



PROCEDURES MANUAL

Created: 02/1992

Revised: 06/1992, 11/1993, 06/1994, 10/1994, 10/1996, 10/1999, 10/2000, 06/2007, 05/2008, 11/2008, 06/2009, 06/2010, 07/2011, 06/2012, 11/2012, 06/2013, 06/2014, 06/2015, 06/2016, 06/2017, 06/2019.

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A1.000 Introduction and Purpose

Standardization of eye banking procedures was one of the founding missions of the Eye Bank Association of America (EBAA) when it was established in 1961. The first edition of the EBAA's Medical Standards was introduced to member eye banks in 1980. A Technician's Manual followed in 1982. The Technician's Manual served as a detailed source of information and training manual for new technicians. This Procedures Manual is not intended to replace the Technician's Manual or to serve as a training manual for new eye bank technicians.

The purpose of this manual is to operationalize the EBAA Medical Standards and to establish clinically accepted baseline practice for each eye banking procedure. It is intended that these procedures are written broadly enough to allow for acceptable variation from one eye bank to another, yet specific enough so that procedures will not vary too widely from one eye bank to another or outside the scope of accepted ophthalmologic practice. Included with most procedures is a suggested list of needed materials. ***Each eye bank should develop its own unique set of procedures that are compatible with EBAA Medical Standards. This manual presents one set of broad procedures believed to be compatible with the EBAA Medical Standards.***

While this Procedures Manual is not a substitute for an eye bank's own procedure manual, we hope it will serve as the framework upon which each eye bank develops its own personalized set of procedures. An individual eye bank's procedure manual should include more specific and personalized information.

Periodic revisions to the EBAA Procedures Manual were performed by members of the Technician Education Committee and now by the Technical Procedures Manual Subcommittee with the final approval by the Medical Advisory Board.

Created February 1992.

Revised: 06/92, 11/93, 06/94, 10/94, 10/96, 10/99, 10/00, 06/07, 05/08, 11/08, 06/09, 06/10, 07/11, 06/12, 11/12, 06/13, 06/14, 06/15, 06/16.

B1.000 Active Membership and Accreditation

Policy: The Eye Bank shall meet all of the requirements for membership and accreditation in compliance with EBAA Bylaws, Medical Standards, Membership Criteria and Criteria for Accreditation.

Reference:

Heck, E. L. (1997). Ch. 33 The Eye Bank Association of America: Purpose, organization, medical standards, and certification. In J. H. Krachmer, M. J. Mannis & E. J. Holland (Eds.), *Cornea, fundamentals of cornea and external disease* (pp. 469-473). St. Louis: Mosby.

Materials: The current version of the following references shall be used:
EBAA Medical Standards
EBAA Criteria for Accreditation
EBAA Criteria for Technician Certification and Re-Certification

Procedure:

Membership

1. New members shall be made to the Eye Bank Association of America (EBAA) by contacting the EBAA office and following the current procedure for membership application.
2. Complete the application forms and required information and submit to the EBAA.
3. The EBAA Constitution and Bylaws Committee will review the application and send a response to the Eye Bank. Admission to membership requires approval of the majority of the Board of Directors.
4. The Eye Bank shall provide all required information to the EBAA together with any prescribed fees and shall keep the EBAA informed as to the Eye Bank Medical Director, Director, required CEBT status, location and any organizational changes that might occur.
5. The eye bank shall register with the International Council for Commonality in Blood Banking Automation (ICCBBA) for a Facility Identification Number (FIN). This is required for all eye banks that assign a DIN or apply an ISBT 128 label to ocular tissue.
6. Current membership status provides each Eye Bank member certain rights and privileges such as access to information, House of Delegate attendance, and votes determined by the preceding years' net ocular revenue that each member reports annually to the Association office.

Accreditation

1. Upon notification from the EBAA, the Eye Bank shall apply for accreditation or re-accreditation as indicated by terms of accreditation and will file the necessary documents and fees for the accreditation visit.
2. Each office and laboratory of the Eye Bank that performs processing, tissue evaluation, donor eligibility determination, storage, and/or distribution of tissue intended for surgical use shall receive an On-Site Accreditation Visit and will strive to meet or exceed the criteria set forth in the current version of the EBAA Medical Standards.
3. The Eye Bank will strive to correct any cited differences identified by the accreditation inspection process by submitting a corrective action plan within the specified time frame. The Eye Bank will also complete corrective actions and provide the necessary documentation to the Accreditation Board Chair within the specified time frames.
4. The Director will ensure that the Eye Bank Policies are in compliance with the current EBAA Medical Standards.
5. The Director will notify the EBAA of any changes in the eye bank's Director, Medical Director, supervisory CEBT, facility location, name, or corporate organization.

