



Medical Standards

**These Standards have the approval of the Eye Banking Committee
of the American Academy of Ophthalmology**

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Table of Contents

A1.000 Introduction and Purpose	5
A1.100 Scope.....	5
B1.000 Active Membership	5
B1.100 Eye Bank Inspection.....	6
B1.200 Inspections by Official Agencies	6
C1.000 Personnel and Governance.....	6
C1.100 Director.....	6
C1.200 Medical Director	7
C1.300 Staff (Technical and Supportive) Performing Tasks Overseen and/or Regulated by the EBAA, FDA, and Other State and Federal Agencies	8
C1.400 Change in Governance	9
C2.000 Training, Certification and Competency Reviews of Personnel Performing Tasks Overseen and/or Regulated by the EBAA, FDA, and Other State Federal Agencies	9
C3.000 Facilities	10
C3.100 Eye Bank Laboratory	10
C3.200 Equipment, Maintenance and Cleaning	10
C3.300 Instruments and Reagents.....	11
C3.400 Procedures Manual.....	11
C3.500 Other Establishments Performing Eye Banking Functions	11
C3.510 Eye Bank Functions Performed by Another Establishment.....	12
C3.600 Infection Control and Personnel Safety	12
C3.700 Biohazardous Waste Disposal.....	13
D1.000 Donor Eligibility Determination.....	13
D1.100 Donor Screening	14
D1.110 EBAA Specific Contraindications to Transplant.....	14
D1.120 Screening for FDA Defined Relevant Communicable Disease Agents and Diseases.....	16
D1.200 Donor Testing	16
D1.210 EBAA Testing Requirements.....	17

D1.220	FDA Testing Requirements	17
D1.230	Non-Required Testing Results	17
D1.300	Documentation of Donor Information	17
D1.400	Method and Authorization for Donation.....	17
D1.500	Donor Age.....	18
D1.600	Interval between Death, Enucleation, Excision, Preservation and Processing	18
D1.700	Eye Maintenance Prior to Recovery	18
D1.800	Living Donors	18
E1.000	Recovery, Processing, and Preservation	18
E1.100	Recovery.....	19
E1.200	Processing and Preservation	19
E1.210	Whole Eye	20
E1.220	Cornea.....	20
E1.221	Processing via Excision of the Corneoscleral Disc from Enucleated Whole Eyes	20
E1.222	Lamellar Tissue Processing.....	20
E1.223	Laser Assisted Processing	20
E1.230	Sclera	20
E1.300	Use of Short or Intermediate Term Storage Solution.....	21
E1.400	Long Term Preservation and Organ Culture	21
F1.000	Tissue Evaluation	21
F1.100	Slit Lamp Examination.....	21
F1.200	Endothelial Cell Density and Pachymetry.....	22
F1.300	Eligibility for Surgical Use.....	22
G1.000	Quality Assurance	22
G1.000	Quality Control	24
G1.200	Microbiologic Culturing	24
G1.300	Tissue Recall or Tissue Withdrawal	25
H1.000	Non-Surgical Donor Tissue.....	25
I1.000	Storage	25
I1.100	Expiration Dating	26

J1.000 Labeling	26
K1.000 Distribution of Tissue	26
K1.100 Review of Donor Medical Information.....	27
K1.200 Distribution Compliance	27
K1.300 Fair and Equitable System	27
K1.400 Returned Tissue.....	27
K1.500 Fraudulent Activity	27
L1.000 Documentation to Accompany Donor Tissue	28
L1.100 Tissue Report Form	28
L1.200 Package Insert Form	29
L2.000 Packaging, Sealing and Packing for Transport.....	30
M1.000 Eye Bank Records	30
M1.100 Length of Storage	30
M1.200 Confidentiality.....	31
M1.300 Donor Screening Forms	31
M1.400 Minimum Information to Be Retained	31
M1.500 Recipient Follow-up Information	32
M1.600 Statistical Reporting	33
N1.000 Amendments	33
Glossary (Definitions of Terms).....	34

EBAA MEDICAL STANDARDS

A1.000 Introduction and Purpose

These standards have been developed to assure consistently acceptable levels of quality, proficiency, and ethics in dealing with ocular tissue for transplantation and define the minimum standards of practice for eye bank functions, as determined by the ophthalmological medical community.

A1.100 Scope

These standards are intended to apply to any and all of the eye bank functions, to include:

- Recovery
- Processing
- Storage
- Tissue evaluation
- Donor eligibility determination
- Distribution

These standards shall be reviewed at least annually and revised as necessary to incorporate current research findings and improved clinical practice.

B1.000 Active Membership

In order for an eye bank to become an active member of the Eye Bank Association of America (EBAA), it must comply with the EBAA Bylaws and the following:

1. Demonstrate compliance with EBAA Medical Standards.
2. Maintain accreditation status by passing the site inspection as administered by the EBAA Accreditation Board.
3. Demonstrate proficiency in any aspect of eye banking including recovery, processing, tissue storage, evaluation, donor eligibility determination and distribution.
4. Proficiency shall be demonstrated by providing documentation, at the time of completing the application, of the handling of at least 25 surgical corneas for each eye bank function for which it is seeking accreditation.
5. Certify compliance with applicable Federal and State regulations.
6. Register with ICCBBA for a Facility Identification Number (FIN) by June 30, 2015.

Once accredited, an eye bank must be inspected and reaccredited at least every three years to maintain active membership in the EBAA.

B1.100 Eye Bank Inspection

The Accreditation Board of the EBAA shall be responsible for inspecting member eye banks as outlined in the written procedures of the Board.

Accreditation and reaccreditation site inspections shall be scheduled following written notification of the impending inspection. Unannounced inspections may be conducted should an allegation of violation of Medical Standards be made to the Accreditation Board, or should the results of inspections by official agencies indicate violation of Medical Standards. Failure to permit an inspection will result in suspension or revocation of an eye bank's accreditation.

Demonstration of proficiency in any and all aspects of eye banking may be required during the site inspection and of any or all technical personnel. The Accreditation Board may review and make a determination to accept findings from outside agencies.

B1.200 Inspections by Official Agencies

Any written documentation of observations, findings, or results (including but not limited to Food and Drug Administration (FDA) Form 483) received by an eye bank which are related to any inspection by an official agency shall be sent to the EBAA office within ten (10) business days of receipt. The EBAA office shall be copied on all future related correspondence.

C1.000 Personnel and Governance

C1.100 Director

All policies and procedures of each eye bank shall be under the supervision of a Director appointed by the eye bank's Board of Directors, Board of Regents or other governing body. The Director shall be responsible for all administrative operations including compliance with these standards.

The Director shall be the individual responsible for the day-to-day operation of the eye bank. It is this individual's responsibility to carry out policies of the eye bank's Board, to determine what functions will be performed by the eye bank, and to prescribe clinically acceptable means to perform these functions.

The Director shall consult with the Medical Director, as well as other medical and legal authorities, in carrying out prescribed responsibilities as necessary. These consultations shall be documented and made available for review during a site inspection.

The Director shall provide all staff members with adequate information to perform their duties safely and competently. Delegation of responsibility for the clinical work of the eye bank shall be as follows:

C1.200 Medical Director

The eye bank must have a Medical Director. When the Medical Director is not available, a back-up Medical Director shall be designated who is capable of fulfilling the responsibilities of the Medical Director on an interim basis.

The Medical Director and a back-up Medical Director must be an ophthalmologist who has completed a corneal fellowship or who has demonstrated expertise in external eye disease, corneal surgery, research or teaching in cornea and/or external disease. If the Medical Director has not served a corneal fellowship, then the eye bank must have and document a consulting relationship with an ophthalmologist who has.

Any physician who provides verification of competency for tissue recovery and preservations shall attend the Medical Directors' Symposium at the annual meeting of the EBAA at least once every three years and a Medical Advisory Board meeting once every three years. A newly appointed Medical Director shall attend a Medical Directors' Symposium and a Medical Advisory Board Meeting within one year of appointment, unless a Co-Medical Director has fulfilled the requirement. The eye bank shall provide written documentation of such attendance at the time of the eye bank site inspection.

The Medical Director shall oversee and provide advice on all medical aspects of the eye bank operations. These include but are not limited to:

1. Formulation, approval, and implementation of medical policies and procedures.
2. Participation in training and oversight of technical staff with regard to eye bank functions.
3. Participation in establishment and operation of a quality assurance program.
4. Responsibility for verification of competency for tissue recovery and preservation by personnel applying for CEBT certification

An eye bank's Medical Director must observe the designated staff trainer or trainers performing the following procedures as applicable on an annual basis:

1. In-situ corneoscleral disc excision or laboratory corneoscleral disc removal from whole eye
2. Posterior lamellar processing procedure that utilizes a microkeratome
3. At least one type of laser-shaped processing procedure

4. Each manual dissection processing procedure(s) for EK and ALK (i.e. DSEK or DMEK)

If an eye bank Medical Director has not designated any individuals as staff trainers, he/she must observe each technician they have qualified to perform any of the above procedures on an annual basis.

The Medical Director may delegate responsibility for eye bank functions to qualified eye bank personnel; however, the Medical Director shall ensure that the eye bank operates in compliance with the EBAA Medical Standards. Ultimate responsibility for the suitability of each tissue for the transplantation in patients rests with the transplanting eye surgeon.

An eye bank has three months to replace a Medical Director who has resigned.

C1.300 Staff (Technical and Supportive) Performing Tasks Overseen and/or Regulated by the EBAA, FDA, and Other State and Federal Agencies.

The Director shall appoint technical and supportive staff and ensure that this staff has the appropriate qualifications and training for the performance of their job responsibilities. The Director shall ensure that there are a sufficient number of qualified eye bank technicians and supportive staff to perform all eye bank laboratory tests and procedures at a level of proficiency established by the bank. The eye bank Medical Director or Medical Director's designee must document in writing those eye bank tasks in which each staff member is qualified and released to perform independently.

Each eye bank must employ at least one EBAA CEBT in a supervisory and training role(s).

If the only function the establishment performs is recovery and/or storage, a documented contractual, consultative relationship with a CEBT and the accredited organization in which the CEBT is employed may be an acceptable alternative to having a CEBT on staff.

An eye bank or other establishment which performs eye banking functions has six months in which to replace their required EBAA CEBT(s) provided that:

1. The establishment notifies the EBAA office in writing that it does not meet this standard.
2. The establishment submits appropriate evidence of its intent to comply with the "required CEBT" standard.
3. A documented interim consultative relationship is established with a CEBT and the accredited organization in which the CEBT is employed.

4. The non-CEBT technician in charge in the interim has demonstrated competency to the Medical Director of the involved establishment.

If a six month deadline cannot be met, the establishment may request an extension by writing to the EBAA office. An extension may be granted on a case-by-case basis after review by the Chair of the Accreditation Board, in consultation with the EBAA CEO or designee.

C1.400 Change in Governance

An eye bank that undergoes a change in governance must notify the EBAA office (in writing) within 30 days. Changes in governance include merger of eye banks, affiliation of two or more eye banks, affiliation of an eye bank with another non-eye bank organization (e.g. tissue banks, organ procurement organizations, hospitals, blood banks, etc.), a change in the name of the eye bank, or a change in required personnel, i.e. Director, Medical Director.

C2.000 **Training, Certification and Competency Reviews of Personnel Performing Tasks Overseen and/or Regulated by the EBAA, FDA, and Other State and Federal Agencies.**

An eye bank or other establishment performing eye banking functions must provide a formal orientation program for each new employee and the employee's participation must be documented.

An eye bank or other establishment performing eye banking functions, must also establish a comprehensive and well-defined training program outlining specific job-related tasks that each employee is being trained to perform. This training program shall contain documentation indicating when each employee is released to perform their job-related tasks independently. This comprehensive training program shall include the implementation and documentation of annual competency reviews of the skills and job-related knowledge of all eye bank employees performing eye banking functions. The person responsible for these competency reviews must be a CEBT or an individual who has been qualified by a CEBT who is part of the organization's comprehensive quality program.

Eye bank technicians seeking to receive EBAA certification or become re-certified must meet the criteria set forth in the EBAA document Criteria for Certification and Recertification of Eye Bank Technicians.

All EBAA accredited eye banks must have one CEBT attend an EBAA sponsored skills workshop once every three years.

C3.000 **Facilities**

Each establishment performing any eye bank function listed in Medical Standard A1.100 (Scope), must have sufficient space, equipment and supplies to accommodate the volume of services performed with optimal accuracy, efficiency, sterility, timeliness and safety. The EBAA office shall be notified (in writing) within 30 days of the relocation, laboratory expansion or addition of a satellite to an eye bank.

C3.100 Eye Bank Laboratory

The laboratory must be a separate area with limited access in which activities directly related to eye banking are carried out. The laboratory shall have a sink with a drain and running water. There must be adequate counter space for preparation of donor material. The room including walls, floor and sink must be kept clean at all times. Appropriate documentation of regular laboratory cleaning schedules must be maintained and kept on file for a minimum of three years.

Each eye bank laboratory must have an adequate stable electrical source and a sufficient number of grounded outlets for operating laboratory equipment.

C3.200 Equipment, Maintenance and Cleaning

Each eye bank laboratory shall have a refrigerator with a device, visible without opening the refrigerator, for recording temperature variations. The temperature recording device should reflect the temperature of the stored tissue under normal storage conditions. Temperature variations must be recorded daily and remain within the range of 2 to 8° Celsius. The refrigerator's continuous temperature recorder must be calibrated against an NIST standard thermometer (or for eye banks outside the U.S.A., a standard thermometer as defined by their countries' regulatory agencies) at least once a year. The refrigerator shall be maintained for the use of tissue and tissue preservation solution and must contain clearly defined and labeled areas for all tissue stored, i.e., quarantined tissue, surgical tissue awaiting distribution, and research tissue. Eye banks must detail required refrigerator cleaning intervals and documentation in their Policies and Procedures manual.

