

TAB 2

Wilma G. Johnson,
Acting Associate Director for Policy Planning
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and Prevention (CDC).

[FR Doc. 97-19893 Filed 7-28-97; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 93N-0453]

Guidance for Screening and Testing of Donors of Human Tissue Intended for Transplantation; Availability

AGENCY: Food and Drug Administration,
HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance document entitled "Guidance for Screening and Testing of Donors of Human Tissue Intended for Transplantation." The purpose of the guidance document is to assist facilities involved in recovery, infectious disease testing, screening, processing, storing, or distributing human tissue intended for transplantation. The guidance document provides information on procedures and practices for donor screening and testing. FDA prepared the guidance document after receiving public input. The topics included in the guidance document were contained in a draft document "Screening and Testing of Donors of Human Tissue Intended for Transplantation" made available for discussion at a public workshop on human tissue held on June 20 and 21, 1995.

DATES: Written comments may be submitted at any time.

ADDRESSES: Submit written requests for single copies of the "Guidance for Screening and Testing of Donors of Human Tissue Intended for Transplantation" to the Office of Communication, Training, and Manufacturers Assistance (HFM-40), Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448. Send one self-addressed adhesive label to assist that office in processing your requests. The document may also be obtained by mail by calling the CBER Voice Information System at 1-800-835-4709 or 301-827-1800, or by fax by calling the FAX Information System at 1-888-CBER-FAX or 301-827-3844.

Persons with access to the Internet may obtain the document using File

Transfer Protocol (FTP), the World Wide Web (WWW), or bounce-back e-mail. For FTP access, connect to CBER at "ftp://ftp.fda.gov/cber/". For WWW access, connect to CBER at "http://www.fda.gov/cber/publications.htm". To receive the document by bounce-back e-mail, send a message to "tissue2@a1.cber.fda.gov".

Submit written comments on the guidance document to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857. Two copies of any comments are to be submitted, except individuals may submit one copy. Requests and comments are to be identified with the docket number found in brackets in the heading of this document. The guidance document and received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

FOR FURTHER INFORMATION CONTACT: Paula S. McKeever, Center for Biologics Evaluation and Research (HFM-630), Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852-1448, 301-594-3074.

SUPPLEMENTARY INFORMATION: In the Federal Register of December 14, 1993 (58 FR 65514), FDA published an interim rule on human tissue intended for transplantation to reduce the risk of transmission of human immunodeficiency virus (HIV) and hepatitis through human tissue intended for transplantation. The interim rule was issued under the authority of sections 215, 311, 361, and 368 of the Public Health Service Act (42 U.S.C. 216, 243, 264, 271) because of an immediate need to protect the public health from the transmission of communicable diseases through the transplantation of human tissue. The interim rule established requirements for the testing of donors of human tissue for HIV Type 1 virus, HIV Type 2 virus, hepatitis B virus, and hepatitis C virus. The interim rule also required that donors be screened for medical history, including behaviors that carry an increased risk of exposure to these viruses (behavioral and high risk information) and for signs and symptoms of infection with these viruses.

In the Federal Register of June 20, 1995 (60 FR 32128), FDA announced the availability for public comment of a draft document entitled "Screening and Testing of Donors of Human Tissue Intended for Transplantation." The availability of the draft document coincided with the workshop on Human

Tissue for Transplantation and Human Reproductive Tissue: Scientific and Regulatory Issues and Perspectives which was held on June 20 and 21, 1995. Comments received on this draft document and the issues discussed at the workshop were considered in the development of the guidance document being announced in this notice.

This guidance document provides general information on the following procedures: (1) Determination of donor suitability, (2) evaluation of screening test performance, (3) application of a plasma dilution algorithm to determine the acceptability of the blood specimen used for testing, (4) screening for behavioral and high risk information, and (5) evaluation of clinical and physical evidence of infection with HIV or hepatitis.

