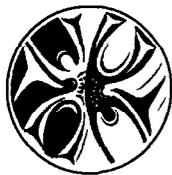


NORTHWEST



TISSUE CENTER

921 Terry Avenue
Seattle, WA 98104

(206) 292-1879

August 23, 2004

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

RE: Docket No. 2004D-0193

Northwest Tissue Center appreciates the opportunity to comment on the May 25, 2004 Draft "Guidance for Industry: Eligibility Determination for Donor of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)".

Northwest Tissue Center is a nonprofit, regional tissue bank that recovers, processes, stores and distributes human musculoskeletal, skin and cardiovascular tissue for transplant. The Tissue Center is a division of a major community blood center, Puget Sound Blood Center. We provide approximately 550 tissue grafts for transplant per month, primarily to hospitals in our recovery area of Washington, northern Idaho and Montana.

We offer the following comments.

DONOR SCREENING

Section III.C.2 in the guidance lists other records that meet the definition of relevant medical records. Police records are listed as an example of information pertaining to risk factors for relevant communicable disease. Very often, tissue establishments cannot obtain access to police records. Even next of kin may be denied access. Our medical/social history questionnaire asks whether the potential donor was ever an inmate of a jail or other correctional facility, affiliated with a gang, or used street drugs. Further information is sought to determine donor eligibility if any of these questions are answered "yes".

Recommendation

Delete "police records".

Section III.C lists the physical examination of a living donor as part of the relevant medical records that must be reviewed when screening a potential donor. This physical examination of a living HCT/P donor is significantly different from the physical examination of a blood donor. According to the

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- University of Washington
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guidance document, the purpose of the physical exam is to assess for physical signs of a relevant communicable disease and for signs suggestive of any risk factor for such disease. The guidance document in section III.G.2 then lists 14 examples of physical evidence to look for. To require an exam of a living donor, particularly for physical evidence of risk of sexually transmitted disease is intrusive and will reduce donation of cord blood and hematopoietic stem cells. A physical exam this exhaustive and intrusive is not required for blood donors, yet the relevant communicable disease concerns are the same.

Recommendation

Delete the requirement for physical examination for volunteer, unpaid living donors.

In section III.E.16 the guidance lists risk factors to look for when screening a donor and recommends that we determine to be ineligible any potential donor who exhibits any of the listed conditions or behaviors. Fever with simultaneous headache is listed as a separate risk factor for relevant communicable diseases, yet in section F.5, fever and headache is listed as clinical evidence for West Nile virus infection. This section also notes that signs and symptoms of WNV can be nonspecific, so the clinical signs and symptoms must be considered in light of other information obtained about the donor in making an eligibility determination.

Recommendation

Delete fever with simultaneous headache as a risk factor for which donors **must** be determined ineligible. Instead allow establishments to consider fever with headache with other information obtained about the donor when determining eligibility.

In section III.E.9 of the guidance, an example of close contact relating to viral hepatitis is given as living in the same household, where sharing of kitchen and bathroom facilities occurs regularly. In section III.E.20.iv, intimate contact of a xenotransplantation product recipient is defined as a person who has engaged in activities that could result in intimate exchange of body fluids, including blood or saliva. Examples of

intimate contact are then listed. This is a more thorough explanation of contact that may transmit disease.

Recommendation

Replace "close contact" in section III.E.9 with "intimate contact" as defined in section III.E.20.iv.

Section III.F.7 of the guidance states that sepsis includes, but is not limited to, bacteremia, septicemia, sepsis syndrome, systemic infection, or septic shock. The guidance goes on to state that if any of the above conditions are specifically noted in the medical records, the donor is ineligible.

Recommendation

Pre-mortem blood cultures may be falsely positive due to improper preparation of the skin. We recommend that blood cultures positive for normal skin flora **not** be considered evidence of bacteremia. In addition, we suggest that an **admit diagnosis** of rule out sepsis, bacteremia, septicemia, sepsis syndrome, systemic infection or septic shock not automatically cause the donor to be ineligible. Review of the relevant medical records for clinical evidence of sepsis would be indicated.

Section III.G.2 lists examples of physical evidence to look for when performing a physical assessment of a donor. One example is physical evidence of risk or sexually transmitted diseases such as herpes simplex.

Recommendation

Clarify whether the presence of genital herpes simplex discovered during physical assessment requires deferral of the donor.

DONOR TESTING

In section V.B.1 of the draft guidance, donors of viable, leukocyte-rich cells or tissue must be tested for anti-CMV. In addition, a procedure must be established governing the release of cells or tissue from donors whose specimens test reactive for CMV and limiting the use of such cells/tissue based on the CMV status of the recipient. Requiring tissue establishments to limit the release of CMV positive HCT/Ps is inappropriate.

Recommendation

The recipient's physician should make this determination based on current information on the potential for disease transmission from the type of HCT/P to be infused/implanted. Blood donors are tested for anti-CMV, yet blood establishments are not required to limit the use of CMV positive units.

The guidance states in section IV.E "you must collect the donor specimen for testing at the same time as cells or tissue are recovered from the donor, or, this is not feasible, within seven days before or after the recovery of cells or tissue."

Recommendation

We recommend deletion of "if this is not feasible". A pre-mortem sample is preferable both for sample quality and to eliminate the risk of hemodilution.

Sections IV.F.1 and IV.F.2 of the guidance outlines circumstances under which transfusions or infusions may dilute plasma, making test results unreliable. It is not clear from reading these sections that if there is a risk of hemodilution, a pre-transfusions/infusion specimen must be tested or an appropriate algorithm applied.

Recommendation

Clarify sections IV.F.1 and IV.F.2 and state that if there is a risk of plasma dilution, a pre-transfusion/infusion specimen must be tested or an appropriate algorithm applied.

We also recommend the following addition to the sentence "Under the regulations, a risk of plasma dilution sufficient that test results may be affected occurs in a donor **with blood loss** over twelve years of age in the following situations:" In addition, we suggest clarifying section IV.F.1.c. We recommend:

- c. The donor received more than 2000 milliliters total of any combination of blood and colloid within the past 48 hours and crystalloid within the past hour as outlined in paragraphs (a) and (b) in section IV.F.1.

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Section V.A.3 states that "if the maternal sample is reactive for HBsAg, you must not collect the cord blood." Our cord blood bank collects the maternal sample at the time of donation. In order to preserve the viability of the cord blood, the unit is processed and store in quarantine before infectious disease testing is completed.

Recommendation

Revise the sentence to "If the maternal sample is reactive for HBsAg, you must not make the cord blood unit available for use".

Section V.B.2 lists examples of viable, leukocyte-rich cells or tissue.

Recommendation

Explain how this categorization of tissues that require testing for HTLV I/II and CMV was made in order to allow classification of other tissues in the future.

Thank you for your consideration of our concerns.

Questions regarding these comments may be directed to Dawn M. Johnson, QA Supervisor, dawnjo@psbc.org or 206-292-2318.

Sincerely,



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Quality Assurance Supervisor

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