In the event of a temperature deviation outside the acceptable range, there must be provision for immediate notification and action to be taken. Testing of the alarm system must be performed and documented on a regular basis. The eye bank laminar airflow cabinet or flow hood must be cleaned before and after each use and at regularly scheduled intervals to prevent cross contamination.

Appropriate maintenance and qualification and/or certification records must be maintained on each piece of equipment. These records must show dates of

inspection, performance evaluations and any maintenance procedures or repairs performed.

The eye bank must include in its procedures manual, the monitoring, inspection and cleaning procedures and schedules for each piece of equipment and laboratory area. Documented cleaning schedules for laboratory equipment must be kept on file for a minimum of three years.

C3.300 Instruments and Reagents

Adequate instrumentation must be available to provide for sterile removal of whole eyes and corneas. Instruments must be inspected frequently enough to assure that they function properly. An eye bank that uses an autoclave to sterilize its instruments shall adhere to the maintenance procedures for autoclaves as recommended in the current Association for the Advancement of Medical Instrumentation (ANSI/AAMI) Standard 79 – “Comprehensive guide to steam sterilization and sterility assurance in health care facilities”. The eye bank must outline these steps in its procedure manual. Annual certification to validate temperature, pressure and time shall be performed and documented. If instruments are sterilized outside of the eye bank, the eye bank shall provide documentation of appropriate sterilization.

All sterilized instruments, supplies and reagents, such as corneal storage solution, must contain sterilization dates, method or appropriate expiration dates that are current at all times if applicable.

C3.400 Procedures Manual

Each eye bank shall maintain its own policies and procedures manual that details all aspects of its specific eye bank functions, and quality assurance practices. Each procedure must be initially approved, signed, and dated by the Director and Medical Director. An annual review of each eye bank’s procedure with signing and dating by the Director and Medical Director is required. Each eye bank must maintain copies of each procedure it uses and the length of time the procedure was in use. Procedures must be readily available to personnel in the area where operations are performed.

Eye banks shall utilize ICCBBA Eye Bank Technical Advisory Group (EBTAG) nomenclature to describe ocular tissue classes and attributes, effective June 30, 2015.

C3.500 Other Establishments Performing Eye Banking Functions

Any establishment performing eye bank functions must employ a CEBT. A recovery and/or a storage-only establishment may meet this requirement by

having a documented consultative relationship with a CEBT and the EBAA accredited organization in which the CEBT is employed.

All establishments performing specialized or specific eye banking functions must have a Medical Director or access to a Medical Director through a documented consultative relationship with an EBAA accredited organization. This Medical Director must meet the requirements of Medical Director as outlined in section C1.200 of these standards. Establishments performing specific eye banking functions may be inspected as part of the EBAA accreditation process of an organization in which they provide services.

C3.510 Eye Bank Functions Performed by Another Establishment

Any EBAA accredited organization engaging with another establishment that performs eye banking functions prior to distribution must either:

1. Document that the establishment is currently EBAA accredited for the eye bank functions performed; or
2. Document that the establishment is in compliance with EBAA medical standards, state and federal regulations appropriate to the eye bank functions performed. This option requires a written agreement and the EBAA accredited organization is responsible for performing compliance audits. Policies and procedures shall describe the audit plan, scope, and frequency.

C3.600 Infection Control and Personnel Safety

Written safety procedures for the eye bank operation shall be established in compliance with the Occupational Safety and Health Act (OSHA Act) of 1970 and the 1991 amendments to Part 1910 of title 29 of the Code of Federal Regulations), Subpart Z and/or applicable state statutes, which may supersede. For eye banks where OSHA regulations do not apply, written safety procedures in compliance with the relevant regulatory agencies are an acceptable substitute. All eye bank personnel must operate under the current Universal Precautions for health care workers issued by the CDC of HHS.¹ These written procedures must be included in the eye bank's procedure manual.

¹ On December 6, 1991, the Occupational Safety and Health Administration (OSHA) of the U.S. Department of Labor (DOL) published its final rules regulating worker occupational exposure to bloodborne pathogens, including but not limited to hepatitis B virus (HBV) and human immunodeficiency virus (HIV). These regulations went into effect March 6, 1992, and make employers responsible for providing and ensuring safe working conditions in all work settings. See the December 6, 1991, *Federal Register*, Vol. 56, no. 235.

C3.700 Biohazardous Waste Disposal

Human tissue and waste items shall be disposed of in such a manner as to minimize any hazard to eye bank personnel and the environment and to comply with state and federal regulations. Dignified and proper disposal procedures shall be used to obviate recognizable human remains and must be documented.

D1.000 Donor Eligibility Determination

Before tissue is made available for distribution, the Donor Eligibility Determination must be made by a responsible person. Reference Appendix II for requirements related to the donor eligibility process.

Prior to making an eligibility determination, the donor must be screened according to D1.200. In addition to donor eligibility determination, tissue must be evaluated for suitability per F1.000.

All donors must be identified by name. All prospective donors shall undergo a physical examination as close as possible to the donation with special attention to physical signs of HIV disease, infectious hepatitis, and injecting drug use. Each eye bank shall have a consistent policy for conducting and documenting this examination. Each eye bank shall also have a consistent policy for examination and documentation of the prospective donor's available medical record and death investigation. Review of all available records on each donor shall be performed by an individual who is qualified by profession, education, or training to do so, and who is familiar with the intended use of the tissue.

Medical and social histories are important aspects of donor eligibility. Adequately determining eligibility includes, but is not limited to:

1. Infectious disease testing (see G1.200)
2. Physical assessment of the donor (see above paragraph)
3. Tissue evaluation (see F1.000)
4. Donor history evaluation: this must include the donor's name, social history and donor information obtained from at least one of the following:
 - a. Pathologist or medical examiner physical assessment of death report
 - b. Police investigation report accompanied by (a) and/or (c)
 - c. Medical examiner's investigative report
 - d. Donor risk assessment interview
 - e. Medical record or hospital chart
 - f. Treating physician interview
 - g. Medical director oversight to review any donor information where questions arise in the above areas (see C1.200). This shall be documented.

D1.100 Donor Screening

The eye donor's relevant medical records must be reviewed for (Reference Appendix III for FDA requirements related to review of relevant medical records):

- EBAA specific contraindications (Ref. D1.110); and
- FDA defined relevant communicable disease agents and diseases (Ref. D1.120); and
- Other diseases as required by the country of import, if exported outside of the United States

D1.110 EBAA Contraindications to Transplant

Tissues from persons with the following are potentially health threatening for the recipient(s) or pose a risk to the success of the surgery and shall not be offered for surgical purposes:

A. All Ocular Donors

1. death of unknown cause and there is likelihood of other exclusionary criteria;
2. congenital rubella;
3. Reye syndrome within the past three months;
4. Active viral encephalitis of unknown origin or progressive encephalopathy (e.g., subacute sclerosing panencephalitis, progressive multifocal leukoencephalopathy, etc.);
5. active bacterial or viral meningitis;
6. active bacterial or fungal endocarditis;
7. suspected rabies and persons who, within the past six months, were bitten by an animal suspected to be infected with rabies;
8. Down Syndrome - exclusive for penetrating keratoplasty or anterior lamellar keratoplasty;
9. intrinsic eye disease;
 - a. retinoblastoma;
 - b. malignant tumors of the anterior ocular segment or known adenocarcinoma in the eye of primary or metastatic origin;
 - c. active ocular or intraocular inflammation: conjunctivitis, keratitis, scleritis, iritis, uveitis, vitreitis, choroiditis, retinitis; or
 - d. congenital or acquired disorders of the eye that would preclude a successful outcome for the intended use, e.g., a central donor corneal scar for

an intended penetrating keratoplasty, keratoconus, and keratoglobus;

10. active leukemias;
11. active disseminated lymphomas;
12. Parkinson, amyotrophic lateral sclerosis, multiple sclerosis, and Alzheimer disease;
13. history of Ebola Virus Disease (EVD).

B. Donors for Penetrating Keratoplasty Procedures

1. Prior intraocular or anterior segment surgery
 - a. Refractive corneal procedures, e.g., radial keratotomy, lamellar inserts, etc.
 - b. Laser photoablation surgery (these corneas may be used for tectonic grafting and posterior lamellar procedures).
 - c. Corneas from patients with anterior segment (e.g., cataract, intraocular lens, glaucoma filtration surgery) may be used if screened by specular microscopy and meet the eye bank's endothelial standards.
2. Pterygia or other superficial disorders of the conjunctiva or corneal surface involving the central optical area of the corneal button.

C. Donors for Anterior Lamellar Keratoplasty Procedures or Tectonic Grafts

Criteria are the same as listed for penetrating keratoplasty, except that tissue with local eye disease affecting the corneal endothelium or previous ocular surgery that does not compromise the corneal stroma, (e.g., donors with a history of endothelial dystrophy or iritis are acceptable).

D. Donors for Epikeratoplasty Procedures

Criteria are the same as listed for penetrating keratoplasty, except that tissue with local eye disease affecting the corneal endothelium, (e.g., donors with a history of endothelial dystrophy or iritis are acceptable). Death to preservation time may be extended.

E. Donors for Endothelial Keratoplasty Procedures

Criteria are the same as listed for penetrating keratoplasty, except that tissue with non-infectious anterior pathology that does not affect the posterior stroma and endothelium is acceptable. Surgeons must be notified of any prior pathology prior to placing tissue for transplant.

F. Scleral Tissue Donors

Criteria are the same as listed for penetrating keratoplasty, except that tissue with local eye disease affecting the cornea is acceptable for use. Death to preservation time may be extended.

D1.120 Screening for FDA Defined Relevant Communicable Disease Agents and Diseases

The FDA defines communicable disease agents and diseases considered relevant (Ref. Appendix I). Tissue from persons exhibiting risk factors for, clinical evidence of, or physical evidence of relevant communicable disease and high risk behavior associated with relevant communicable disease must not be used for transplant purposes (Ref. Appendix II).

D1.200 Donor Testing

The eye donor must be tested according to:

- EBAA testing requirements (D1.210)
- FDA testing requirements (D1.220). Eye banks located outside of the United States are not bound by FDA testing requirements, but must test in accordance with national and local regulations in the jurisdiction in which they are located.
- State requirements
- Other testing requirements of the country of import, if exported outside of the United States

A review of written results of infectious disease testing shall be received by the eye bank prior to releasing tissue designated for surgical use.

The infectious disease testing laboratory and test kits used must meet FDA regulatory requirements (Ref. Appendix IV). Eye banks outside the U.S. must use a laboratory that is accredited by, and whose tests are approved by their own countries' regulatory agencies.

If plasma dilution sufficient to affect the results of communicable disease testing is suspected, the donor should be considered ineligible, unless a pre-transfusion or infusion sample drawn up to 7 days before recovery is tested; or

an algorithm designed to evaluate volumes administered in the 48 hours before specimen collection is used, showing that plasma dilution sufficient to affect the results has not occurred (Ref. Appendix IV).

Eye banks outside of the U.S.A. shall use a plasma dilution algorithm which meets the requirements of their own countries' regulatory agencies. If no such requirements exist, they shall use an algorithm which meets FDA requirements.

D1.210 EBAA Testing Requirements

The results of the following EBAA required testing must be negative or non-reactive for the tissue to be eligible for transplant:

- anti-HIV-1, anti-HIV-2 (or combination test)
- Hepatitis B surface antigen (HBsAg)
- anti-HCV

D1.220 FDA Testing Requirements

Refer to Appendix IV for FDA donor testing requirements and recommendations. Results must be negative or non-reactive for the tissue to be eligible for transplant except as indicated for syphilis.

D1.230 Non-Required Testing Results

All non-required positive infectious disease tests must be reported to the eye bank's medical director, who must review and act on them, or the eye bank must have a standard policy regarding the action to be taken in response to the individual test.

D1.300 Documentation of Donor Information

Donor screening forms and/or copies of relevant medical records reviewed must be completed and retained on all donated eye tissue as part of the donor record. See Section L1.000.

A unique donor identifying number, i.e., medical examiner or coroner case number, hospital medical record number, social security or driver's license number, shall be obtained and recorded in the donor record.

D1.400 Method and Authorization for Donation

Documentation of legal authorization for recovery is essential for medical-legal reasons. Authorization procedures and forms must conform with state law and documentation for authorization must be retained. In medical

examiner's/coroner's cases, the eye bank shall adhere to the regulations specified by the medical examiner's or coroner's legislation in its state. In each case the authorization designation and restrictions, if any, must be adhered to and cannot be altered without the witnessed resigning or redesignation of the legally appropriate person.

D1.500 Donor Age

Since no definite relationship has been established between the quality of donor tissue and age, the upper and lower age limit is left to the discretion of the Medical Director.

D1.600 Interval between Death, Enucleation, Excision, Preservation, and Processing

Acceptable time intervals from death, enucleation or excision to preservation may vary according to the circumstances of death and interim means of storage of the body. It is generally recommended that corneal preservation occur as soon as possible after death. All time intervals for each donor, i.e., the time of death to the time of enucleation and preservation and/or the time to corneal excision, and/or the time to additional tissue processing, shall be recorded. The time that cooling of ocular tissues and/or refrigeration of the body was begun shall be recorded, if applicable.

D1.700 Eye Maintenance Prior to Recovery

The prospective donor's corneal integrity should be maintained. Recommended procedures for eye maintenance shall be found in the procedures manual. Each individual eye bank's procedure is left to the discretion of the Medical Director and shall be clearly documented.