As technical standards change over time due to an increased understanding of infectious diseases and improved technology for testing, FDA may issue future guidance to help ensure that the regulatory process reflects the current level of knowledge. The recommendations in this guidance document should be considered in addition to voluntary standards developed and used by human tissue organizations.

This document is not being issued under the authority of 21 CFR 10.90(b) because FDA is in the process of revising this section. As with other guidance documents, FDA does not intend this document to be all-inclusive. This document does not bind the agency and does not create or confer any rights, privileges, or benefits for or on any person. Tissue facilities may follow the guidance document or may choose to use alternative procedures not provided in the guidance document. If a tissue facility chooses to use alternative procedures, the facility may wish to discuss the matter further with the agency to prevent expenditure of resources on activities that may be unacceptable to FDA.

Interested persons may, at any time, submit written comments to the Dockets Management Branch (address above) regarding this guidance document. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Continued comment by the human tissue industry is encouraged, and comments will be continuously accepted by the Dockets Management Branch.

FDA periodically will review written comments on the guidance document to

determine whether future revisions to the guidance document are warranted.

Dated: January 21, 1997.

William B. Schultz,

Deputy Commissioner for Policy.

[FR Doc. 97-19821 Filed 7-28-97; 8:45 am]

BILLING CODE 4160-01-F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Health Care Financing Administration

[Document Identifier: HCFA-P-15A]

Agency Information Collection Activities: Proposed Collection; Comment Request

AGENCY: Health Care Financing Administration.

In compliance with the requirement of section 3506(c)(2)(A) of the Paperwork Reduction Act of 1995, the Health Care Financing Administration (HCFA), Department of Health and Human Services, is publishing the following summaries of proposed collections for public comment. Interested persons are invited to send comments regarding this burden estimate or any other aspect of this collection of information, including any of the following subjects: (1) The necessity and utility of the proposed information collection for the proper performance of the agency's functions; (2) the accuracy of the estimated burden; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) the use of automated collection techniques or other forms of information technology to minimize the information collection burden.

1. *Type of Information Collection Request:* Extension of a currently approved collection; *Title of Information Collection:* Medicare Current Beneficiary Survey (MCBS) Rounds: 20-32; *Form No.:* HCFA-P-15A (OMB# 0938-0568); *Use:* The MCBS is a continuous, multipurpose survey of a nationally representative sample of aged and disabled persons enrolled in Medicare. The survey provides a comprehensive source of information on beneficiary characteristics, needs, utilization, and satisfaction with Medicare-related activities; *Frequency:* Other (3 times a year per respondent); *Affected Public:* Individuals and households; *Number of Respondents:* 16,000; *Total Annual Responses:* 48,000; *Total Annual Hours:* 48,000.

To obtain copies of the supporting statement and any related forms for the proposed paperwork collections

referenced above, E-mail your request, including your address and phone number, to Paperwork@hcfa.gov, or call the Reports Clearance Office on (410) 786-1326. Written comments and recommendations for the proposed information collections must be mailed within 60 days of this notice directly to the HCFA Paperwork Clearance Officer designated at the following address: HCFA, Office of Information Services, Information Technology Investment Management Group, Division of HCFA Enterprise Standards Attention: John Rudolph, Room C2-26-17, 7500 Security Boulevard, Baltimore, Maryland 21244-1850.

Dated: July 9, 1997.

John P. Burke III,

HCFA Reports Clearance Officer, Division of HCFA Enterprise Standards, Health Care Financing Administration.

[FR Doc. 97-19924 Filed 7-28-97; 8:45 am]

BILLING CODE 4120-03-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Institute; Notice of Closed Meeting

Pursuant to Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following National Cancer Institute Special Emphasis Panel (SEP) meeting:

Name of SEP: Genetic Epidemiology of Lung Cancer I and II.

Date: August 4, 1997.

Time: 11:00 a.m. to 12:30 p.m.

Place: Teleconference, National Cancer Institute, Executive Plaza North, Room 635G, 6130, Executive Boulevard, Bethesda, MD 20892.