Inspections by Official Agencies

Any written documentation of observations, findings, or results (including but not limited to 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.

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

Purpose:

To outline the requirements for training, certification, and continuing education of eye bank technical personnel.

Reference:

Heck, E. L. (1997). Ch. 33 The Eye Bank Association of America: Purpose, organization, medical standards, and certification. In J. H. Krachmer, M. J. Mannis & E. J. Holland (Eds.), *Cornea, fundamentals of cornea and external disease* (pp. 469-473). St. Louis: Mosby.

Materials needed:

Eye bank training syllabus
Form or method to record attendance of staff

Procedure	Rationale
1. All new full and part-time technicians must attend an eye bank orientation training program. This training program shall comply with any state laws relating to retrieval of donor eye tissue or enucleator certification. Each eye bank must document technical staff participation in all training sessions.	1. To ensure complete and effective training of new eye bank technical personnel.
2. Perform and document annual competency testing on all staff members performing eye banking functions.	2. To ensure staff members are performing tasks according to written protocols.
3. At least one member of the eye bank's technical staff must be EBAA certified by successfully completing the EBAA Technician Certifying Examination. This certification must be renewed every three years.	3. See EBAA Medical Standards section C1.300.

4. Provide continuing education programs for each technical staff member.
 5. Maintain a written record of all technical meetings.
 6. Any Medical Director who provides verification of competency for tissue recovery and preservations must 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.
 7. 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.
 8. The eye bank shall provide written documentation of such attendance at the time of the eye bank site inspection.
 9. The Medical Director shall review the eye bank's technical policies and procedures manual annually and make changes as necessary in accordance with any changes in EBAA Medical Standards or scientific/clinical advances in the practice of eye banking.
 10. The Medical Director shall meet with the eye bank's technical staff on a periodic basis to review technical operations.
 11. The Medical Director must designate in writing all non-EBAA certified technicians who are qualified and authorized to perform eye bank laboratory procedures.
4. See EBAA Medical Standards section C2.000.
 6. To ensure that Medical Directors stay current and knowledgeable about the EBAA Medical Standards and regulations.
 7. See EBAA Medical Standards section C1.200
 9. To ensure active participation and approval by the medical director on technical policies and procedures.
 11. See EBAA Medical Standards section C1.300.

C3.000 Facilities

C3.100 Eye Bank Laboratory

Purpose:

To provide an environment suitable for processing human eye tissue for surgical and research use that is in compliance with the EBAA Medical Standards and applicable federal and state regulations.

Reference:

- Danneffel, M. B. (1997). Ch. 32 structure and function of eye banks. In J. H. Krachmer, M. J. Mannis & E. J. Holland (Eds.), *Cornea, fundamentals of cornea and external disease* (pp. 463-467). St. Louis: Mosby.
- Heck E. (2005) Ch. 31 Structure and function of eye banks. In Krachmer, Mannis, Holland (Eds) *Cornea, fundamentals diagnosis and management.* (pp 407-409), Philadelphia: Elsevier.

Materials needed:

Room with limited access, i.e., locked door
Sink with a drain and running water or appropriate non-water based surgical hand antisepsis system
Adequate counter space
Adequate stable electrical source
Storage space for supplies and instruments
Appropriate space for tissue processing, i.e. ISO Class 5 Hood or Biosafety Cabinet, Processing Room
Refrigerator with temperature recording device, (alarm system suggested)
Slit lamp biomicroscope
Specular microscope

Procedure

Rationale

- | | |
|--|---|
| <ol style="list-style-type: none">1. The eye bank laboratory must be large enough to carry out the volume of eye banking functions handled and to accommodate the number of technicians working at any given time.2. Ideally, the laboratory should be in close proximity to the eye bank's administrative offices, as well as to the medical director. | <ol style="list-style-type: none">1. See EBAA Medical Standards section C3.100. |
|--|---|