D1.800 Living Donors

Eye tissue that is removed and intended for surgical use from a living donor shall have the same standards applied as for all cadaveric tissue, e.g., the same donor medical history shall be obtained, the same records, infectious disease tests, etc. No extended quarantine period, outside the usual 24-48 hours for infectious disease test results, shall be required for corneal tissue used for transplantation that is stored in short or intermediate term storage solution.

E1.000 **Recovery, Processing, and Preservation**

Recovery, processing, and preservation must be done using aseptic technique. AORN's "*Recommended Practices for Surgical Hand Antisepsis/Hand Scrubs*" and "*Recommended Practices for Maintaining a Sterile Field*" shall be used as guidance for aseptic technique during ocular tissue recovery and processing.

All procedures must be documented.

Specific recovery, processing, and preservation procedures can be found in the EBAA Procedures Manual. EBAA Procedures Manual is available for use as a Guidance Document. This manual is periodically reviewed and modified as necessary by the Technician Education Committee. Revisions and modifications are approved by the Medical Advisory Board.

The Medical Director is responsible for establishing the eye bank's procedures for recovery, processing, and preservation of tissue. The Medical Director and Director are responsible for assuring that eye bank personnel comply with all applicable procedures for the recovery, processing, and preservation of tissue.

E1.100 Recovery

The donor's identity shall be verified prior to recovery. Recovery may be performed via enucleation or in situ method.

Povidone-iodine solution shall contact the surface of any ocular tissue intended for transplantation at least once between the time of the donor's death and tissue preservation (e.g. corneoscleral disc in Optisol-GS or whole eye in moist chamber). Excess povidone-iodine solution should be irrigated from the ocular surface prior to preservation. The concentration, volume of solution, and the duration of ocular surface exposure to the solution shall be specified in the eye bank's operating procedures.

The corneoscleral disc shall initially be examined with a penlight or portable slit lamp for clarity, epithelial defects, foreign objects, contamination and scleral color prior to enucleation or in situ corneoscleral disc excision.

Standard Precautions shall be followed during donor physical examination, recovery, and all tissue handling procedures to protect eye bank staff from potential exposure to infectious diseases. Tissue from donors with the following is hazardous to eye bank personnel:

- Active Viral Hepatitis
- Acquired Immunodeficiency Syndrome (AIDS) or HIV seropositivity
- Active viral encephalitis or encephalitis of unknown origin
- Creutzfeldt-Jakob Disease (CJD)
- Rabies

E1.200 Processing and Preservation

Processing must be performed in a) a laminar air flow hood or cabinet which meets ISO Class 5 standards, b) in an accredited operating room, or c) in another environment documented annually to have less than 25 colony forming units per 90 mm settle plate per one hour exposure.

Tissue must be processed in such a way as to prevent cross-contamination and labeling mix-ups (e.g., tissue from different donors may not be processed simultaneously).

E1.210 Whole Eye

Eye banks that preserve and store whole eyes for lamellar or refractive keratoplasty may use preservation methods such as moist chamber at 2-8 degrees Celsius, freezing below zero degrees Celsius, or some other validated method.

E1.220 Cornea

Eye banks that process corneas intended for transplant may use one of the following methods. The Medical Director must develop appropriate tissue selection criteria and approve the procedure for each method utilized. All processes must be validated. When changes or process deviations occur, the eye bank shall review and evaluate the process and perform revalidation where appropriate.

E1.221 Processing via Excision of the Corneoscleral Disc from Enuclated Whole Eyes

E1.222 Lamellar Tissue Processing

Processing of lamellar tissue may be performed using manual or automated methods (e.g. microkeratome).

E1.223 Laser Assisted Processing

Lasers may be used to process lamellar tissue or custom wound architecture (e.g. femtosecond laser).

E1.230 Sclera

There are various methods of processing sclera, including utilizing ethanol (70% or greater ethyl alcohol), sterile glycerol, cryopreservation, radiation sterilization, or some other validated method.

E1.300 Use of Short or Intermediate Term Storage Solution

Eye banks shall use an appropriate corneal storage solution that has been manufactured in accordance with FDA Good Manufacturing Practices. The solution shall be used and stored according to the manufacturer’s recommendations for temperature, date and other factors. The manufactured solution purchased and shipped to the eye bank shall be inspected for damage upon arrival. The lot number of storage solution used for each cornea shall be recorded on the tissue report containing the unique identification number of the tissue to allow tracking and recall.

E1.400 Long Term Preservation and Organ Culture

Some eye banks employ preservation techniques such as long term preservation of corneal tissue and organ culturing. An eye bank that uses long term preservation and/or organ culture shall carefully document the procedure(s) in their procedures manual, and adhere to rigid aseptic technique

F1.000 **Tissue Evaluation**

The performing of any and /or all of the following on corneal tissue intended for transplant: slit lamp examination, endothelial cell density, and pachymetry measurement; according to Matrix I.

The ultimate responsibility for determining the suitability of the tissue for transplantation rests with the transplanting surgeon.

Matrix I:

Post-Processing Tissue Evaluation Matrix			
Processing Type	Slit Lamp Biomicroscopy	Specular Microscopy	Pachymetry
<i>PKP</i>	X	X	
<i>DSAEK</i>	X	X	X
<i>DSEK</i>	X	X	X
<i>DMAEK</i>	X	X	
<i>DMEK</i>	X	X	
<i>ALK</i>	X		X
<i>Long-term preservation</i>			

F1.100 Slit Lamp Examination

The corneoscleral disc shall be examined for epithelial and stromal pathology and in particular endothelial disease using slit lamp biomicroscopy. Whole eyes to be distributed for lamellar processing must have the same

examination. Corneoscleral discs that have been processed for lamellar keratoplasty procedures shall be re-evaluated by slit lamp biomicroscopy to ensure that there was no damage to the relevant transplantable tissue.

Document the observations of the slit lamp examination with particular attention to the epithelium, stroma, and endothelium such as, but not limited to, scars, edema, significant arcus, striae, epithelial defects, guttata, polymegathism, pleomorphism, infiltrates, or foreign bodies.

F1.200 Endothelial Cell Density and Pachymetry

Determination of endothelial cell density via specular microscopy (or quantitative light microscopy for organ cultured corneas) shall be a standard method of corneal tissue evaluation (according to Matrix I) for all member eye banks of the EBAA, effective December 2001. Minimal endothelial cell count limits are left to the discretion of the Medical Director. When it is impossible to obtain an endothelial cell count, this requirement may be waived on a case-by-case basis by the Medical Director. Calibration of endothelial cell counting equipment shall be done according to manufacturer guidelines, when applicable, and on at least an annual basis. Calibration procedures shall include specific directions and limits for accuracy.

F1.300 Eligibility for Surgical Use

The eye bank responsible for evaluation of ocular tissue shall specify whether the tissue meets the criteria for penetrating keratoplasty, anterior lamellar keratoplasty, endothelial keratoplasty, keratolimbal allograft, and/or tectonic use.

G1.000 **Quality Assurance**

Each eye bank shall have a formally established quality assurance program. This program shall include:

- Establishment and maintenance of procedures for all functions performed by the eye bank (including review, approval, and revision)
- Monitoring and evaluation of functions through periodic audits by an individual(s) not regularly involved in the processes being monitored
- Identification of problems and complaints relating to activities (receiving, investigating, evaluating, and documenting information relating to eye banking requirements)
- Development of plans for corrective actions, including monitoring for effectiveness

The quality assurance program shall address applicable requirements relating to the following areas:

1. Facilities
2. Environmental control
3. Equipment
4. Supplies and reagents
5. Recovery
6. Processing and processing controls
7. Labeling controls
8. Storage
9. Receipt, pre-distribution shipment, and distribution
10. Donor eligibility determinations, donor screening, and donor testing
11. Tissue evaluation

Each eye bank shall document all aspects of its quality assurance program. Records relating to the quality assurance program shall be maintained for a minimum of ten years. These records shall be made available at the time of site inspection.

The Quality Assurance Program shall establish a system for reporting, documenting, and investigation of deviations. Deviations for distributed tissue relating to core CGTPs must be reported to the federal regulators and EBAA.

The eye bank's quality assurance program shall include a method for the receiving surgeon to report adverse reactions from the transplantation of corneal, scleral, or other ocular tissue to the distributing eye bank. The distributing eye bank must forward the adverse reaction information to the source eye bank, which made the donor eligibility determination. The source bank must perform an investigation and must report the adverse reaction information within 30 days to the EBAA office for review by the Medical Advisory Board. In accordance with FDA 1271.350, adverse reactions involving a relevant communicable disease must be reported to the FDA within 15 calendar days of receipt of the information if the adverse reaction is fatal, life-threatening, results in permanent impairment or damage or requires medical or surgical intervention.

The source bank must notify all entities involved in the recovery, processing, storage, distribution, tissue evaluation, and donor eligibility determination of the results of the investigation. Each of the involved entities must maintain documentation of the adverse event and results of the investigation forwarded to it by the source bank.

Infection of a systemic nature that the medical director's investigation determines to be possibly, likely/probable or definitely due to donor tissue must be communicated to all entities that recovered organs or received or recovered tissues from that donor.

An adverse reaction reportable to the EBAA is any communicable or other disease that is possibly, reasonably likely/probable, or definite/certain to have been transmitted by

transplantation of donor eye tissue, including infection (as manifested by endophthalmitis, keratitis or systemic disease) and biologic dysfunction (such as immediate endothelial failure, donor corneal dystrophy, malignancy, or evidence suggestive of prior refractive surgery). If systemic infectious disease such as HIV, hepatitis, syphilis, West Nile Virus (WNV), or Creutzfeldt Jakob Disease (CJD) develops in a recipient, whether or not it is suspected to be due to donor tissue, this must be reported to the EBAA office. The Medical Director shall receive and review all adverse reaction reports, documenting any corrective actions he/she determines are indicated.

G1.100 Quality Control

The Director shall prescribe tests and procedures for measuring, assaying or monitoring properties of tissues essential to the evaluation of their safety for transplantation, e.g., hepatitis B surface antigen and human immunodeficiency virus (HIV) antibody, and conform with federal requirements as well as individual state laws. Results of all such tests or procedures, together with evaluations based on these findings, shall become part of permanent record of all tissues intended for surgical use.

G1.200 Microbiologic Culturing

Culturing of eye bank donor eyes may be performed despite the recognition by many that bacteriologic contamination of donor eyes does not necessarily lead to infection and that presurgical or surgical cultures may not correlate with postoperative infection if it should occur. Cultures may be performed either before and/or at the time of surgery.

a. Presurgical Cultures

Eye banks may elect to perform corneoscleral disc cultures at the time of corneal preservation in storage solution. Positive culture reports shall be reported to the receiving surgeon or recipient eye bank.

b. Surgical Culturing

Each eye bank shall indicate on the information sheet accompanying the tissue for transplantation whether corneoscleral disc cultures were performed prior to distribution. Positive results in cases of postoperative infection shall be reported to the eye bank that recovered the tissue as well as to the eye bank that distributed the tissue.

G1.300 Tissue Recall or Tissue Withdrawal

Eye banks must have a policy and procedure for potential recall of tissue.

Positive test results or information about behavioral risks or medical history, received after release of tissue, that indicate a risk for transmission of a relevant communicable disease must be reported to the:

- Eye bank's medical director
- Consignee (i.e. the transplanting surgeon, processor or distributing eye bank), within 45 days
- EBAA office, within 45 days
- FDA or other appropriate government agency, within 45 days

Consignee notification of positive test results or information that does not indicate a risk of transmission of a relevant communicable disease does not require EBAA notification.

H1.000 **Non-Surgical Donor Tissue**

The use of ocular tissue from a donor determined to be ineligible is not prohibited for non-clinical uses, so as long as they bear the Bio-hazard legend and are labeled “For Non-clinical Use Only”.

Tissue distributed for non-clinical purposes (e.g., teaching and/or research) from a donor who has been determined to be ineligible for transplantation due to results of required testing and/or screening or from donors who have not been tested for required infectious diseases, must have a label affixed to the individual tissue container which contains the information below.

1. “For Non-clinical Use Only”
2. “Bio-hazardous” or bio-hazard legend

I1.000 **Storage**

All tissue shall be transported and stored in quarantine from the time of recovery until the donor eligibility determination has been completed. Quarantined tissue must have a label designating the tissue as “quarantine” affixed to the individual tissue container.

All surgical tissue shall be stored in quarantine in a physically separate area clearly identified for such use, or through use of other procedures such as automatic designation, until a donor eligibility determination has been made.

If a donor is determined ineligible, the tissue must be stored or identified in a physically separate area labeled for such use, or other procedures must be followed that are adequate to prevent improper release.

All tissue shall be stored aseptically at a temperature appropriate to the method of preservation used. Eye banks must precisely document their procedures for storage of corneal tissue, whether it is in the form of the whole eye or the corneoscleral disc in an appropriate storage solution.

11.100 Expiration Dating

Where appropriate, an expiration date must be assigned based upon methods of processing, preservation, storage, and packaging.

J1.000 **Labeling**

All ocular tissue distributed for surgical use shall be in a container which is clearly and indelibly labeled to include at least the information below.