Contact Person: Sally A. Mulhern, Ph.D., Scientific Review Administrator, National Cancer Institute, NIH, Executive Plaza North, Room 635G, 6130 Executive Boulevard, MSC 7410, Bethesda, MD 20892-7410, Telephone: 301/496-7413.

Purpose/Agenda: To evaluate and review grant applications.

This notice is being published less than 15 days prior to the meeting due to the urgent need to meet timing limitations imposed by the review and funding cycle.

The meeting will be closed in accordance with the provisions set forth in secs. 552b(c)(4) and 552b(c)(6), Title 5 U.S.C. Applications and the discussions could reveal confidential trade secrets or commercial property such as patentable material and personal information concerning individuals associated with the applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

(Catalog of Federal Domestic Assistance Program Numbers: 93.393, Cancer Cause and

Prevention Research; 93.394, Cancer Detection and Diagnosis Research; 93.395, Cancer Treatment Research; 93.396, Cancer Biology Research; 93.397, Cancer Centers Support; 93.398, Cancer Research Manpower; 93.399, Cancer Control)

Dated: July 22, 1997.

LaVerne Y. Stringfield,

Committee Management Officer, NIH.

[FR Doc. 97-19848 Filed 7-28-97; 8:45 am]

BILLING CODE 4140-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Cancer Institute; Notice of Closed Meetings

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following National Cancer Institute Special Emphasis Panel (SEP) meetings:

Name of SEP: Pivotal Clinical Trials for Chemoprevention Agent Development.

Date: August 18-19, 1997.

Time: August 18—7:00 a.m.—5:00 p.m.;

August 19—8:00 a.m.—5:00 p.m.

Place: Double Tree Hotel, 1750 Rockville Pike, Rockville, Md 20852.

Contact Person: Ray Bramhall, Ph.D., Scientific Review Administrator, National Cancer Institute, NIH, Executive Plaza North, Room 636, 6130 Executive Boulevard, MSC 7410, Bethesda, Md 20892-7410, Telephone: 301/496-3428.

Purpose/Agenda: To evaluate and review grant applications.

Name of SEP: Chemoprevention in Genetically-Identified High-Risk Groups: Interactive Research and Development Project.

Date: August 25-26, 1997.

Time: August 25—8:30 a.m.—5:00 p.m.;

August 26—8:00 a.m.—5:00 p.m.

Place: Hyatt Regency Bethesda, 1 Bethesda Metro Center, Bethesda, Md 20814.

Contact Person: Ray Bramhall, Ph.D., Scientific Review Administrator, National Cancer Institute, NIH, Executive Plaza North, Room 636, 6130 Executive Boulevard, MSC 7410, Bethesda, Md 20892-7410, Telephone: 301/496-3428.

Purpose/Agenda: To evaluate and review grant applications.

These meetings will be closed in accordance with the provisions set forth in secs. 552b(c)(4) and 552b(c)(6), Title 5, U.S.C. Applications and the discussions could reveal confidential trade secrets or commercial property such as patentable material and personal information concerning individuals associated with the applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

(Catalog of Federal Domestic Assistance Program Numbers: 93.393, Cancer Cause and Prevention Research; 93.394, Cancer Detection and Diagnosis Research; 93.395,

Guidance for Industry

Screening and Testing of Donors of Human Tissue Intended for Transplantation

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
July 1997**

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GUIDANCE FOR INDUSTRY:¹

SCREENING AND TESTING OF DONORS OF HUMAN TISSUE INTENDED FOR TRANSPLANTATION

PURPOSE

This guidance provides general information on donor screening and testing procedures and practices for those entities involved in the recovery, screening, testing, processing, storage, or distribution of human tissue intended for transplantation and may assist in complying with the requirements in Title 21, Code of Federal Regulations (21 CFR) Part 1270.

