferral should occur if past 28 days.		

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2-2-16	<p>Joint UKBTS Professional Advisory Committee (JPAC);</p> <p>See Change Notification No. 14 - 2016 for Tropical Viruses</p>	<p>Issued by the Human Tissue Authority as: Guidance for HTA-licensed organisations on Zika Virus</p>	<p>Obligatory:</p> <p>Must not donate if:</p> <p>c) In other cases it is less than four weeks from a donor's return from a Tropical Virus Risk endemic area.</p>	<p>Obligatory:</p> <p>Must not donate if:</p> <p>a) It is less than six months from a donor's return from a Tropical Virus Risk endemic area and the donor has been diagnosed with chikungunya, dengue or zika virus infection whilst there or following their return to the UK.</p> <p>b) It is less than six months from a donor's return from a Tropical Virus Risk endemic area and the donor has either had a history of symptoms suggestive of chikungunya, dengue or zika virus infection whilst there or following their return to the UK.</p>	<p>Discretionary:</p> <p>All donors may be accepted six months after their return from an affected area or resolution of symptoms. This may be reduced to four weeks, if they have had neither symptoms nor evidence of infection.</p>
2-9-16	<p>US FDA/CBER</p>	<p>(notice of plan to issue guidance for blood donation and for HCT/Ps) See AATB Bulletin</p>			<p>Both are described as "Guidance" versus "Draft Guidance" or "Final Guidance" so that determination may not have been made at</p>

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					<p>this time. When any guidance is issued, comments to CBER may be submitted. How soon guidance will be issued is not divulged but this topic can be expected to be a priority.</p>
2-10-16	<p>NHS Blood And Transplant Organ Donation and Transplantation Zika Virus and Transplantation of Solid Organs From Deceased Donors</p>	<p>Issued by the Human Tissue Authority as: Guidance for HTA-licensed organisations on Zika Virus</p>	<p>Travel hx +; “Donor characterisation includes a full recent travel history; when the potential donor has travelled to Latin America or other affected areas, the SNOD should enquire whether the donor had been bitten by mosquitos and about any associated illness: this should be documented on the Donor Characterisation Form”</p>		<p>Risk:benefit</p>
2-21-16	<p>European CDC; Zika virus disease epidemic; 21 January 2016</p>	<p>Recommendations ; rec’d verbal report they are working on recommendations for medical products derived</p>	<p>Travel hx</p>		<p>“Tissue establishments for assisted reproduction may foresee a</p>

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		from SoHO (substances of human origin)			need to defer potential semen donors for 28 days after returning from affected areas as a viable virus was detected in semen more than two weeks after recovery from an illness consistent with Zika virus infection."
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There are numerous references. Here are a few:

<http://www.cdc.gov/zika/index.html>

http://www.cdc.gov/mmwr/zika_reports.html

- [Zika Virus Spreads to New Areas — Region of the Americas, May 2015–January 2016](#)
- [Possible Association Between Zika Virus Infection and Microcephaly — Brazil, 2015](#)
- [Interim Guidelines for the Evaluation and Testing of Infants with Possible Congenital Zika Virus Infection — United States, 2016](#)
- [Local Transmission of Zika Virus — Puerto Rico, November 23, 2015–January 28, 2016](#)
FEBRUARY 12, 2016

On December 31, 2015, the Puerto Rico Department of Health reported the first locally acquired case of Zika virus disease in a jurisdiction of the United States in a patient from southeastern Puerto Rico. Zika virus is expected to continue to spread throughout the territory, and the 3.5 million residents of Puerto Rico, including approximately 43,000 pregnant women per year, are at risk for Zika virus infection.

- [Notes from the Field: Evidence of Zika Virus Infection in Brain and Placental Tissues from Two Congenitally Infected Newborns and Two Fetal Losses — Brazil, 2015](#)
FEBRUARY 10, 2016

A surge in the number of children born with microcephaly has been noted in regions of

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Brazil with a high prevalence of suspected Zika virus disease. This report describes evidence of a link between Zika virus infection and microcephaly and fetal demise through detection of viral RNA and antigens in brain tissues from infants with microcephaly and placental tissues from early miscarriages.