All tissues:

1. Name of source eye bank.
2. Tissue identification number. There must be a unique identification number for each ocular tissue or fraction thereof.
3. Type of tissue (e.g. cornea, whole eye, sclera).
4. If cornea has had additional processing (e.g. lamellar, laser shaped), clearly indicate this on the label.
5. Expiration date of tissue.
6. A statement that the tissue is intended for single patient application only.
7. A statement that the tissue is not to be considered sterile unless tissue has been subjected to a validated process to ensure sterility.
8. Type of storage solution.
9. Utilize ISBT 128 identifiers to label ocular tissue products, effective January 1, 2016. These identifiers include the Donation Identification Number (DIN), Product Code, and all dates.
10. ISBT 128 data structures shall be used within two-dimensional (2-D) symbols (Data Matrix) to label ocular tissue products distributed internationally, effective January 1, 2017.

Short and intermediate term preserved tissues:

1. Date and time of donor's death.
2. Date and time of initial corneal/scleral preservation.

K1.000 **Distribution of Tissue**

K1.100 Review of Donor Medical Information

Prior to distribution of tissue for transplantation, the Medical Director or his/her designee shall review and document that the medical and laboratory information is in accordance with medical standards, and that any departures from procedure do not increase the risk of communicable disease transmission.

K1.200 Distribution Compliance

Compliance with EBAA medical standards shall be maintained in eye bank functions performed through distribution. An eye bank performing distribution shall inform the consignee, in writing, of requirements for tracking and traceability, outcomes and adverse reaction reporting. Compliance with applicable laws, regulations and standards in eye bank functions performed after distribution is the responsibility of the consignee.

K1.300 Fair and Equitable System

Eye banks shall establish and document a system of distribution for transplant tissue that is just, equitable and fair to all patients served by the eye bank. Documentation of distribution requests for, offers of, and delivery of eye tissue shall be available for inspection by the Accreditation Board. Access to tissue shall be provided without regard to recipient sex, age, religion, race, creed, color or national origin.

K1.400 Returned Tissue

For transplant tissue returned and redistributed, tissue transportation and storage information must be documented and made available to the eye bank and transplanting surgeon. For special research studies, by recommendation of the Medical Advisory Board and approval by the EBAA Board of Directors, such tissue transportation and storage information may be withheld from the transplanting surgeon.

K1.500 Fraudulent Activity

If the eye bank discovers fraudulent activity has occurred in the distribution, shipping or labeling of any tissue imported or exported by the eye bank, an investigation shall be performed to identify the root cause of the occurrence. The eye bank shall report the occurrence and their findings to the EBAA within 10 days following identification of the fraudulent activity. The EBAA office shall notify the appropriate regulatory bodies of the alleged fraudulent activity. The eye bank will copy the EBAA on all future correspondence related to the fraudulent activity during their follow up.

L1.000 **Documentation to Accompany Donor Tissue**

L1.100 Tissue Report Form

For special research studies, by recommendation of the Medical Advisory Board and approved by the EBAA Board of Directors, certain specific data may be masked on the tissue report form and label. A copy of the tissue report form shall accompany the tissue. The tissue report shall contain the following:

All Tissues:

1. Name of (Source) eye bank
2. Location of eye bank
3. Telephone number of eye bank
4. Eye bank identification number unique to each tissue graft. Effective January 1, 2016, utilize ISBT 128 Donation Identification Number (DIN) and Product Code.
5. Type of storage solution
6. If cornea is processed, clearly indicate the type of processing performed or the indicated use (e.g. endothelial keratoplasty, posterior lamellar keratoplasty, anterior lamellar keratoplasty, laser assisted keratoplasty, etc.).
7. Report requirements by processing type according to Matrix II.
8. Name and EBAA Accreditation Status of each establishment that performs any of the following steps in the preparation of tissue: recovery, processing, storage, evaluation, donor eligibility determination and distribution.
9. A summary of records reviewed regarding the eligibility of tissue for transplant.

Short and intermediate term preserved tissues:

1. Age of donor
2. Cause of death
3. Death date and time
4. Preservation date and time
5. Additional tissue processing date and time
6. The time that cooling of ocular tissues and/or refrigeration of the body was begun
7. Name of technician who enucleated, excised, processed, and evaluated the tissue
8. Report requirements by processing type according to Matrix II.

Matrix II:

Post-Processing Reporting Requirements					
Processing Type	Morphology and Dimensions of Cut	Diameter of Cut	Pachymetry	Pre/Post-Processing Slit Lamp Exam	Pre/Post-Processing Endothelial Cell Density Reports
LAK	Yes	No	No	Yes	Yes
DSAEK	No	Yes	Yes	Yes	Yes
DSEK	No	Yes	Yes	Yes	Yes
DMAEK	No	No	No	Yes	Yes
DMEK	No	No	No	Yes	Yes
ALK	No	Yes	Yes	Yes	No
Short Term Preservation	As above	As above	As above	Yes*	Yes**
Intermediate Term Preservation	As above	As above	As above	Yes*	Yes**
Long Term Preservation	As above	As above	As above	Yes*	Yes**

*only for tissue intended for optical, as opposed to tectonic surgeries

**only for tissue deemed suitable for procedures in which the transplant outcome is dependent upon viable endothelium

L1.200 Package Insert Form

A “Package Insert” form that meets the EBAA requirements defined below shall accompany the tissue for transplantation. This form shall include the following:

1. Recommended storage temperature for specific type of tissue (cornea; sclera; whole eye). Specific emphasis on DO NOT FREEZE for corneas.
2. That the surgeon should check for integrity of the seal and immediately report to the eye bank any evidence of possible tampering.
3. For corneas in intermediate-term storage solution, a color change per the manufacturer’s guidelines may indicate a change in pH, in which case the tissue should not be used and a report made immediately to the eye bank.
4. Whether pre-surgical microbiologic cultures were performed by the eye bank.
5. The form shall also advise the receiving surgeon that the tissues are delivered with no warranty as to merchantability or fitness for a particular purpose, and that the receiving surgeon is ultimately responsible for judging if the tissue is suitable for use.
6. The form shall advise the consignee that they are responsible for tracking of the tissue recipient’s name, unique identification number, age and/or date of birth, diagnosis, date of surgery, location of surgery, type

of surgery, and the name of the transplanting surgeon when the tissue is transplanted. This information is needed to track the tissue from the donor to consignee and from the consignee to the recipient.

7. Infectious disease tests were performed by a CLIA certified and FDA registered laboratory.
8. That FDA approved tests were used for infectious disease testing as required by the FDA and EBAA, some of which are approved for pre-mortem blood and that FDA approved tests for cadaveric blood were used where available.
9. A list of infectious disease test results for that specific donor.

This information may be included on the eye bank's donor screening form as long as it is easily noticed; otherwise a separate package insert form is advised.

L2.000 Packaging, Sealing and Packing for Transport

Each tissue for distribution shipment shall be individually packaged and sealed with a tamper-evident seal or enclosed in a tamper evident container.

Each tissue for predistribution shipment transported by a secondary carrier shall be sealed with a tamper-evident seal or enclosed in a tamper-evident container.

Corneal tissue in intermediate-term storage solution shall be packaged using a method designed to maintain cool conditions and prevent freezing. The package content should demonstrate remaining coolant effect at the time of use or removal to mechanical storage or replacement of the coolant. For tissue preserved by other methods such as long-term preserved, organ culture, or short-term preserved tissue, the packaging method shall be appropriate to the method of preservation used. Packing shall be done so that the tissue label and documentation to accompany the tissue do not become wet. Special instructions shall be included on a Package Insert. See *Section L1.200*.

M1.000 Eye Bank Records

Eye banks shall utilize ICCBBA Eye Bank Technical Advisory Group (EBTAG) nomenclature to describe ocular tissue classes and attributes, effective June 30, 2015.

All records shall utilize ISBT 128 identifiers, effective January 1, 2016. This includes the Donation Identification Number (DIN) and Product Code.

M1.100 Length of Storage

All records shall be kept for a minimum of ten years from the date of transplantation/implantation, distribution or whichever is longer.

M1.200 Confidentiality

All eye bank records and communications between the eye bank and its donors and recipients shall be regarded as confidential and privileged.

M1.300 Donor Screening Forms

Donor screening forms shall contain information regarding the circumstances surrounding the death of a donor and adequate medical history so that the eligibility of the tissue for transplantation may be judged.

M1.400 Minimum Information to Be Retained

Forms for retaining donor and recipient or consignee information shall be established and shall be readily accessible for inspection by the EBAA Accreditation Board. Eye bank records shall include the following minimum information:

See Section L1.000 for information to be included on the Tissue Report Form.

1. Eye bank identification number unique to each tissue graft
2. Name of eye bank
3. Type of storage solution
4. Storage solution lot numbers
5. Unique donor identification number
6. Name of donor (or if import tissue, name of importing eye bank and their unique ID number)
7. Age of donor
8. Cause of death
9. Death date and time
10. Enucleation or in situ excision date and time
11. Preservation date and time
12. The time that cooling of ocular tissues and/or refrigeration of the body was begun
13. Additional tissue processing date and time
14. Slit lamp report(s)
15. Endothelial cell density(ies) (if applicable)
16. Name of enucleator/processor/evaluator/technician
17. Name of surgeon or consignee receiving tissue
18. Tissue readily traceable from donor to consignee for each unique graft number (See Section M1.500)
19. Date, time, method of transportation
20. Utilization of tissue: i.e., surgical, research, training
21. Printed results of all EBAA required and non-required infectious disease screening tests
22. Microbiologic screening results if performed

23. Microbiologic reports of positive donor rim cultures from the receiving surgeon if reported
24. Adverse reactions if reported
25. Documentation that post-operative outcome information from the transplanting surgeon has been requested

M1.500 Recipient Follow-Up Information

1. Each distributing eye bank shall obtain consignee name and address information for each eye tissue used for human transplantation distributed by the bank.
2. Each distributing eye bank shall seek:
 - Patient's name (if allowed by law)
 - Unique identification according to the following order of preference:
 - a. Social security number
 - b. Driver's license number
 - c. Hospital information number
 - d. Alien identification
 - e. Passport number
 - f. Other unique identifier appropriate to the health care delivery system where surgery is performed
 - Age and/or Date of Birth
 - Diagnosis
 - Name of surgeon receiving transplanting tissue
 - Date of surgery
 - Location of surgery
 - Post-operative complications (tissue related)
 - Type of surgery performed, e.g. penetrating keratoplasty, anterior lamellar keratoplasty, endothelial keratoplasty, keratolimbal allograft, and/or tectonic
3. Corneas and scleral tissue that can be used beyond 14 days post-mortem may be stocked at an institution only if it is for single patient use; the distributing eye bank must be able to track the tissue to the consignee.
4. Each distributing establishment must request postoperative outcome information between three and six months after transplant from the consignee concerning possible adverse reactions on all cornea tissue, except long term preserved, used for human transplantation that was distributed to the consignee by that bank. This request must be addressed to the transplanting surgeon and delivered separately from the documentation that accompanies the eye tissue. For special research studies where postoperative outcomes are monitored by other means, by recommendation of the Medical Advisory Board and approval by the

EBAA Board of Directors, eye bank solicitation of postoperative outcome information and documentation of such solicitation (under M1.400 item 25) will not be required.

M1.600 Statistical Reporting

Each eye bank shall report statistics to the EBAA in accordance with a policy established by the EBAA Board.

Each source eye bank shall report information on surgical technique and indications for surgery.

N1.000 Amendments

These standards may be amended as required.

The Medical Advisory Board shall be charged with proposing amendments to these standards as medical technology, techniques and information require. A comment period may be provided prior to the intended effective date.

Glossary Definition of Terms

***Note:** The Eye Bank Association of America (EBAA) Glossary pertains to association members, which are required to meet EBAA Medical Standards and follow applicable federal and state regulations.*

Where applicable, the EBAA uses ICCBBA Eye Bank Technical Advisory Group (EBTAG) nomenclature to describe ocular tissue classes, storage state, storage solution, and pathogen reduction methodology.

Adverse Reaction (EBAA reportable). Any communicable or other disease that is possibly, reasonably likely/probable or definite/certain to have been transmitted by transplantation of donor eye tissue including infection and biologic dysfunction. See also **Eye Bank Association of America (EBAA) Medical Standard G1.000**. (Reference: Guidance Document for Investigating and Reporting Adverse Reactions to the EBAA)

Ambient Storage. Stored in a solution at ambient temperature.

Anterior and Posterior Layers. A pre-cut cornea where both the anterior and posterior layers are present.

Anterior Lamellar Keratoplasty. Transplantation of the anterior stroma of the cornea.

Anterior Layer. Corneal stroma without endothelium. May include epithelium.

Aseptic Technique. Method by which contamination with microorganisms is prevented.

Audit. A documented review of procedures, records, personnel functions, equipment, materials, facilities, and/or vendors to evaluate adherence to the written SOP, standards, or federal, state and/or local laws and regulations.

Autologous use. The implantation, transplantation, infusion, or transfer of human cells or tissue back into the individual from whom the cells or tissue were recovered.

CDC. An abbreviation for the *Centers for Disease Control and Prevention*, Atlanta, Georgia.

CFR. An abbreviation for the *Code of Federal Regulations*. Published by the Office of the Federal Register, National Archives and Records Administration, Washington, DC.

CJD. An abbreviation for *Creutzfeldt-Jakob Disease*.

Colloid. A protein or polysaccharide solution such as albumin, dextran, or hetastarch that can be used to increase or maintain osmotic (oncotic) pressure in the intravascular compartment, or certain blood components, such as plasma and platelets.

Complaint. Any written or oral communication concerning dissatisfaction with the identity, quality, packaging, durability, reliability, safety, effectiveness, or performance of tissue.

Competency. The ability of an employee to acceptably perform tasks concomitant with his/her educational level for which he/she has been trained.

Competency Assessment. The evaluation of the ability of an employee to acceptably perform tasks that are expected of the employee for the duties/responsibilities assigned to him/her.