SCOPE

Because the Food and Drug Administration (FDA) is in the process of revising 21 CFR 10.90(b), this document is not being issued under the authority of 21 CFR 10.90(b), and the document does not bind the agency and does not create or confer any rights, privileges, or benefits for or on any person. Tissue establishments may follow the guidance or may choose to use alternative procedures not provided in this guidance document. If a tissue establishment chooses to use alternative procedures, the establishment may wish to discuss the matter further with the agency to prevent expenditure of resources on activities that may be unacceptable to the FDA:

This guidance applies to human tissue intended for transplantation procured on or after the effective date of the final rule contained in 21 CFR 1270 and supersedes previous guidance issued by FDA on the screening and testing of donors of human tissue intended for transplantation. FDA may amend this guidance periodically as needed.

¹This guidance document represents FDA's current thinking on screening and testing of donors of human tissue intended for transplantation. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both. Written requests for single copies of this document may be submitted to the Office of Communication, Training and Manufacturers Assistance (HFM-40), Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852-1448. The document may also be obtained by mail by calling the CBER Voice Information System at 1-800-835-4709 or 301-827-1800, or by fax by calling the FAX Information System at 1-888-CBER-FAX- or 301-827-3844. Persons with access to the INTERNET may obtain the document using the World Wide Web (WWW) or bounce-back e-mail. For WWW access, connect

to CBER at "<http://www.fda.gov/cber/publications.htm>." To receive the document by bounce-back e-mail, send a message to "tissue2@a1.cber.fda.gov."

INTRODUCTION

On December 14, 1993, FDA published 21 CFR Part 1270¹, entitled Human Tissue Intended for Transplantation, to reduce the risk of transmission of the human immunodeficiency virus (HIV) and hepatitis viruses through human tissue intended for transplantation. The regulation was issued as an interim rule under the authority of Sections 215, 311, 361, and 368 of the Public Health Service Act (42 U.S.C. 216, 243, 264, 271), because of an immediate need to protect the public health from exposure to the human immunodeficiency virus (HIV), hepatitis B (HBV) and hepatitis C (HCV) viruses through transplantation of tissue from donors infected with these viruses. On July 29, 1997, FDA issued a final rule, 21 CFR Part 1270, clarifying and modifying provisions contained in the interim rule for human tissues intended for transplantation.

DONOR TESTING

Required Tests

All human tissue intended for transplantation should be procured from donors who are tested and found to be negative for antibodies to the human immunodeficiency virus, Type 1 and Type 2 (anti-HIV-1 and anti-HIV-2), hepatitis B surface antigen (HBsAg), and antibodies to the hepatitis C virus (anti-HCV) using FDA licensed tests. The testing should be performed by laboratories appropriately certified for these tests under the Clinical Laboratories Improvement Amendments (CLIA) of 1988. Tissue determined to be suitable for transplantation should be accompanied by a summary of records or copies of original records as required by 21 CFR Part 1270 indicating that the testing was performed and that the samples were found to be negative for anti-HIV-1, anti-HIV-2, HBsAg, and anti-HCV using an FDA licensed screening test. For samples of cadaveric blood, i.e., taken from a donor whose heart beat has ceased, screening tests which have been licensed for testing cadaveric blood should be used, when such tests become available.

FDA recommended that blood banks screen blood using HIV antigen testing.² At present, FDA is not recommending HIV antigen testing for donors of human tissue intended for transplantation. Because blood storage, temperature and other factors may affect test results; and because the test kit specificity and sensitivity has not been addressed for cadaveric blood, HIV antigen testing is not a requirement at this time. If, however, donors are tested using an HIV antigen test, or any other non-required HIV test, the tissue establishment should reject tissue from a donor who tests positive by that test.

