U.S. FOOD & DRUG ADMINISTRATION

Infectious Disease Screening and Testing for Donors of HCT/Ps

FDA-ISCT Liaison Meeting

October 19, 2016

Overview

- Relevant Communicable Disease Agents and Diseases (RCDADs)
- WNV screening and testing
- ZIKV screening and testing

RELEVANT COMMUNICABLE DISEASE AGENTS AND DISEASES (RCDADS)

Donor Eligibility (DE) Determination

(§ 1271.50)

- A donor eligibility (DE) determination is based on screening and testing of HCT/P donors for ***relevant communicable diseases or disease agents (RCDADs)***

http://divinebehavioralservicesinc.com/wp-content/uploads/2014/07/eligibility.jpg

- A DE determination is required for all donors of cells and tissues (HCT/Ps), except as provided in § 1271.90
- An HCT/P must not be implanted, transplanted, infused, or transferred until the donor has been determined to be eligible, except as provided in §§ 1271.60(d), 1271.65(b), and 1271.90

When is a Donor Eligible?

(§ 1271.50)

- Donor screening (described in § 1271.75) must indicate that the donor:
  - Is free from risk factors for, and clinical evidence of, infection due to RCDADs; and
  - Is free from communicable disease risks associated with xenotransplantation.
- Donor testing results for relevant communicable disease agents (described in § 1271.80 and § 1271.85) must be negative or nonreactive, except as provided in § 1271.80(d)(1).

Incomplete DE Determination

- § 1271.60(d) – Use in cases of urgent medical need
  - Documented urgent medical need
    - No comparable HCT/P is available, and the recipient is likely to suffer death or serious morbidity without the HCT/P (§ 1271.3(u))
  - Special labeling and physician notification requirements apply
  - You must complete the DE determination during or after the use of the HCT/P, and you must inform the physician of the results of the determination

Exceptions in 21 CFR Part 1271

- Use of HCT/Ps from an ineligible donor (§ 1271.65(b)):
  - Allogeneic use in a 1st or 2nd degree blood relative
  - Urgent medical need (§ 1271.3(u))
  - ★ Special labeling & notification requirements (§ 1271.65(b)(2)-(3))
- DE determination not required (§ 1271.90(a)):
  - Cells and tissue for autologous use
  - ★ Special labeling requirements apply (§ 1271.90(c))

What is an RCDAD?

§ 1271.3(r)(2)

(i) May be a risk of transmission by an HCT/P because the disease agent or disease:

(A) Is potentially transmissible by an HCT/P, and

(B) Either of the following applies:

(1) The disease agent or disease has sufficient incidence and/or prevalence to affect the potential donor population, or

(2) The disease agent or disease may have been released accidentally or intentionally in a manner that could place potential donors at risk.

(ii) Could be fatal or life-threatening, could result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of body function or permanent damage to a body structure; and

(iii) Appropriate screening measures have been developed and/or an appropriate screening test for donor specimens has been licensed, cleared, or approved for such use by FDA and is available.

What are the current RCDADs?

(§ 1271.3(r) & DE Guidance III.D.)

For all cells and tissues:

- Human immunodeficiency virus, types 1 and 2 (HIV-1/2)
- Hepatitis B virus (HBV)
- Hepatitis C virus (HCV)
- Human transmissible spongiform encephalopathy (hTSE), including Creutzfeldt-Jakob disease (CJD)
- *Treponema pallidum* (agent that causes syphilis)
- Vaccinia*
- Sepsis*
- West Nile virus (WNV)*
- Zika virus (ZIKV)**

For viable, leukocyte-rich cells and tissues:

- Human T-lymphotropic virus, type I and type II (HTLV-I/II)

For reproductive cells and tissues:

- *Chlamydia trachomatis* (CT)
- *Neisseria gonorrhea* (NG)

* Additional information is provided in section III.D. of the 2007 DE Guidance

** Additional information is provided in the March 2016 ZIKV Guidance

WNV SCREENING AND TESTING

WNV Screening

- 2007 Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (Donor Eligibility/DE Guidance)
- Section III.D. – Identified WNV as an RCDAD
- Section IV.E. – Risk Factors or Conditions
- Section IV.F. – Clinical Evidence

http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/UCM091345.pdf

WNV Testing

Use of Nucleic Acid Tests to Reduce the Risk of Transmission of West Nile Virus from Living Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)

Guidance for Industry

- Final guidance posted September 12, 2016
- Implementation within 6 months (March 12, 2017)
- Recommendations apply to all HCT/Ps recovered on or after the implementation date

http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/UCM372084.pdf

WNV Testing Recommendations

- Living HCT/P donors should be tested for WNV using a licensed NAT donor screening test
  - U.S. (50 states + D.C.): June 1st – October 31st
  - Other locations: year-round
- Any HCT/P donor whose specimen tests negative (or non-reactive) for WNV NAT should be considered to be negative (or non-reactive) for WNV for purposes of determining donor eligibility

Timing of Testing

- § 1271.80(b) – You must collect the donor specimen for testing at the time of recovery of cells or tissue from the donor; or up to 7 days before or after recovery, except:
  - For donors of peripheral blood stem/progenitor cells, bone marrow (if not excepted under §1271.3(d)(4)), or oocytes, you may collect the donor specimen for testing up to 30 days before recovery
- WNV Guidance – "Because of the increased susceptibility to infection in these immunosuppressed patients, and the potential for donors to contract WNV infection between DE determination and HPC recovery during certain months, medical practitioners may wish to order supplemental testing of the donor at the time of HPC recovery. This additional "day of" test is not required for determining donor eligibility, but may be a useful medical practice in post-HPC transplant care."