Conjunctiva. Transparent mucous membrane passing over the inner surface of the eyelids and reflected over the front part of the sclera

Consent. A process where approval for donation is obtained from the donor (called “First Person consent” or “FP”) or the donor’s next of kin or other legally recognized representative.

Consignee. Any eye bank, eye banking intermediary or transplanting surgeon (whether individual, agency, institution, or organization) that receives tissue and assumes responsibility for any step in the processing, storage, distribution and/or use of such tissue.

Container. A receptacle that is used to contain tissues and is in direct contact with the tissue.

Contract Services. Those functions pertaining to the recovery, screening, testing, processing, storage, and/or distribution of tissue that another establishment agrees to perform for an eye bank.

Cornea. Transparent anterior part of the outer fibrous coat of the eye bounded by an outer stratified epithelium and an inner monolayer of endothelial cells. The major refractive component of the eye.

Corneal Button. Cornea with scleral rim removed.

Corneoscleral Disc. Cornea excised with scleral rim which may include some conjunctiva.

Cross-Contamination. The transfer of infectious agents from one tissue to another tissue, or from one donor’s tissue to another donor’s tissue.

Cryopreserved. Preserved by freezing or vitrification in the presence of a cryoprotectant and using a method validated to maintain cellular viability and/or preserve tissue matrix structure. The information about the cryoprotectant may be specified using the storage solutions attribute group or on the tissue container label or in accompanying documentation.

Crystalloid. A balanced salt and/or glucose solution, such as saline, TPN (total parenteral nutrition), Ringer’s lactate solution, or 5 percent dextrose in water, used to replace electrolytes or to increase intravascular volume.

Decontamination. The use of physical or chemical means to remove, inactivate, or destroy bloodborne pathogens on a surface or item to the point where they are no longer capable of transmitting infectious particles and the surface or item is rendered safe for handling, use, or disposal.

Dehydration. The removal of water from cells and/or tissue.

Departure from Procedure/Accident. A planned excursion from a SOP. If the SOP is relevant to preventing risks of communicable disease transmission, a responsible person must determine the departure does not increase the risks of communicable disease transmission and must document the decision.

Designee. A person authorized by responsible party to perform assigned duties.

Deviation/Error. An unplanned excursion from a current good practice, applicable standard, or established specification.

Disinfectant. An agent that reduces the number of viable cellular microorganisms.

Disinfection. A process that reduces the number of viable cellular microorganisms, but does not necessarily destroy all microbial forms, such as spores and viruses.

Disposition. The final destination of tissue, including use for transplantation, education, research, or discard.

Distributing Eye Bank. An entity that is reimbursed for or invoices for providing tissue to the end user. Shall be responsible for tracking recipient or consignee information, post op follow up and reporting any adverse reaction to the source establishment.

Distribution. A process of allocation of tissue for transplant, research or educational use. This process includes receipt of request, selection, inspection and release of tissue, to a consignee such as a surgeon, surgical center or educational research center. The principles of tracking, traceability and adverse reaction reporting will be maintained throughout the process of distribution.

Donor. A living or deceased individual who provides the source of tissue for transplantation, education, or research.

Donor Eligibility Determination. The evaluation of all available information about a potential donor to assess whether the donor meets qualifications specified in the SOP and standards. This includes, but is not limited to: medical, social, and sexual histories; laboratory test results; physical assessment or physical examination; and autopsy findings (if performed).

Donor Referral Sources. Entities such as hospitals, medical examiners, coroners and individual allied health care professionals or others who identify potential eye tissue donors and refer them to eye banks.

Donor Risk Assessment Interview. A documented dialogue in person or by telephone with an individual or individuals who would be knowledgeable of the donor's relevant medical history and social behavior. For example this may be: the donor, if living; the next of kin; the nearest available relative; a member of the donor's household; other individual with an affinity relationship (e.g., caretaker, friend, significant life partner); and/or the primary treating physician. Alternatively, a living donor may complete a written questionnaire. Relevant social history is elicited by questions regarding certain activities or behaviors that are considered to place such a potential donor at increased risk for a relevant communicable disease agent or disease.

Donor Screening. See **EBAA Medical Standard D1.100.**

End User. A hospital, surgeon, surgicenter, research center or any entity that utilizes tissue provided by an eye bank.

Endothelial Keratoplasty. Transplantation of the corneal endothelium attached to a carrier.

Enucleation. Recovery of the whole eye.

Equipment Qualification. Protocols designed to adequately evaluate, prior to use, whether or not pieces of equipment will perform to expectation, and normally function within the required tolerance limits.

Evaluation. The assessment of an entity, tissue, equipment, personnel, performance in relation to predetermined expectations or standards.

Expiration Date. The date after which instruments, supplies or tissues are deemed no longer suitable for use.

Eye Bank. An entity that provides or performs one or more functions involving ocular tissue from living or deceased individuals for transplantation, research, and/or educational purposes. See Eye Bank Functions.

Eye Bank Functions. Functions performed by an eye bank that subject the eye bank to accreditation policies of the EBAA, including 1) recovery, 2) processing, 3) storage, 4) tissue evaluation, 5) donor eligibility determination, and 6) distribution.

FDA. An abbreviation for the United States *Food and Drug Administration*.

Fraudulent activity. Any activity that involves potentially falsified tissue, tissue documents or labeling of tissue containers of imported or exported tissue for transplant or research

Freeze Dried. (Lyophilized) Preservation in the dried state achieved by freezing followed by sublimation of water under vacuum to very low residual moisture content.

Freezing. The cooling of tissues to a set temperature below 0°C without the addition of a cryoprotectant.

Frozen. Stored in the frozen state, but without additives specifically to protect cells/matrix and/or without the controlled freezing conditions required for cryopreservation.

Graft. Tissues prepared for use in transplantation.

HBc. An abbreviation for *hepatitis B core*.

HBsAg. An abbreviation for *hepatitis B virus surface antigen*.

HCV. An abbreviation for *hepatitis C virus*.

HIV. An abbreviation for *human immunodeficiency virus*.

HTLV. An abbreviation for *human T-cell lymphotropic virus*.

Hypothermic Storage. Stored in a solution at 2 to 8°C

Identification Number. A unique numeric or alphanumeric designation assigned to, and thus associated with, a donor or recipient, a specific establishment (or facility) and tissues for the purpose of tracking and confidentiality. If donated ocular tissue is divided, a unique donor identification number is distinctly assigned to each part.

Intermediate Term Preservation. Cornea or corneal section preserved in a solution that maintains cellular and/or ultrastructure viability for 14 days. Intermediate term preservation is currently utilized at 2-8°C storage temperatures. Examples of intermediate term storage media are: Life4°C, Optisol GS, and Eusol.

Laser Assisted Keratoplasty. Corneal surgeries in which wound architecture is processed by laser.

- a. **Laser Assisted Anterior Keratoplasty.** Anterior keratoplasty in which the lamellar and/or side dissection of the donor tissue is processed using a laser.
- b. **Laser Assisted Endothelial Keratoplasty.** Endothelial keratoplasty (surgery) in which the lamellar and/or side dissection of the donor tissue is processed using a laser.
- c. **Laser Assisted Penetrating Keratoplasty.** Penetrating keratoplasty in which the donor and recipient wound architecture are processed by laser.

Laser Shaped. Full-thickness cornea shaped to a specific edge profile using laser technology.

Limbal Tissue. Tissue bridging the junction between the cornea and sclera.

Long Term Preservation. Cornea or corneal section stored in a solution that is designed to maintain tissue ultrastructure for greater than 14 days and up to five years depending on the technique. Viability is not maintained. Examples are ethanol and glycerin preservation. Other media, such as albumin, may be used in conjunction with ionizing radiation to preserve the tissue ultrastructure.

Medical Director. See **EBAA Medical Standard C1.200.**

Microorganism. A microscopic organism; viruses, while sometimes included in this classification, are not included here.

Moist Chamber. Whole eye stored at 2 to 8°C in a humid environment.

Next Of Kin. The person(s) most closely related to a deceased individual as designated by applicable law such as the Uniform Anatomical Gift Act.

NIST. An abbreviation for the *National Institute of Standards and Technology.*

ODO. An abbreviation for *organ donation organization.*

OPO. An abbreviation for *organ procurement organization.*

Organ Culture. Stored in a nutrient medium at 28° to 37° Celsius.

Package. A labeled carton, receptacle, or wrapper containing one or more containers and accompanying labeling and package insert materials.

Package Insert. The written material accompanying tissue bearing further information about the tissue, directions for use, and any applicable warnings.

Pathogen Reduction. Describes the method of sterilization, disinfection or decontamination of the product.

Physical Assessment. A limited autopsy or recent ante-mortem or post-mortem physical examination of the donor to assess for signs of a relevant communicable disease and for signs suggestive of any risk factor for a relevant communicable disease.

Physical Examination. See Physical Assessment.

Plasma Dilution. A decrease in the concentration of the donor's plasma proteins and circulating antigens or antibodies resulting from the transfusion of blood or blood components and/or infusion of fluids, i.e., colloid(s) and/or crystalloid(s).

Policies and Procedures Manual. A group of standard operating procedures (SOPs) that detail the specific policies of an eye bank and the procedures used by the staff/personnel. This includes but is not limited to, procedures to assess donor eligibility; this includes operations such as;

screening, recovery, processing, evaluation, testing, quarantine, labeling, storage, distribution, tracking, disposition, and recalling tissue.

Posterior Layer. Endothelium on Descemet membrane with or without a supporting layer of posterior stroma.

Pre-Cut Tissue. Corneal tissue in which lamellar or vertical dissection has been processed for surgical use, by eye bank or other organization, prior to distribution for surgical use.

Pre-Distribution Shipment. Shipment of tissue in quarantine within an establishment or between establishments (recovering eye bank to processing eye bank) of tissue that has not been released for distribution. Tissue must be shipped in quarantine.

Preservation. The use of chemical agents, alterations in environmental conditions or other means to prevent or retard biological or physical deterioration of ocular tissues.

Primary Graft Failure. Corneal edema present from the time of keratoplasty that does not clear after eight weeks and in which there is no known operative or postoperative complication or underlying recipient condition that would explain the biologic dysfunction

Procedure. A series of steps, which when followed, are designed to result in a specific outcome.

Process Controls. A system of checks and balances incorporated into standard operating procedures involving critical operations to prevent errors.

Process Validation Studies. The process of demonstrating a specific process or procedure will consistently produce expected results within predetermined specifications.

Processing. Any activity performed on the eye tissue, other than recovery, donor screening, donor testing, storage, labeling, packaging, or distribution, such as: testing for microorganisms; preparation, sterilization, steps to inactivate or remove adventitious agents; preservation for storage; manipulation/sizing and removal from storage. Any manipulation of the ocular tissue intended for transplant that involves opening a previously sealed container after recovery.

Processing Establishment. The entity that performs post-recovery tissue processing.

Procurement. See **Recover(y)**.

Proficiency. An evaluation of laboratory methods and test results that assesses the quality of standard operating procedures, equipment, supplies, and reagents, as well as the skill of the personnel performing the testing.

QA. An abbreviation for *quality assurance*.

QC. An abbreviation for *quality control*.

Qualification. The method of establishing confidence that equipment, reagents, and ancillary systems are capable of consistently operating within established limits and tolerances. Process performance qualification is intended to establish confidence that the process is effective and reproducible.

Qualified. Deemed competent by a recognized authority.

Quality. The conformance of ocular tissue or a process with pre-established specifications or standards.

Quality Assurance (QA) Program. A program that: 1) defines the policies and environment required to meet standards of quality and safety and, 2) provides confidence that the processes and tissue consistently conform to requirements for quality. Dimensions of QA may include quality control, auditing and process control, standards for personnel, facilities, procedures, equipment, testing, and record keeping activities.

Quality Control (QC). Specific tests defined by the eye bank's QA Program to be performed to monitor retrieval, processing, preservation and storage, tissue quality, and test accuracy. These may include, but are not limited to: performance evaluations, inspection, testing, and controls used to determine the accuracy and reliability of the eye bank's equipment and operational procedures, as well as the monitoring of supplies, reagents, equipment, and facilities.

Quarantine. The identification of ocular tissue as not currently eligible for transplantation, including ocular tissue that has not yet been characterized as being eligible for transplantation. Quarantine includes the storage of such tissue in an area clearly identified for such use, or other procedures, such as automated designation, to prevent the premature release of such ocular tissue for transplantation.

Recall. An action taken to locate and retrieve tissue from distribution and dispensary inventories. Removal or correction of a marketed product that the FDA considers to be in violation of the laws it administers and against which the agency would initiate legal action, e.g., seizure. Recalls may be conducted on a firm's own initiative, by FDA request, or by FDA order under statutory authority. (Reference: EBAA Tissue Recall Guidance Document)

Receiver. An establishment (facility or entity) or individual that accepts shipment of distributed tissues for transplantation (e.g. physicians, dentist, institutions, and other eye banks).

Recipient. An individual who receives an ocular tissue transplant.

Recover(y). The removal, acquisition, recovery, or collection of donor tissue.

Recovery Establishment. Entity that recovers tissue from a donor.

Relevant Communicable Disease. Any communicable disease relevant to transplantation of tissue in humans as defined by FDA regulations, FDA guidance documents or US law.

Relevant Medical Records. A collection of documents including a current donor risk assessment interview, a physical assessment/physical examination of the donor, laboratory test results (in addition to results of testing for required relevant communicable disease agents), relevant donor records, existing coroner and autopsy reports, as well as information obtained from any source or records that may pertain to donor eligibility regarding high risk behaviors, and clinical signs and symptoms for any relevant communicable disease agent or disease (RCDAD), and/or treatments related to medical conditions suggestive of such risk.