Viral Marker Test Performance

All tissue from donors that test repeatedly reactive on a required screening test should be quarantined and should not be used for transplantation. Donor sample testing, using FDA licensed tests, should be performed and test results interpreted according to the manufacturer's instructions in the package insert

for the particular viral marker. Below is a summary for conducting laboratory testing of donor samples using currently licensed kits^{3,4,5,6}:

- (1) A single test should be performed on a donor sample from each donor whose tissue is intended for transplantation. This test is referred to as the initial test.
- (2) If the initial test result is nonreactive, the donor sample is considered negative for the particular viral marker, and the tissue from the donor may be used for transplantation, provided all other donor suitability requirements are met.
- (3) If the initial test result is reactive, the donor sample is considered to be initially reactive. The sample should be retested in duplicate, preferably within a single run (not necessarily the same test kit lot), using the same procedure and same manufacturer's test kit as that used for the initial test. If both repeat test results are non-reactive for the viral marker, the donor sample is considered negative for the particular viral marker, and the tissue from the donor may be used for transplantation provided all other donor suitability requirements are met. If either one or both of the repeat test results are reactive, the test is considered to be repeatedly reactive, and the tissue from the donor should not be used for transplantation.

Plasma Dilution and Testing Algorithm

21 CFR Part 1270 states that tissue shall be determined to be unsuitable for transplantation if transfusion or infusion has been sufficient to affect test results. Transfusion or infusion in the absence of blood loss should not normally be sufficient to affect test results. When blood loss is known or suspected to have occurred, the potential tissue donor was transfused or infused, and no adequate pre-transfusion/infusion sample is available for infectious disease testing; then an algorithm should be used to determine that there has not been plasma dilution sufficient to affect test results. For adults, if administration of more than 2000 milliliters of whole blood, reconstituted blood, red blood cells (RBC) and/or colloid occurs within the 48 hours immediately preceding the collection of a blood sample for testing; or the administration of more than 2000 milliliters of crystalloids occurs within the one hour immediately preceding the taking of a blood sample for testing; or a combination of more than 2000 milliliters of the above occurs, and there is no pre-transfusion/infusion blood sample, then the algorithm defined in the tissue establishment's standard operating procedure (SOP) should be applied. If a donor is 12 years of age or under and there is no pre-transfusion/infusion sample, then an algorithm should be applied when any transfusion or infusion has occurred to determine that there has not been plasma dilution sufficient to affect test results.

The following is an example of a suitable algorithm (see Attachments 1 and 2):

For donors in the 45-100 kilogram range: the blood volume in milliliters may be determined by dividing the body weight in kilograms by 0.015, and the plasma volume in milliliters may be determined by dividing the body weight in kilograms by 0.025. In a circumstance of blood loss with replacement:

If the combined volume of colloid given in the 48 hours preceding sampling plus the volume of crystalloid given in the one hour preceding sampling exceeds the donor's total plasma volume or if the combined volume of the blood given in the 48 hours preceding sampling, plus the volume of colloid given in the 48 hours preceding sampling, plus the volume of crystalloid given in the one hour preceding sampling exceeds the donor's total blood volume then plasma dilution is sufficient to affect test results and the donor should be rejected. (If any one element has not been transfused/infused then it is simply a zero in the calculation.)

For purposes of clarification and definition:

- (1) Blood - refers to whole blood, reconstituted blood, and/or red blood cells transfused in the 48 hours preceding sampling. Reconstituted blood is considered to be red blood cells suspended extracorporeally, in a volume of colloid or crystalloid sufficient to produce a product with a hematocrit in the normal range.
- (2) Colloid - refers to plasma, platelets, albumin, hetastarch, dextran, or a combination of these administered in the 48 hours preceding sampling.
- (3) Crystalloid - refers to saline, dextrose in water, Ringer's lactate, and other balanced electrolyte solutions administered in the one hour before sampling.

Because every possible clinical situation cannot be predicted, the medical director should determine additional circumstances where application of an algorithm would be applied, document the application, and explain the circumstances. Examples of these additional circumstances are a donor who has had blood loss previously, stabilizes, then expires, but has received fluids in the 48 hours prior to sampling; a donor who is obese; a donor who in the absence of bleeding may have received large amounts of infusions which the medical director or designee believes may affect test results; or a donor who is less than 45 kilograms or greater than 100 kilograms.