3. The eye bank laboratory must have the following:
 - A. Door that can be locked, to ensure limited access to eye bank personnel only.
 - B. Sufficient grounded outlets from a stable electrical source.
 - C. Adequate countertop space.
 - D. Sink with drain and running water or appropriate non-water based surgical hand antisepsis system.
 - E. A laminar air flow hood or cabinet which meets ISO Class 5 standards or a processing room that maintains fewer than 25 colony forming units per 90mm settling plate per 60 minute exposure
 - F. Refrigerator with a temperature-recording device and either an emergency power source or a power failure alarm.
- 3B. Any equipment that would be damaged by power fluctuations requires surge protection.
- 3F. Eye bank equipment such as the refrigerator used to store eye tissue and corneal storage medium must have an emergency back-up power supply or an alarm system that will notify someone in the event of a power failure. See EBAA Medical Standard C3.200.

C3.200 Equipment, Maintenance and Cleaning

Purpose:

To ensure and document that all equipment is inspected, maintained and cleaned on a regular basis.

Reference:

ANSI/AAMI ST79:2010/A4:2013

Philips, N. F. (2013). Ch. 18 Sterilization. In S. Schreffer, & L. Wilson (Eds.), *Berry & Kohn's operating room technique* (Twelfth ed.) (pp. 303-327). St. Louis: Mosby.

Phillips, N. F. (2013). Ch. 17 Decontamination and Disinfection. In S. Schreffer, & L. Wilson (Eds.), *Berry & Kohn's operating room technique* (Twelfth ed.) (pp. 285-301). St. Louis: Mosby.

Phillips, N. F. (2013). Ch. 14 Surgical Microbiology and Antimicrobial Therapy. In S. Schreffer, & L. Wilson (Eds.), *Berry & Kohn's operating room technique* (Twelfth ed.) (pp. 233-251). St. Louis: Mosby.

EBAA Accreditation Board. *Final Temperature Probe White Paper*. August 2011.

Materials needed:

ISO Class 5 Hood or Biosafety Cabinet or Processing Room
 Refrigerator with temperature recording device
 Slit lamp biomicroscope
 Specular microscope (optional)
 Cleaning logs
 Maintenance logs
 Inspection and certification records for ISO Class 5 Hood or Biosafety Cabinet or Processing Room
 Autoclave, if used
 Incubator, if used
 CDC recommended / EPA-registered cleaning agent

Procedure	Rationale
<p>1. The ISO Class 5 Hood or Biosafety cabinet must be inspected and certified at least annually and each time it is moved. Certification documentation must be maintained for 10 years after the date of administration, or if unknown, 10 years after the date of tissue distribution, disposition or expiration, whichever is latest (FDA requirement 1271.270(d)) and be available for review at time of site inspection.</p> <p>A. If tissue processing occurs in a processing room, the processing room must be verified annually. The annual verification records must be maintained for ten years and available for the EBAA site inspection.</p>	<p>1. To assure proper functioning of the HEPA filters.</p>
<p>2. The hood, biosafety cabinet or processing room shall be cleaned with a CDC recommended cleaning agent such as 10% sodium hypochlorite in water or an EPA registered disinfectant before and after each use. Each cleaning shall be recorded. These records shall be kept for 3 years after the date of administration, or if unknown, 3 years after the date of distribution, disposition or expiration, whichever is latest (FDA requirement 1271.270(d)) and must be available for EBAA site inspection.</p>	<p>2. Appropriate cleaning and disinfection of the tissue processing area is essential for infection control and to prevent cross contamination.</p>
<p>3. If an incubator is used for cultures by the Eye Bank:</p> <p>A. The incubator must be cleaned in accordance with manufacturers' instructions using a CDC recommended, n EPA-registered cleaning agent. All cleaning and maintenance records must be kept for three years and must be available for EBAA site inspection.</p>	<p>3. .</p> <p>A. Routine cleaning ensures that no cross contamination of specimens occur.</p>

4. The refrigerator with temperature recording device that can be checked without opening the refrigerator. Temperature probe must reflect the temperature of the stored tissue under normal storage conditions.
 - A. Must be recorded daily to ensure that the refrigerator temperature remains within 2-8°C. Document any deviations and corrective action taken.
 - B. Recording graph paper must be changed as prescribed by the cycle it covers, i.e., daily, weekly or monthly. Alternatively, electronic monitoring methods should be checked and backed up at regular intervals.
 - C. Check recording device temperature for accuracy at least once a year against an NIST calibrated thermometer.
 - D. In the event of a power failure, there must be a provision for immediate notification and action to be taken.
 - E. The inside of the refrigerator must be cleaned periodically with a CDC recommended, EPA-registered cleaning solution.
 - F. All cleaning and maintenance records must be kept for 3 years after the date of administration, or if unknown, 3 years after the date of distribution, disposition or expiration, whichever is latest (FDA requirement 1271.270(d)) and be available for EBAA site inspection
 - G. The refrigerator must be maintained for the exclusive use of eye banking.
 - H. The refrigerator must have clearly labeled areas for quarantined tissue, surgical tissue awaiting distribution, and research tissue.