Repeat Reactive. A blood sample that is reactive on initial testing and is still reactive in at least one of two duplicate samples when the same test is repeated using the same blood sample.

Resolution. Adjustment, clarification, and/or correction of practices and/or procedures that results in compliance with the SOPM and/or standards.

Responsible Party. A person who is authorized to perform designated functions for which he or she is trained and qualified.

Retrieval. See Recover(y).

Safety. A level of quality of tissue that indicates handling according to acceptable standards and assures substantial freedom from the potential for harmful effects to recipients. The condition of being protected from risk or injury associated with occupational exposure.

Satellite Facility. An establishment in a location physically separate from its main facility where any activities occur that contribute to screening, recovery, transport, processing, evaluation, testing, quarantine, labeling, storage, distribution, tracking, disposition, or recall of ocular tissue under the management or direct supervision of the same corporate entity or its employee(s).

Sclera. Fibrous white outer part of the eye remaining after excision of the corneoscleral disc and removal of intraocular content and extraneous surface tissue.

Secondary Carrier. Any transporter of tissue that is not directly employed by the eye bank. Examples include, but are not limited to, contracted couriers, volunteer drivers, and commercial carriers.

Services to Donor Families. A defined policy or program that implements an eye bank's recognition of the value of donation by the consenting party. These may include written communications regarding: potential uses of tissue; recovery outcome information; bereavement support; provision of a copy of the Document of Consent; and/or guidance describing how to contact the eye bank if any questions arise regarding the donation. Frequency of follow-up and program maintenance is at the discretion of the Executive Director.

Shall. A figure of speech used interchangeably with "must."

Short term preservation. Eye tissue preservation techniques that maintain viability and/or ultrastructure for less than 5 days. Examples are whole eyes preserved in a moist chamber at 2-8°C and MK medium.

Should. A figure of speech used to indicate a recommendation; advisory, indicating a commonly accepted activity for which there may be effective alternatives.

SOP. An abbreviation for *standard operating procedures*.

Source Establishment (or Facility). The entity that releases tissue following donor eligibility determination, and is responsible for maintaining donor records and evaluating adverse reaction reports

Standard Precautions. Guidelines recommended by the Centers for Disease Control and Prevention for reducing the risk of transmission of bloodborne and other pathogens. Standard precautions apply to (1) blood; (2) all body fluids, secretions, and excretions except sweat, regardless of whether or not they contain blood; (3) non-intact skin; and (4) mucous membranes. Standard Precautions includes hand hygiene, and the use of appropriate personal protective equipment such as gloves, gown, mask, eye protection, or face shield, whenever touching or exposure to patients' body fluids is anticipated.

Standards. The Medical Standards of the EBAA.

Sterile. The absence of detectable, viable, microorganisms (refer to ANSI/AAMI ST79:2010).

Sterilization. A validated method used to render instrumentation and ocular tissue free from viable microorganisms, including spores (refer to ANSI/AAMI ST79:2010/A4:2013).

Store or Storage. The maintenance of ocular tissue for future use.

Storage Establishment. The entity that stores tissue at any time prior to distribution to the end user.

Storage Solution. Specifies the solution in which the tissue is stored.

Summary of Records. A condensed version of the required testing and screening records that contains the identity of the testing laboratory, the listing and interpretation of all required infectious disease tests, a listing of the documents reviewed as part of the relevant medical records, and the name of the person or establishment determining the eligibility of the ocular tissue for transplantation.

Time of Death. For purposes of eye donation, the time of death is the cessation of heartbeat, cardiac death, asystole, cross-clamp, last known alive (LKA), or it can be the time of death established by core temperature, when applicable and with appropriate documentation from a medical professional.

Tissue. A functional group of ocular cells, such as cornea, sclera. Tissues may be transplanted as viable cells or otherwise preserved or fixed. Tissue does not include perfusable organs for transplantation.

Tissue Bank. An entity that provides or engages in one or more services involving tissue from living or deceased individuals for transplantation, research, and/or educational purposes. These services include but are not limited to assessing donor suitability (including screening), recovery, processing, evaluation, testing, quarantine, labeling, storage, distribution, tracking, disposition, and recall of tissue.

Tissue Evaluation. The performing of any and/or all of the following on eye tissue intended for transplant: slit lamp examination, endothelial cell density, and pachymetry measurement.

Tissue Identification Number. Any unique combination of letters, numbers, and/or symbols assigned to ocular tissue and linked to a donor, from which the complete history of the collection, processing, packaging, quarantine, labeling, storage, and distribution of ocular tissue can be traced.

Tissue Type. Refers to whole eye or a specific portion of the eye, such as cornea or sclera.

Tolerance Limits. The limits that define a range of acceptable values established for each testing procedure that, when exceeded, require the implementation of corrective actions designed to produce results within the acceptable range in future tests.

Traceability. The act or ability to locate ocular tissue during any step of its recovery, processing, evaluation, testing, quarantine, labeling, storage, distribution, disposition, or recall. It includes the capacity to identify the surgeon, consignee, or medical facility receiving the tissue and the ability of the surgeon, consignee, or medical facility to identify the storage, recipient or final disposition of the tissue.

Tracking. The act or ability to locate individual tissue during any step of its recovery, processing, evaluation, testing, quarantine, labeling, storage, distribution, disposition, and recalling. It includes the capacity of the distributing eye bank to identify the consignee and the consignee to identify the recipient.

Transplantation. The transfer of tissue to a recipient.

Transplant Program. An organization of medical personnel and allied health care professionals, operating in one or more transplant centers, with the responsibility for the transplantation of one or more types of tissues, and/or organs.

Transport Medium. Any microbiological medium capable of maintaining cellular viability during the transport of ocular tissue.

Universal Precautions. An approach to infection control, in which all human blood, certain body fluids, as well as fresh tissues and cells of human origin are handled as if they are known to be infected with HIV, HBV, and/or other blood-borne pathogens.

Validation. The method of establishing documented evidence that provides a high degree of assurance that specific process will consistently produce the predetermined outcome.

Variance. A departure from *Standards* that is pre-approved by the EBAA, Medical Director, Executive Director, or governing authority prior to implementation.

Verification. The confirmation by examination and provision of objective evidence that specified requirements have been fulfilled.

Wet Ice Temperatures. Temperatures ranging from 1-10°C.

Withdrawal (or Market Withdrawal). Removal or correction of a distributed product by an eye bank that involves a minor violation that would not be subject to legal action by the FDA, or that involves no violation. Does not involve a relevant communicable disease. No notification to FDA or EBAA is required. (Reference: EBAA Tissue Recall Guidance Document)

EBAA Medical Standards Appendix I: FDA Defined Relevant Communicable Disease Agents and Diseases

Introduction

As referenced in EBAA Medical Standard D1.120, this appendix contains excerpts from FDA guidance and reference to FDA regulation pertaining to definition of relevant communicable disease and disease agents. The FDA guidance does not establish legally enforceable responsibilities, but describes the FDA's current thinking on the contained topics and should be viewed only as recommendations unless specific regulatory or statutory requirements are cited. The use of the word "should" in the FDA's guidance means that something is suggested or recommended, but not required.

Further, the EBAA has interpreted the guidance in this appendix. Reformatting, editing, and specific additions have been performed. For direct information from the FDA, one should refer to the documents cited in the below references section. The purpose of this appendix is not only to provide interpretation of the above named document, but to allow the EBAA Medical Standards to be independent of FDA guidance and regulation.

Note: Standard text contains language directly from the FDA guidance whereas text in bold/italics is an interpretation or amendment by the EBAA for clarification in this appendix.

EBAA Guidance

- I. Relevant communicable disease and disease agents specifically listed in § 1271.3(r)(1)
 - a. The following communicable diseases and disease agents are relevant for *ocular tissue* (§ 1271.3(r)(1)(i)):
 - i. Human immunodeficiency virus (HIV), types 1 and 2;
 - ii. Hepatitis B virus (HBV);
 - iii. Hepatitis C virus (HCV);
 - iv. Human transmissible spongiform encephalopathy (TSE); including Creutzfeldt-Jakob disease (CJD); and
 - v. *Treponema pallidum* (syphilis).
- II. A communicable disease agent or disease meeting the criteria described in § 1271.3(r)(2), but not specifically listed in § 1271.3(r)(1), is relevant if it is one
 - a. For which there may be a risk of transmission by *ocular tissue*, either to the recipient of the *ocular tissue* or to those people who may handle or otherwise come in contact with the *ocular tissue*, such as medical personnel, because the disease agent or disease:
 - i. is potentially transmissible by *ocular tissue*; and
 - ii. either (1) has sufficient incidence and/or prevalence to affect the potential donor population (§ 1271.3(r)(2)(i)(B)(1)), or (2) may have

been released accidentally or intentionally in a manner that could place potential donors at risk of infection (§ 1271.3(r)(2)(i)(B)(2));

- b. That 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 (§ 1271.3(r)(2)(ii)); and
- c. For which appropriate screening measures have been developed and/or an appropriate screening test for donor specimens has been licensed, approved, or cleared for such use by FDA and is available (§ 1271.3(r)(2)(iii)).
- d. ***Additional RCDADs not specifically listed in § 1271.3(r)(1), identified in FDA Guidance as relevant include:***
 - i. ***West Nile Virus***
 - ii. ***Sepsis***
 - iii. ***Vaccinia***

References:

21 CFR 1271 Human Cells, Tissues, and Cellular and Tissue-Based Products, rev. 4/1/2009

Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products, August 2007

EBAA Medical Standards Appendix II: FDA-defined Contraindications to Transplant

Introduction

As referenced in EBAA Medical Standard D1.120, this appendix contains excerpts from FDA guidance and reference to FDA regulation pertaining to contraindications for release of ocular tissue for transplant use. The FDA guidance does not establish legally enforceable responsibilities, but describes the FDA's current thinking on the contained topics and should be viewed only as recommendations unless specific regulatory or statutory requirements are cited. The use of the word "should" in the FDA's guidance means that something is suggested or recommended, but not required.

Further, the EBAA has interpreted the guidance in this appendix. Reformatting, editing, and specific additions have been performed. For direct information from the FDA, one should refer to the documents cited in the below references section. The purpose of this appendix is not only to provide interpretation of the cited FDA documents, but to allow the EBAA Medical Standards to be independent of FDA guidance and regulation.

Note: Standard text contains language directly from the FDA guidance whereas text in bold/italics is an interpretation or amendment by the EBAA for clarification in this appendix.

EBAA Guidance

I. Risk Factors

Following is a list of conditions and behaviors that increase the donor's relevant communicable disease risk. Except as noted in this section, and in accordance with § 1271.75(d), you should determine to be ineligible any potential donor who exhibits one or more of the following conditions or behaviors.

- a. Men who have had sex with another man in the preceding 5 years (risk factor for HIV and Hepatitis B).
- b. Persons who have injected drugs for a non-medical reason in the preceding 5 years, including intravenous, intramuscular, or subcutaneous injections (risk factor HIV, Hepatitis B and Hepatitis C).
- c. Persons with hemophilia or other related clotting disorders who have received human-derived clotting factor concentrates in the preceding 5 years (risk factor for HIV, Hepatitis B and Hepatitis C). A donor who received clotting factors once to treat an acute bleeding event more than 12 months ago may be eligible to donate.
- d. Persons who have engaged in sex in exchange for money or drugs in the preceding 5 years (risk factor for HIV, Hepatitis B and Hepatitis C).
- e. Persons who have had sex in the preceding 12 months with any person described (*as above in I.a-d*) or with any person who has HIV infection, including a positive or reactive test for HIV virus, hepatitis B infection, or clinically active (symptomatic) hepatitis C infection.
- f. Persons who have been exposed in the preceding 12 months to known or

suspected HIV, HBV, and/or HCV-infected blood through percutaneous inoculation (e.g., needle stick) or through contact with an open wound, non-intact skin, or mucous membrane.