The establishment's SOPs should define those elements necessary to make a determination whether a pre-transfusion/infusion blood sample for infectious disease testing is adequate. For example, the amount of hemolysis, storage conditions, and age of the sample may be considered relevant. Therefore, the medical director or designee should review these factors and document that a determination of unsuitability of the sample was made.

The tissue establishment should include in its SOPs the algorithm established [see 21 CFR 1270.31(a)].

There should be written procedures prepared and followed for all significant steps in the infectious disease testing process under section 1270.21 which should conform to the manufacturers' instructions for use contained in the package inserts for the required tests. These procedures should be readily

available to the personnel in the area where the procedures are performed. Any deviation from the written procedures should be recorded and justified.

DONOR SCREENING

Sources of Information

In addition to the testing and plasma dilution determination, 21 CFR Part 1270 requires identification of the donor and screening of all tissue donors for relevant behavioral high risk criteria and for clinical and physical evidence of HIV or hepatitis infection. This screening should include an interview with the donor, if living, or an interview with one or more individuals who can provide reliable information concerning the donor's medical history, if the donor is deceased. The donor medical history interview as defined in the final rule means a documented dialogue with an individual or individuals who would be knowledgeable of the donor's medical history and relevant social behavior. The relevant social history would include questions to elicit whether or not the donor met certain descriptions or engaged in certain activities or behaviors considered to place the donor at increased high risk for HIV and hepatitis. The individual interviewed may be the donor's next of kin, a relative, a member of the donor's household, an individual with an affinity relationship with the donor, or the donor's primary treating physician. In addition, a review of all available records including the donor's medical records, autopsy reports or any physical assessment reports including the medical examiner report, police records and other available information, should be used to make a donor suitability determination.

Review of such records should be performed by an individual who is qualified by profession, education and training and who is familiar with the intended use of the tissue. Determining the acceptability of each donor should be the responsibility of the medical director or designee, who, upon review of all available records makes such a determination following the establishment's standard operating procedures, existing medical standards, and federal, state or territorial laws and regulations. The medical director or designee should determine that adequate information has been obtained to assess donor suitability and should have the discretion to reject tissue where information is incomplete or should document the rationale for the release of such tissue based upon the available adequate information.

A number of state and territorial legislative consent laws permit corneal retrieval under specified circumstances of consent. FDA requires in 21 CFR Part 1270, consistent with the 1994 PHS guidelines⁷, that the corneal tissue be accompanied by the summary of records documenting that the corneal donation was procured under legislative consent law and determined to be suitable in the absence of a donor medical history screening interview. For corneal tissue procured under legislative consent where a donor medical history screening interview has not occurred, a physical assessment of the donor is required and other available information should be reviewed and should support a determination that the cornea is suitable for transplantation. FDA recommends that, whenever possible, a donor medical history screening interview be performed.

Behavioral and High Risk Information

The donor medical history screening interview should include questions about the following behavioral

and high risk criteria and tissue should not be accepted for transplantation from donors who have any positive evidence of the following exclusionary risk factors:

- (1) men who have had sex with another man within the preceding 5 years⁷;
- (2) persons who have injected drugs for a non-medical reason in the preceding 5 years, including intravenous, intramuscular, and subcutaneous injections⁷;
- (3) persons with hemophilia or related clotting disorders who have received human-derived clotting factor concentrates^{4,7,8};
- (4) persons who have had sex in exchange for money or drugs in the preceding 5 years⁷;
- (5) persons who have had sex in the preceding 12 months with any person described in the 4 items above or with any person suspected of having HIV, hepatitis B virus, or hepatitis C virus infection^{4,7};
- (6) persons who have been exposed within the last 12 months to known or suspected HIV, HBV, and/or HCV infected blood through percutaneous inoculation (e.g. needlestick) or through contact with an open wound, non-intact skin, or mucous membrane^{4,7,8};
- (7) children 18 months of age or less born to mothers HIV-infected or at risk for HIV infection and who have been breast fed within the preceding 12 months, regardless of HIV status⁷;

NOTE: Children over 18 months of age born to mothers infected with HIV or at risk for infection, who have not been breast fed within the preceding 12 months, and whose HIV antibody test, physical examination, and review of medical records do not indicate evidence of HIV infection can be accepted as donors⁷.