ZIKV SCREENING AND TESTING

ZIKV Screening

Donor Screening Recommendations to Reduce the Risk of Transmission of Zika Virus by Human Cells, Tissues, and Cellular and Tissue-Based Products

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Guidance for Industry

This guidance is for immediate implementation.

- Published online March 1st, 2016
- Implemented within 4 weeks after publication of the guidance
- Recommendations apply to all HCT/Ps recovered on or after the implementation date

★ Identified ZIKV as a RCDAD for all donors of HCT/Ps

Recommendations for living donors

- Living donors of HCT/Ps should be considered ineligible if they have any of the following risk factors:
  1. Medical diagnosis of ZIKV infection in the past 6 months.
  2. Residence in, or travel to, an area with active ZIKV transmission within the past 6 months.
  3. Sex within the past 6 months with a male who is known to have either of the risk factors listed in items 1 or 2, above.

Recommendations for living donors

- Additionally, donors of umbilical cord blood, placenta, or other gestational tissues should be considered ineligible if the birth mother who seeks to donate gestational tissues has any of the following risk factors:
  4. Medical diagnosis of ZIKV infection at any point during that pregnancy.
  5. Residence in, or travel to, an area with active ZIKV transmission at any point during that pregnancy.
  6. Sex at any point during that pregnancy with a male who is known to have either of the risk factors listed in items 1 or 2, above (on previous slide).

Areas with active ZIKV transmission

- From the guidance: an area with "active ZIKV transmission" is an area included on the CDC website listing of countries and U.S. states and territories with local vector-borne (i.e., mosquito-acquired) transmission of ZIKV: http://www.cdc.gov/zika/geo/index.html
- Link for "Blood and Tissue Collection Community" (http://www.cdc.gov/zika/areasatrisk.html)
- Contains a listing of the active areas in the U.S. and their effective date
- Also contains a list of other countries considered to be active and the date those notifications were posted

Areas with active ZIKV transmission

Areas At Risk For Locally Acquired Vector-borne Zika Cases

Language: English

Zika virus information for the blood and tissue collection community

CDC is working with state health departments and blood and tissue collection organizations to help ensure the safety of our blood and tissue supply and reduce the risk of Zika virus transmission through blood transfusions and tissue transplants. Zika virus disease is a nationally notifiable condition. Cases are reported to CDC by state and local health departments using standard case definitions.

Areas of Active Transmission in the United States

To protect the US blood and tissue supply, CDC in collaboration with the US Food and Drug Administration (FDA) defines areas of active Zika virus transmission as having two or more locally acquired cases of Zika virus infection within 45 days. These defined areas of risk can be different from areas for which CDC has issued travel guidance because of concerns about potential risk for blood and tissue safety.

The following are areas of active transmission of Zika virus in the continental United States for the purpose of blood and tissue safety intervention:

- Miami-Dade County, Florida - As of July 29, 2016
  Florida Department of Health Confirms Local Transmission – click to view announcement
- Palm Beach County, Florida - As of August 24, 2016
  Florida Department of Health Zika Update - click to view announcement

Travel notice posting dates for countries and territories with reported local mosquito transmission of Zika virus.

Country or Territory	Date Travel Notification Posted
American Samoa	2/1/2016
Anguilla	6/29/2016
Antigua & Barbuda	8/3/2016

http://www.cdc.gov/zika/areasatrisk.html

Donor Testing for ZIKV

- Currently, FDA does not provide any recommendations on HCT/P donor testing
- If testing is performed, you must consider the results of the test when you make a DE determination
  - A positive test result must be considered a risk factor for ZIKV infection, even if an investigational test was used
  - However, any negative or nonreactive test results obtained would not override any risk factors identified in the March 2016 ZIKV guidance
- FDA is committed to working with U.S. government partners and manufacturers interested in developing tests for HCT/P donors
- FDA will consider appropriate recommendations for use of such tests upon their availability

★ Exceptions in §1271.65(b) (use from an ineligible donor) and § 1271.90 (no DE required) may apply.

Contact Information

Manufacturers Assistance
Industry.Biologics@fda.hhs.gov

Consumer Questions About Products
ocod@fda.hhs.gov

Regulatory Questions
CBEROCTGTRMS@fda.hhs.gov

http://www.fda.gov/BiologicsBloodVaccines/default.htm