- g. Children born to mothers with or at risk for HIV infection, ***if the child is 18 months of age or younger, or if the child was breast-fed within the preceding 12 months.***
- h. Persons who have been in juvenile detention, lock up, jail or prison for more than 72 consecutive hours in the preceding 12 months (risk factor for HIV, Hepatitis B and Hepatitis C).
- i. Persons who have lived with (resided in the same dwelling) another person who has hepatitis B or clinically active (symptomatic) hepatitis C infection in the preceding 12 months.
- j. Persons who have undergone tattooing, ear piercing or body piercing in the preceding 12 months, in which sterile procedures were not used, e.g., contaminated instruments and/or ink were used, or shared instruments that had not been sterilized between uses were used.
- k. Persons who have had a past diagnosis of clinical, symptomatic viral hepatitis after their 11th birthday, unless evidence from the time of illness documents that the hepatitis was identified as being caused by hepatitis A virus, Epstein-Barr Virus (EBV), or cytomegalovirus (CMV).
- l. Persons who are deceased and have a documented medical diagnosis of sepsis or have documented clinical evidence consistent with a diagnosis of sepsis that is not explained by other clinical conditions at the time of death. ***An eye bank should make a determination on how to routinely handle situations of clinical history proximal to death in which sepsis was suspected at the time of admission or part of a differential diagnosis during admission in which the patient may have been shown through clinical data not to be septic prior to death.***
- m. Persons who have had smallpox vaccination (vaccinia virus) in the preceding 8 weeks should be evaluated as follows:

For persons who had no vaccinia complications (***including eczema vaccinatum, generalized vaccinia, progressive vaccinia, postvaccinial encephalitis, or vaccinial keratitis***):

- 1. You should defer the donor until after the vaccination scab has separated spontaneously, or for 21 days post-vaccination, whichever is the later date, and until the physical examination or physical assessment includes a confirmation that there is no scab at the vaccination site.
- 2. In cases where a scab was removed before separating spontaneously, you should defer the donor for two months after vaccination.
- 3. ***In cases where the eye bank cannot determine how the scab separated, you should defer if the vaccination was less than 21 days ago. Deferral is not necessary if the scab is not visible upon external examination and the vaccination was greater than 21 days ago.***

4. For persons who have experienced vaccinia complications, you should defer the donor until 14 days after all vaccinia complications have completely resolved. ***Deferral is not necessary if the date of vaccinia complication resolution is indeterminate and there are no visible signs of vaccinia complications.***
 5. Persons who acquired a clinically recognizable vaccinia virus infection by contact with someone who received the smallpox vaccine (i.e., touching the vaccination area or the scab, including the covering bandages, or touching clothing, towels, or bedding that might have come into contact with an unbandaged vaccination area or scab).
 6. ***For cadaveric donors who have received a smallpox vaccination or had close contact with the smallpox vaccination site of someone else, you should examine the skin and defer if a scab or other signs of vaccinia are present.***
 7. You should defer persons who developed other complications of vaccinia infection acquired through contact with a vaccine recipient until 14 days after all vaccinia complications have completely resolved. ***Deferral is not necessary if the date of vaccinia complication resolution is indeterminate and there are no visible signs of vaccinia complications. Deferral is not necessary for anyone who did not develop vaccinia complications.***
- n. Persons who have had a medical diagnosis or suspicion of WNV infection (based on symptoms and/or laboratory results, or confirmed WNV viremia) you should defer for 120 days following diagnosis or onset of illness, whichever is later.
 - o. Persons who have tested positive or reactive for WNV infection, using an FDA-licensed or investigational WNV NAT donor screening test in the preceding 120 days.
 - p. Persons who have been treated for or had syphilis within the preceding 12 months. We do not recommend deferral of donors if evidence is presented that the treatment occurred more than 12 months ago and was successful.
 - q. Persons who have been diagnosed with vCJD or any other form of CJD (Refs. 3 and 75). Note: If the individual knowledgeable about the donor's medical and travel history is not familiar with the term "Creutzfeldt-Jakob Disease" or "variant Creutzfeldt-Jakob Disease," you may try to describe those in layman's terms. If the person being interviewed is still not familiar with those terms, you may consider the lack of familiarity with those terms as a negative response to questions using those terms.
 - r. Persons who have been diagnosed with dementia or any degenerative or demyelinating disease of the central nervous system or other neurological disease of unknown etiology (Refs. 3 and 75). Potential donors who have a diagnosis of delirium (e.g., delirium caused by toxic/metabolic diseases or recent head trauma) would not necessarily be considered to have a diagnosis of dementia and should be evaluated by the Medical Director. (***Ocular tissue*** from

donors with dementia confirmed by gross and microscopic examination of the brain to be caused by cerebrovascular accident or brain tumor and who are confirmed not to have evidence of TSE on microscopic examination of the brain may be acceptable based on an evaluation by the Medical Director).

- s. Persons who are at increased risk for CJD. Donors are considered to have an increased risk for CJD if they have received a non-synthetic dura mater transplant, human pituitary-derived growth hormone, or have one or more blood relatives diagnosed with CJD.
- t. Persons who have a history of CJD in a blood relative unless the diagnosis of CJD was subsequently found to be an incorrect diagnosis, the CJD was iatrogenic, or the laboratory testing (gene sequencing) shows that the donor does not have a mutation associated with familial CJD.
- u. Persons who spent three months or more cumulatively in the United Kingdom (*England, Northern Ireland, Scotland, Wales, the Isle of Man, the Channel Islands, Gibraltar, and the Falkland Islands*) from the beginning of 1980 through the end of 1996.
- v. Persons who are current or former U.S. military members, civilian military employees, or dependents of a military member or civilian employee who resided at U.S. military bases in Northern Europe (Germany, Belgium, and the Netherlands) for 6 months or more cumulatively from 1980 through 1990, or elsewhere in Europe (Greece, Turkey, Spain, Portugal, and Italy) for 6 months or more cumulatively from 1980 through 1996.
- w. Persons who spent 5 years or more cumulatively in Europe (*Albania, Austria, Belgium, Bosnia-Herzegovina, Bulgaria, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Liechtenstein, Luxembourg, Macedonia, Netherlands, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, United Kingdom, and Yugoslavia*) from 1980 until the present (note this criterion includes time spent in the U.K. from 1980 through 1996).
- x. Persons who received any transfusion of blood or blood components in the U.K. or France between 1980 and the present.
- y. ***If the eye bank is not testing for HIV I/II using a test kit specifically labeled as sensitive for detection of HIV group O antibodies, then deferral includes*** persons or their sexual partners who were born or lived in certain countries in Africa (Cameroon, Central African Republic, Chad, Congo, Equatorial Guinea, Gabon, Niger, or Nigeria) after 1977 (risk factor for HIV group O).
- z. ***If the eye bank is not testing for HIV I/II using a test kit specifically labeled as sensitive for detection of HIV group O antibodies, then deferral includes*** persons who have received a blood transfusion or any medical treatment that involved blood in *Cameroon, Central African Republic, Chad, Congo, Equatorial Guinea, Gabon, Niger, or Nigeria*, after 1977 (risk factor for HIV group O).
- aa. Persons who are xenotransplantation product recipients or intimate contacts of a

xenotransplantation product recipient. *Xenotransplantation* is any procedure that involves the transplantation, implantation, or infusion into a human recipient of either: (1) live cells, tissues, or organs from a nonhuman animal source; or (2) human body fluids, cells, tissues, or organs that have had ex vivo contact with live nonhuman animal cells, tissues, or organs.

Xenotransplantation products include live cells, tissues, or organs used in xenotransplantation. Biological products, drugs, or medical devices sourced from nonliving cells, tissues or organs from nonhuman animals, including but not limited to porcine insulin and porcine heart valves, are not considered xenotransplantation products. *Xenotransplantation product* recipient means a person who undergoes xenotransplantation. *Intimate contact of a xenotransplantation product* recipient means a person who has engaged in activities that could result in intimate exchange of body fluids, including blood or saliva, with a xenotransplantation product recipient. ***Intimate partners of recipients of the xenotransplantation product Epicel™ need not be deferred.***

II. Clinical Evidence

Except as noted in this section and in accordance with § 1271.75(d), you should determine to be ineligible any potential donor who exhibits one or more of the following examples of clinical evidence of relevant communicable disease.

- a. HIV Infection
 1. A prior positive or reactive screening test for HIV;
 2. Unexplained weight loss;
 3. Unexplained night sweats;
 4. Blue or purple spots on or under the skin or mucous membranes typical of Kaposi's sarcoma;
 5. Disseminated lymphadenopathy (swollen lymph nodes) for longer than one month;
 6. Unexplained temperature of >100.5°F (38.6°C) for more than 10 days;
 7. Unexplained persistent cough or shortness of breath;
 8. Opportunistic infections;
 9. Unexplained persistent diarrhea; and/or
 10. Unexplained persistent white spots or unusual blemishes in the mouth.
- b. Hepatitis Infection:
 1. A prior positive or reactive screening test for hepatitis B virus or hepatitis C virus;
 2. Unexplained jaundice;
 3. Unexplained hepatomegaly; and/or
 4. Past diagnosis of clinical, symptomatic viral hepatitis after the 11th birthday, unless evidence from the time of illness documents that the hepatitis was identified as caused by hepatitis A virus, EBV, or CMV.

Note: Records of the following laboratory data might assist you in making the donor-eligibility determination in the face of an inconclusive history of hepatitis infection: alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin or prothrombin time. If these tests are

abnormal, but a cause other than viral hepatitis was established, we do not recommend that you defer the donor.

- c. Syphilis Infection:
 - 1. Persons who have had or have been treated for syphilis, in the preceding 12 months. We do not recommend deferral of donors who have had or have been treated for syphilis more than 12 months ago, if evidence is presented that treatment occurred more than 12 months ago and was successful.
- d. Vaccinia Infection:
 - 1. Recent smallpox vaccination;
 - 2. Eczema vaccinatum;
 - 3. Vesicular rash indicative of generalized vaccinia in a person who has had recent smallpox immunization or who is a contact of someone with recent smallpox immunization, as specified in I.m.5. and I.m.6.;
 - 4. Progressive necrosis in an area of vaccination consistent with vaccinia necrosum;
 - 5. Postvaccinial encephalitis; and/or
 - 6. Vaccinial keratitis.
- e. WNV Infection:
 - 1. Mild symptoms might include fever, headache, body aches, or eye pain;
 - i. mild symptoms might also occasionally be accompanied by a skin rash on the trunk of the body; or
 - ii. swollen lymph glands.
 - 2. Severe illness;
 - i. severe illness might include encephalitis, meningitis, meningoencephalitis, and acute flaccid paralysis;
 - ii. signs and symptoms of severe illness might include headache, high fever, neck stiffness, stupor, disorientation, coma, tremors, convulsions, and muscle weakness or paralysis.
- f. Sepsis (including, but not limited to, bacteremia, septicemia, sepsis syndrome, systemic infection, systemic inflammatory response syndrome (SIRS), or septic shock):
 - 1. Clinical evidence of infection; and
 - 2. Two or more of the following systemic responses to infection if unexplained:
 - i. Temperature of $>100.4^{\circ}$ F (38° C);
 - ii. Heart rate >90 beats/min;
 - iii. Respiratory rate >20 breaths/min or PaCO₂ <32 ; or
 - iv. WBC $>12,000$ cells/mm³, $<4,000$ cells/mm³, or $>10\%$ immature (band) forms.
 - 3. More severe signs of sepsis include unexplained hypoxemia, elevated lactate, oliguria, altered mentation, and hypotension.
 - 4. Positive (pre-mortem) blood cultures might be associated with the above signs.

III. Physical Evidence

You should determine ineligible for transplant any potential donor who exhibits one or more of the following examples of physical evidence of RCDADs or high-risk behavior associated with these RCDADs.

- a. Physical evidence for risk of sexually transmitted diseases such as genital ulcerative disease, herpes simplex, chancroid (you should consider these signs in light of other information obtained about the donor in making a donor eligibility determination) (seen in HIV, Hepatitis B virus, *Chlamydia trachomatis*, and *Neisseria gonorrhoeae*).
- b. Physical evidence for risk of, or evidence of syphilis.
- c. For a male donor, physical evidence of anal intercourse including perianal condyloma (seen in HIV and Hepatitis B).
- d. Physical evidence of nonmedical percutaneous drug use such as needle tracks; your examination should include examination of tattoos, which might be covering needle tracks (seen in HIV, Hepatitis B and Hepatitis C).
- e. Physical evidence of recent tattooing, ear piercing, or body piercing. Persons who have undergone tattooing, ear piercing, or body piercing in the preceding 12 months, in which sterile procedures were not used (e.g., contaminated instruments and or/ink were used), or instruments that had not been sterilized between uses were used (seen in HIV, Hepatitis B and Hepatitis C).
- f. Disseminated lymphadenopathy (seen in HIV).
- g. Unexplained Oral thrush (seen in HIV).
- h. Blue or purple spots consistent with Kaposi's sarcoma (seen in HIV).
- i. Unexplained jaundice, hepatomegaly, or icterus (seen in Hepatitis B and Hepatitis C). Note: Hepatomegaly may not be apparent in a physical assessment unless an autopsy is performed.
- j. Physical evidence of sepsis, such as unexplained generalized rash or fever.
- k. Large scab consistent with recent history of smallpox immunization.
- l. Eczema vaccinatum (seen in vaccinia).
- m. Generalized vesicular rash (generalized vaccinia).
- n. Severely necrotic lesion consistent with vaccinia necrosum.
- o. Corneal scarring consistent with vaccinia keratitis.

References:

21 CFR 1271 Human Cells, Tissues, and Cellular and Tissue-Based Products, rev. 4/1/2009

Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products, August 2007

EBAA Medical Standards Appendix III: Donor Eligibility Determinations

Introduction

As referenced in EBAA Medical Standard D1.000, this appendix contains excerpts from FDA guidance and reference to FDA regulation pertaining to donor eligibility determination processes, records, and informational sources. The FDA guidance does not establish legally enforceable responsibilities, but describes the FDA's current thinking on the contained topics and should be viewed only as recommendations unless specific regulatory or statutory requirements are cited. The use of the word "should" in the FDA's guidance means that something is suggested or recommended, but not required.

Further, the EBAA has interpreted the guidance in this appendix. Reformatting, editing, and specific additions have been performed. For direct information from the FDA, one should refer to the documents cited in the below references section. The purpose of this appendix is not only to provide interpretation of the cited FDA documents, but to allow the EBAA Medical Standards to be independent of FDA guidance and regulation.

Note: Standard text contains language directly from the FDA guidance whereas text in bold/italics is an interpretation or amendment by the EBAA for clarification in this appendix.

