

Relevant Communicable Diseases in HCT/Ps

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Relevant Communicable Diseases in HCT/Ps

- ZIKA Virus
 - HCT/Ps derived from peripheral blood, bone marrow
 - Cord blood
- West Nile Virus
- Other arthropod-borne viruses
 - Dengue, Chikungunya
 - Similar challenges: asymptomatic viremia; likely transmissible; lack of approved test
 - Various geographic distributions

ZIKA Virus

- RNA flavivirus transmitted by various *Aedes* species mosquitoes
- Clinical Disease:
 - Associated with neurologic manifestations; Guillain-Barré syndrome
 - Associated with birth defects [microcephaly] in newborns
 - 80% of infected individuals are asymptomatic
- Viremia – 10 days or more after symptoms
 - Also in saliva, urine, breast milk, semen [62 d; 10 weeks]
- Transmission:
 - Sexual transmission [male to female]
 - Transfusion
 - Gestational tissues: amniotic membrane/fluid; placenta; cord blood
- Relevant communicable disease agent under 21 CFR 1271.3
[GUIDANCE FOR INDUSTRY, March 2016]

HCT/P Donor Eligibility

- March 2016 HCT/P Guidance: Donor ineligible if
 - Medical diagnosis of ZIKV infection – 6 months
 - Residence in or travel to area active ZIKV transmission
 - Sex in past 6 months with male with either risk factor
- If not possible to determine [3 above] = incomplete
- Confusion exists regarding how to label product if
 - ZIKV assessment “incomplete”
 - Ineligible for another reason: [lived in Europe or UK; +HBc]

HCT/P Donor Eligibility

- Under the unified tiered approach to HCT/P regulation, all HCT/Ps are regulated together
- Different HCT/Ps may have different communicable disease risk based on source of cells and disease agent
- HPC, Apheresis products from normal volunteer donors similar to other apheresis-derived blood components:
 - Low risk donor population
 - Method of collection
 - Actual tissue components present in end product

HCT/P Donor Eligibility

- August 2016 Guidance allows testing of volunteer blood donors with investigational test for ZIKA virus
- Such testing not permitted for HPC, Apheresis donors due to all HCT/Ps regulated together
 - Result is more ineligible donors [6 month deferral/ ineligibility]
 - Decisions based upon presumed risk and clinical need
- Is there consideration to treat the apheresis-derived HCT/Ps more like apheresis platelets for this assessment of eligibility?

ZIKA Virus / Cord Blood

- Strong association between risk of microcephaly and first trimester ZIKV infection; negligible in second and third trimester
- Recent studies – association between ZIKV infection in any trimester and adverse pregnancy outcome
- Little is known about effects of mild or asymptomatic ZIKV infections at any time, or of infections in early pregnancy - women may be unaware of pregnancy

ZIKA Virus / Cord Blood

- Challenge to CBB:
 - Can exclude clearly affected infants or symptomatic mothers
 - Residence in “area of active transmission” at any time 6 months pre-pregnancy through entire pregnancy make donor ineligible?
- Cord blood banking in Latin America is rapidly growing
- Snapshot of accredited cord blood banks:

| | FLORIDA | BRAZIL | SINGAPORE | PANAMA |
|--------------|---------|--------|-----------|--------|
| FACT-NetCord | 3 | 1 | 3 | |
| AABB | 4 | | 3 | 1 |

ZIKA Virus / Cord Blood

- CBB affiliated with NMDP also report potential issues with decreased collections and bankable units
 - July 2016 survey; 17 CBB respondents
 - Various methods of regulatory compliance
 - Negative impact on the national inventory of CB units
- Is there a potential to utilize a test under IND for either the maternal samples, the stored maternal samples, or stored cord blood unit samples?
 - Selected products with travel history / residence only [no symptomatic disease]

West Nile Virus

West Nile Virus

- Endemic in the United States
 - First recognized in US in 1999
 - Outbreaks of disease recognized annually
 - Mosquitoes that transmit are present in US
 - Human to human transmission well documented
 - Asymptomatic illnesses
 - Universal donor screening available and used
- On-going research:
 - Genetic variability and mutation
 - Impact on virulence
 - Variants escape detection; need to maintain relevant reagents
 - Potential approaches to increase sensitivity of current assays

West Nile Virus

- West Nile Virus is a relevant communicable disease
 - HCT/P donors screened / tested within 30 days of collection
 - Day of collection testing eliminated by registries
 - Probably most valuable test, but not useful – products already infused
- FDA Guidance [2007; referenced 9/2016]

“...persons who have tested positive in the preceding 120 days should be considered ineligible...”
- FDA Guidance [09/2016]

“Any HCT/P donor with a negative test should be considered to be negative for WNV for eligibility determination.”

West Nile Virus

- Is there specific guidance related to time frame required since last positive test to call a donor “eligible”?
- How long is the period of ineligibility after a positive test?

Thank you