- (8) current inmates of correctional systems (including jails and prisons) and individuals who have been incarcerated for more than 72 consecutive hours during the previous 12 months^{7,9};
- (9) persons who have had close contact with another person having viral hepatitis within 12 months preceding donation^{3,8};
- (10) persons who have had or have been treated for syphilis or gonorrhea during the preceding 12 months⁴;
- (11) persons who within 12 months of donation have undergone tattooing, acupuncture, ear or body piercing in which shared instruments are known to have been used³;

NOTE: Though not currently within the scope of 21 CFR 1270, FDA is aware that screening for possible risks of exposure to Creutzfeldt-Jakob disease is recommended in voluntary standards such as the American Association of Tissue Banks and the Eye Bank Association of America. The relevant factors are:

- (12) persons with a diagnosis of Creutzfeldt-Jakob Disease or known family history (blood relative) of a person with non-iatrogenic Creutzfeldt-Jakob Disease¹⁰;
- (13) persons who have received injections of human pituitary-derived growth hormone (pit-hGH)¹¹;
or
- (14) persons who are known to have received transplants of dura mater¹⁰.

21 CFR 1270.31(b), states that written procedures should be prepared and followed for all significant steps for obtaining, reviewing, and assessing the relevant medical records. As noted in the definition of relevant medical records, those records include a donor medical history screening interview. FDA believes that the establishment should develop and follow SOPs incorporating direct questions addressing the above risk factors and that direct questions should be asked in the donor medical history screening interview to determine if these events occurred. The questions should be framed in a way to elicit the information being sought. Available records should also be reviewed to determine if any of the above risk factors are reported. If these risk factors are reported to have occurred within the specified time period the tissue should not be used.

Clinical Evidence

In addition to the requirements in 21 CFR Part 1270 that a donor should test negative on FDA screening tests for HIV, HBV, HCV and be screened and found to have none of the relative risk factors, a donor should also be free from clinical signs and symptoms of HIV and hepatitis. Based on the available information from a donor's medical history, physical examination, medical records, autopsy report and laboratory test results, tissue donors should be free from evidence of:

- (1) HIV infection or Acquired Immunodeficiency Syndrome (AIDS) which could include clinical signs and symptoms such as unexplained weight loss, unexplained night sweats, blue or purple spots on the skin or mucous membranes typical of Kaposi's sarcoma, disseminated lymphadenopathy of longer than one month, unexplained temperature of over 100.5°F (38.6°C) for more than 10 days, unexplained persistent cough or shortness of breath, opportunistic infections, unexplained persistent diarrhea^{4,7}, and
- (2) Hepatitis B or C infection, which could include clinical signs and symptoms of hepatitis such as unexplained yellow jaundice or hepatomegaly (records of laboratory data such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin or prothrombin time may assist in making a donor suitability determination)⁶.

Physical Evidence

Physical assessment of all tissue donors aids in donor suitability determinations because it provides an additional level of assessment for high risk behaviors or clinical evidence of infection with HIV or hepatitis. 21 CFR 1270 defines a physical assessment as a limited autopsy or recent antemortem or postmortem physical examination of the donor to assess for any evidence of high risk behavior and signs of HIV and hepatitis infection. If any of the following signs are observed on physical assessment and are deemed to be an indication of either high risk behavior or an indication of HIV or hepatitis infection then the tissue should be rejected.