5. If an autoclave is used by the Eye Bank:
 - A. The autoclave must be cleaned as often as recommended by manufacturer with a CDC recommended cleaning solution. All cleaning and maintenance records must be kept for three years and available for EBAA site inspection.
 - B. Chemical indicators or sterilization process indicators must be placed inside each

4. To ensure that ocular tissue and preservation media are stored at the prescribed temperature. See EBAA Accreditation Board Final Temperature Probe White Paper.
 - A. See EBAA Medical Standards section C3.200.
 - B. The recording pen should never print over the same time period more than one time.
 - C. This is to verify the accuracy of the recording device.
 - D. See EBAA Medical Standards section C3.200.
 - E. Routine cleaning of the tissue storage area is essential for infection control and to prevent transfer of microorganisms.
 - H. See EBAA Medical Standards section C3.200.

instrument tray or wrapped kit. Indicators should be placed in an area that is the most difficult for the sterilant to penetrate.

- C. All articles to be sterilized must be wrapped in materials that meet recommended sterilization standards (See ANSI/AAMI ST79:2010/A4:2013)). Items for Immediate-Use Steam Sterilization (IUSS), formerly called flash sterilization, or for other validated non-steam sterilization methods (for example Steris) do not require wrapping.
 - D. Place indicator tape on the outside of each package. A lot number and expiration date must be noted on each item sterilized.
 - E. Record the date, lot number, load contents, the exposure time and pressure, operator name, and whether a biological indicator test was used and the results for each sterilization cycle.
 - F. Annual certification to validate temperature, pressure and time must be conducted and documented.
 - G. Monitor the efficiency of the sterilization process at least once each week with a reliable biological indicator that employs spores of established resistance. For steam sterilizers, this is *Bacillus stearothermophilus*. All items from this run must be quarantined until results are received, usually at 48 hours, and/or a written protocol for recall of all items must be in place.
6. Biological-indicator test packs shall be used during initial installation testing of steam sterilizers and following any major repairs. Biological-indicator test packs should also be used routinely in sterilization loads at least weekly, but preferably daily. Composition of a 16-towel challenge pack can be found in AAMI Standards.
7. Cleaning and maintenance records for all other instruments and equipment used, such as the slit lamp biomicroscope, centrifuge, and specular

indicators used in test packs such as the Bowie Dick Test Pack. Indicators do not prove sterility has been achieved, but they do allow detection of certain procedural errors and equipment malfunctions.

- C. Terminally sterilized items should be wrapped appropriately, and marked with expiration information. IUSS should not be used as a substitute for sufficient instrument inventory.
 - D. External indicators are used to differentiate processed from non-processed items, not to establish whether adequate sterilization has taken place.
6. The condition of the equipment, the expertise of the sterilization operator, and other factors determining success or failure of a steam sterilization cycle may vary. The less frequently a sterilizer is used, the greater the opportunity for an unnoticed problem that could affect sterilization. Biological-indicator test packs provide a useful means to monitor the efficiency of sterilization practices.

microscope must be kept for three years and be available for EBAA site inspection.

8. All cleaning and maintenance procedures must be recorded for each piece of equipment used. All cleaning procedures should clearly delineate the type of cleaning solution used and the frequency of cleaning.
8. Cleaning and maintenance records shall be available for EBAA site visit inspection. They shall be kept for at least three years.

C3.300 Instruments, Cleaning and Maintenance

Purpose:

To maintain instruments to assure that they function properly, to minimize or prevent trauma to eye tissue during procurement and preservation, and to adequately clean for effective sterilization.

Reference:

ASCRS-ASORN Special Report, *Recommended Practices for Cleaning and Sterilizing Intraocular Surgical Instruments*, www.ascrs.org/upload/ASORNSpecialTaskForceReport.pdf, 4/3/07.