EBAA Guidance

- I. *The Process of Donor Eligibility Determinations:*
 - a. A donor-eligibility determination is a conclusion ***by a responsible person (Medical Director or Designee)*** that an *ocular tissue* donor is either eligible or ineligible to donate ***for clinical use***, based on the results of donor screening (§ 1271.75) and testing (§§ 1271.80 and 1271.85). Under § 1271.50(b), a donor is eligible ***for clinical use*** only if screening shows that the donor is free from risk factors for, and clinical evidence of, infection due to relevant communicable disease agents and diseases (***RCDADs***), and is free from communicable disease risks associated with xenotransplantation; and test results for relevant communicable disease agents are negative or nonreactive, except as provided in § 1271.80(d)(1) for non-treponemal screening tests for syphilis.
 - b. You must establish and maintain procedures for all steps that you perform in testing, screening, determining donor eligibility, and complying with all other requirements of part 1271, subpart C (§ 1271.47(a)). A responsible person must review and approve all procedures before their implementation (§ 1271.47(b)). These procedures must be readily available to personnel in the area where the procedures are performed, or if this is not practical, in a nearby area (§ 1247(c)). You are authorized under §1271.47(e) to use appropriate standard procedures developed by another organization, provided that you have verified that the procedures are consistent with and at least as stringent as the requirements in part 1271.
 - c. Under § 1271.47(d), at the time a departure occurs, you must record and

justify that departure from a procedure relevant to preventing risks of communicable disease transmission. Before making available for distribution *ocular tissue* from a donor whose eligibility is *to be* determined under such a departure, a responsible person must determine that the departure did not increase the risk of communicable disease transmission. A departure is an intended change from an established procedure, including a standard operating procedure (SOP), which occurs before the *ocular tissue* is distributed, and is consistent with applicable regulations and standards. A departure is different from a deviation, which under § 1271.3(dd) is defined as an event that is inconsistent with applicable regulations, standards, or established specifications, or is unexpected or unforeseeable.

II. Records to Accompany Ocular Tissue After Determination of Donor Eligibility

- a. A distinct identification code (such as an alphanumeric code) affixed to the *ocular tissue* container, that relates the *ocular tissue* to the donor and to all records pertaining to the *ocular tissue* and does not include an individual's name, social security number, or medical record number
- b. A statement *that* based on the results of screening and testing, the donor is determined to be eligible
- c. A summary of the records used to make the donor-eligibility determination, *including*:
 - i. A statement that the communicable disease testing was performed by a laboratory or laboratories certified to perform such testing on human specimens under the Clinical Laboratory Improvement Amendments of 1988 (42 U.S.C. 263a) and 42 CFR part 493 or meeting equivalent requirements, as determined by the Centers for Medicare and Medicaid Services (CMS)
 - ii. A listing and interpretation of the results of all tests performed for relevant communicable disease agents or diseases
 - iii. The name and address of the establishment that made the donor-eligibility determination

III. Information Sources for Review for Donor Eligibility Determination

- a. When you screen *an ocular donor*, you must review relevant medical records for risk factors for, and clinical evidence of *RCDADS* (see Appendix II). Relevant medical records, as defined under § 1271.3(s), means a collection of documents that includes: (1) a current donor medical history interview; (2) a current report of the physical assessment of a cadaveric donor or the physical examination of a living donor; and (3) other available records listed in § 1271.3(s)(1) through (4).
 - i. The donor medical history interview (§ 1271.3(n)) is a documented dialogue concerning the donor's medical history and relevant social behavior with a living donor or if the donor is not living or is unable to participate in the interview, then with one or more individuals who can

provide the information sought. These individuals might be the donor's next of kin, the nearest available relative, a member of the donor's household, an individual with an affinity relationship with the donor (e.g., caretaker, friend, partner), or the donor's primary treating physician.

- ii. The purpose of the physical assessment of a cadaveric donor or the physical examination of a living donor is to assess for physical signs of a relevant communicable disease and for signs suggestive of any risk factor for such a disease (reference Appendix II). For a cadaveric donor, the physical assessment means a limited autopsy, or a recent antemortem or postmortem physical examination (§ 1271.3(o)). For living donors, you may examine only those parts of the body that are necessary to evaluate for **RCDADs** based upon relevant donor history that has been obtained during the interview and review of available records. You may rely on records of a recent report of a physical examination by other health care professionals. Because this is a step in determining donor eligibility, you must establish and maintain standard operating procedures (SOPs) for the conduct of the physical assessment or physical examination (§ 1271.47).
- iii. If they are available, other records that also meet the definition of relevant medical records (§ 1271.3(s)) include
 - laboratory test results (other than the results of testing required for the donor-eligibility determination);
 - medical records;
 - coroner and autopsy reports; and
 - records or other information received from any source pertaining to risk factors for relevant communicable disease (e.g., social behavior, clinical signs and symptoms of relevant communicable disease, and treatments related to medical conditions suggestive of risk for relevant communicable disease). Examples of these records include: medical examiner reports, police records, and information from other tissue or medical establishments, if applicable. ***NOTE: In the absence of autopsy reports available in time for release of transplant use of corneas, an eye bank should review the presumed cause of death and other relevant preliminary autopsy findings, then review the autopsy report when it becomes available after release of tissue.***

References:

21 CFR 1271 Human Cells, Tissues, and Cellular and Tissue-Based Products, rev.

20100331 Appendix III-Eligibility

Rev. 4

Page 3 of 4

4/1/2009

Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products, August 2007

EBAA Medical Standards Appendix IV: Testing

Introduction

As referenced in EBAA Medical Standard D1.220, this appendix contains excerpts from FDA guidance and reference to FDA regulation pertaining to donor testing requirements and recommendations. The FDA guidance does not establish legally enforceable responsibilities, but describes the FDA's current thinking on the contained topics and should be viewed only as recommendations unless specific regulatory or statutory requirements are cited. The use of the word "should" in the FDA's guidance means that something is suggested or recommended, but not required.

Further, the EBAA has interpreted the guidance in this appendix. Reformatting, editing, and specific additions have been performed. For direct information from the FDA, one should refer to the documents cited in the below references section. The purpose of this appendix is not only to provide interpretation of the cited FDA documents, but to allow the EBAA Medical Standards to be independent of FDA guidance and regulation.

Note: Standard text contains language directly from the FDA guidance whereas text in bold/italics is an interpretation or amendment by the EBAA for clarification in this appendix.

EBAA Guidance

I. Donor Testing

- a. You must test all donors of *ocular tissue* for the RCDADs listed below, as required in § 1271.85(a). You must use an FDA-licensed, approved, or cleared screening test (§ 1271.80(c)). ***You must use a donor screening test specifically labeled for cadaveric specimens instead of a more generally labeled donor screening test when applicable and when available. Testing must be performed at a testing facility that has been certified under the requirements of the Clinical Laboratory Improvement Amendments (CLIA) or equivalent requirements as determined by the Centers for Medicare and Medicaid Services.*** You must determine a donor ineligible whose specimen tests reactive for a screening test for a relevant communicable disease agent, ***except for the Treponema pallidum exception below.***

Testing is required for the following RCDADs:

- i. Human immunodeficiency virus, type 1 (HIV-1)
- ii. Human immunodeficiency virus, type 2 (HIV-2)
- iii. Hepatitis B virus (HBV)
- iv. Hepatitis C virus (HCV)
- v. *Treponema pallidum* (Syphilis)

- b. Recommended screening tests per the FDA document titled Guidance for***

Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products, August 2007 for ocular tissue include:

- i. ***HIV, type 1 (FDA-licensed screening test either for anti-HIV-1 or combination test for anti-HIV-1 and anti-HIV-2; and FDA-licensed screening NAT test for HIV-1, or combination NAT); (if the screening test used is not labeled as sensitive for group O antibodies, donors must be evaluated for risk factors associated with HIV group O, described in Appendix II, I.y-z.)***
 - ii. ***HIV, type 2 (FDA-licensed screening test either for anti-HIV-2 or combination test for anti-HIV-1 and anti-HIV-2)***
 - iii. ***HBV (FDA-licensed screening test for Hepatitis B surface antigen (HBsAg) and for total antibody to Hepatitis B core antigen (anti-HBc)(IgG and IgM)***
 - iv. ***HCV (FDA-licensed screening test for anti-HCV; and FDA-licensed screening NAT test for HCV, or combination NAT)***
 - v. ***Treponema pallidum (FDA-cleared screening test for syphilis or FDA-cleared diagnostic serologic test for syphilis). As an exception for syphilis test results under § 1271.80(d)(1), you may determine to be eligible a donor whose specimen tests positive or reactive on a non-treponemal screening test for syphilis and negative or nonreactive on a specific treponemal confirmatory test (e.g., fluorescent treponemal antibody with absorption test (FTA-ABS), so long as all other required testing and screening are negative or nonreactive. A donor whose specimen tests positive or reactive on either a specific treponemal confirmatory test for syphilis or on a treponemal screening test is not eligible. If a cadaveric specimen is too hemolyzed to interpret the Rapid Plasma Reagin (RPR) test result, you should use another test, such as the FTA-ABS test result.***
- c. Current FDA-licensed donor ***screening tests*** for HIV, Hepatitis B, Hepatitis C, and HTLV are listed at the website:
www.fda.gov/cber/products/testkits.htm. You may also ***check this website:***
<http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/TissueSafety/ucm095440.htm#approved> ***for links to HCT/P-related, FDA-licensed, approved or cleared donor screening tests.***

II. Assessment of Donor Specimens for Testing Suitability

You must collect the donor specimen for testing at the same time as tissue is recovered from the donor, or within seven days before or after the recovery of tissue. As you are permitted under § 1271.80(b) to collect the donor specimen up to seven days before recovery of tissues, you may use a premortem specimen to test a cadaveric donor, as long as the specimen is collected within that timeframe. Although there is no requirement that specifies when to test the collected specimen, you should perform testing as soon as possible after collection and in accordance with the time limits stated in the

manufacturer's instructions for use of the test kit.

For adult donors who have suffered blood loss sufficient to require fluid replacement, certain volumes of transfusions and/or infusions should be suspected of affecting test results. Blood loss might occur internally or externally. For donors 12 years of age or younger, you should suspect that any transfusion or infusion might affect test results regardless of blood loss. There might be other clinical situations involving transfusion or infusion that should also be suspected of affecting test results. Autologous blood removed pre-operatively or peri-operatively and reinfused during the same surgical procedure would not need to be included in plasma dilution calculations.

- a. For adult donors, in accordance with § 1271.80(d)(2)(ii)(A), you must suspect plasma dilution sufficient to affect the results of communicable disease agent testing where blood loss is known or suspected in a donor over 12 years of age in any of the following situations (see *Definitions* below for a definition of plasma dilution):
 1. The donor received a transfusion or infusion of more than 2000 milliliters of blood or colloids either (see *Definitions* below for definitions of blood and colloids):
 - i. Within the 48 hours immediately preceding the collection of a pre-mortem specimen for testing; or
 - ii. Within the 48 hours immediately preceding death, if the specimen for testing is collected post-mortem, whichever occurred earlier.
 2. The donor received more than 2000 milliliters of crystalloids within either (see *Definitions* below for a definition of crystalloids):
 - i. The one hour immediately preceding the collection of a pre-mortem specimen for testing; or
 - ii. Within the one hour immediately preceding death, if the specimen for testing is collected post-mortem, whichever occurred earlier.
 3. The donor received more than 2000 milliliters of any combination of whole blood, red blood cells, colloids, and/or crystalloids within the applicable time frames set out in (1) and (2) in this section.
- b. For pediatric donors, in accordance with § 1271.80(d)(2)(ii)(B), you must suspect plasma dilution sufficient to affect the results of communicable disease agent testing, regardless of the presence or absence of blood loss, in a donor 12 years of age or under, in any of the following situations.
 1. Any transfusion of blood or colloids:
 - i. Within the 48 hours immediately preceding the collection of a pre-mortem specimen for testing; or
 - ii. Within the 48 hours immediately preceding death, if the specimen is collected post-mortem, whichever occurred earlier.
 2. Any crystalloids:
 - i. Within the one hour immediately preceding the collection of a pre-mortem specimen for testing; or
 - ii. Within the one hour immediately preceding death, if the specimen is collected post-mortem, whichever occurred earlier.
- c. There may be other clinical situations that may cause reasonable suspicion of a specimen to be diluted. As the establishment that collects donor specimens for

testing, you might be aware of additional circumstances in which plasma dilution might affect test results. Your SOPs should identify any additional circumstances where you believe plasma dilution might have occurred, and you should use a pre-transfusion/infusion specimen or apply an algorithm in those instances.

1. Example 1: A donor who has previously had blood loss, stabilizes, then expires, but has received fluids in the 48 hours before specimen collection.
 2. Example 2: A donor who is obese.
 3. Example 3: 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.
 4. Example 4: A donor who weighs less than 45 kilograms or more than 100 kilograms.
- d. As part of establishing procedures for all steps in testing in accordance with § 1271.47(a), establishments making donor eligibility determinations must have SOPs that define those elements necessary to determine whether a pre-transfusion/infusion blood specimen is adequate for infectious disease testing (e.g., the amount of hemolysis, storage conditions, and age of the specimen). Testing laboratories must perform tests in accordance with the manufacturer's instructions (§ 1271.80(c)), including any instructions concerning factors that might affect specimen stability.

Definitions:

Blood component means a product containing a part of human blood separated by physical or mechanical means (§ 1271.3(i)).

Colloid means: (1) a protein or polysaccharide solution, such as albumin, dextran, or hetastarch, that can be used to increase or maintain osmotic (oncotic) pressure in the intravascular compartment; or (2) blood components such as plasma and platelets (§ 1271.3(j)).

Crystalloid means an isotonic salt and/or glucose solution used for electrolyte replacement or to increase intravascular volume, such as saline solution, Ringer's lactate solution, 5 percent dextrose in water (§ 1271.3(k)), or total parenteral nutrition (TPN).

Plasma dilution means a decrease in the concentration of the donor's plasma proteins and circulating antigens or antibodies resulting from the transfusion of blood or blood components and/or infusion of fluids (§ 1271.3(p)).

References:

21 CFR 1271 Human Cells, Tissues, and Cellular and Tissue-Based Products, rev. 4/1/2009

Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products, August 2007