For all donors, the following should be determined by limited autopsy and/or recent antemortem or postmortem physical examination, and noted if reported in any other available record:

- (1) Physical evidence for risk of sexually transmitted diseases such as genital ulcerative disease, herpes simplex, syphilis, chancroid;
- (2) Physical evidence of anal intercourse including perianal condyloma;
- (3) Physical evidence of nonmedical percutaneous drug use such as needle tracks;
- (4) Disseminated lymphadenopathy;
- (5) Oral thrush;
- (6) Blue or purple spots consistent with Kaposi's sarcoma;
- (7) Needle tracks, including examination of tattoos which may be covering needle tracks;
- (8) Unexplained jaundice, hepatomegaly or icterus; or
- (9) If the body was rejected for routine autopsy due to infectious criteria or if the autopsy was done in an infectious disease control room or under any special precautions and the reasons for these procedures.

REFERENCES

1. FDA Interim Rule for Human Tissue Intended for Transplantation, December 14, 1993, Federal Register, Vol 58, No. 238, p 65514.
2. FDA Recommendations to Blood Establishments for Donor Screening with a Licensed Test for HIV-1 Antigen," 8/8/95.
3. FDA Revised Recommendations to Blood Establishments for "Testing Whole Blood, Blood Components, Source Plasma and Source Leukocytes for Antibody to Hepatitis C Virus Encoded Antigen (Anti-HCV)," 4/23/92.
4. FDA Revised Recommendations to Blood Establishments for "The Prevention of Human Immunodeficiency Virus (HIV) Transmission by Blood and Blood Products," 4/23/92.
5. FDA Recommendations to Blood Establishments for "The Management of Donors and Units that are Initially Reactive for Hepatitis B Surface Antigen (HBSAG)," 12/2/87.
6. FDA Recommendations to Blood Establishments for "Donor Suitability Related to Laboratory Testing for Viral Hepatitis and a History of Viral Hepatitis," 12/22/93.
7. PHS Guideline for Preventing Transmission of HIV through Transplantation of Human Tissue and Organs, MMWR 1994:43, 1-17.
8. PHS Guideline for Screening Donors of Blood, Plasma, Organs, Tissue and Semen for Evidence of Hepatitis B and Hepatitis C, MMWR 1991:40, 1-17.
9. FDA Recommendations to Blood Establishments for "Deferral of Current and Recent Inmates of Correctional Institutions as Donors of Whole Blood, Blood Components, Source Leukocytes, and Source Plasma," 6/8/95.
10. FDA Recommendations to Blood Establishments for "Precautionary Measures to Further Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease by Blood and Blood Products," 8/8/95.
11. FDA Recommendations to Blood Establishments for "Deferral of Blood and Plasma Donors based on Medications," 7/28/93.

Reject Donor

ATTACHMENT 2: EXAMPLE OF A PLASMA DILUTION WORKSHEET

DONOR ID# _____

Date and Time of sampling..... _____ am/pm

Donor weight in kg..... _____ kg

Plasma Volume (PV)

PV = Donor weight (kg) _____ ÷ .025..... _____ ml

Blood Volume (BV)

BV = Donor weight (kg) _____ ÷ .015..... _____ ml

A. Total Volume of Blood Transfused/48h

Volume of: RBC's transfused/48h _____ ml
 whole blood transfused/48h _____ ml
 reconstituted blood transfusion _____ ml

TOTAL: **A** = _____ ml

B. Total volume of Colloid Infused/48h

Volume of: dextran _____ ml
 plasma _____ ml
 platelets _____ ml
 albumin _____ ml
 hetastarch _____ ml

Other: _____ ml
 _____ ml
 _____ ml

TOTAL: **B** = _____ ml

C. Total volume of Crystalloid Infused/1h

Volume of: saline _____ ml
 dextrose in water _____ ml
 Ringer's lactate _____ ml

Other: _____ ml
 _____ ml
 _____ ml

TOTAL: **C** = _____ ml

DETERMINATION OF SUITABILITY

1. Is B + C > PV? Y N
 2. Is A + B + C > BV? Y N

If answer to both 1 and 2 are NO then test sample.
 If answer to either 1 or 2 is YES then reject donor.

COMMENTS: _____

INITIALS: _____