Phillips, N. F. (2013). Ch. 18 Sterilization. In S. Schreffer, & L. Wilson (Eds.), *Berry & Kohn's operating room technique* (Twelfth ed.) (pp. 303-327). St. Louis: Mosby.

Phillips, N. F. (2013). Ch. 17 Decontamination and Disinfection. In S. Schreffer, & L. Wilson (Eds.), *Berry & Kohn's operating room technique* (Twelfth ed.) (pp. 285-301). St. Louis: Mosby.

Phillips, N. F. (2013). Ch. 14 Surgical Microbiology and Antimicrobial Therapy. In S. Schreffer, & L. Wilson (Eds.), *Berry & Kohn's operating room technique* (Twelfth ed.) (pp. 233-251). St. Louis: Mosby.

Materials needed:

Instruments to be cleaned
Instrument cleaner
Instrument lubricant
Mechanism for instrument sterilization

Procedure	Rationale
1. Protective apparel, including protective clothing, head cover, gloves, mask and eye protection shall always be worn while cleaning instruments.	1. Observe Standard Precautions to protect against transmission of bloodborne pathogens (HIV and hepatitis) and other infectious diseases.
2. Decontaminate instruments to remove all potentially biohazardous material such as tissue or blood by immersion in a CDC recommended disinfectant solution such as 10% sodium hypochlorite. Be sure that all blades are in a fully open position.	2. To reduce or minimize the opportunity for potentially infectious microorganisms to remain on instruments.
3. Transfer instruments to a solution of warm water	3. Low sudsing detergents minimize wear and tear

- and low sudsing, non-corrosive detergent that does not contain phosphates or alkali metals.
4. Soak instruments according to manufacturers' guidelines/directions.
 5. Use a hard bristle brush to remove stubborn stains.
 6. Rinse instruments thoroughly using tap water, then use a final rinse with sterile distilled or sterile deionized water, and dry carefully.
 7. Visually inspect Instruments for debris and damage, preferably under magnification, immediately after cleaning and before packaging for sterilization to ensure removal of visible debris. Send any dull or faulty instruments immediately for sharpening, repair and/or replacement.
 8. Lubricate all instruments, particularly those with moveable parts by immersion in instrument lubricant if cleaner does not contain lubricant. Allow the lubricant to work in to the moveable joints by opening and closing them while submerged in the solution.
 9. Remove the instruments from the lubricant and allow them to dry. Do not rinse or wipe the lubricant off.
 10. Package or wrap instruments for sterilization and note the expiration date and lot number on the outside to ensure kits are used within the appropriate time period or within the appropriate period which guarantees sterility based on the type of packaging used. Steam sterilization at 121°C (250°) for 30 minutes is recommended. Chemical indicators or sterilization process indicators must be placed inside each kit.
 11. Glassware, such as eye jars should first have all tissue removed, followed by soaking according to manufacturers' instructions in a CDC recommended disinfectant. Using a brush and detergent, scrub caps and jars thoroughly. Rinse carefully with pyrogen-free water and allow to air dry.
 12. Package separately for sterilization or include within enucleation instrument tray.
- of the instruments; less dulling and rusting occurs.
4. Soaking helps remove debris, tissue, and blood that may stain instruments.
 5. To avoid debris becoming baked on instruments, use a brush for scissors, especially in the box joints.
 6. Instruments should be dried thoroughly to avoid rusting. Use of sterile distilled or deionized water as a final rinse avoids bacterial toxin and chemical contamination to minimize TASS.
 7. To ensure adequate cleaning and to remove any dull or poorly functioning instruments from use.
 8. Protects instruments against rusting, staining, and corrosion.
 9. Improves function, lessens growth of bacteria, and allows for steam penetration.
 10. See Procedure C3.200, 5(b).

The lot number should include the date of sterilization and the cycle number. This can be used for stock rotation.

If event-related sterility is followed, items are considered sterile unless the integrity of the packaging is compromised (i.e., torn, soiled, wet, or showing evidence of tampering).

C3.400 Procedures Manual

Purpose:

To describe the method for developing, updating and archiving a Policy and Procedures manual.

Material Needed:

Computer word processing program (
Paper and printer
EBAA Medical Standards
FDA Rule 21 CFR Parts 16, 1270 and 1271
Applicable State regulations
Occupational Health and Safety Administration Guidelines
Centers for Disease Control - Standard Precautions

Procedure	Rationale
1. Determine an alphanumeric format to identify each policy and outline each procedure.	1. This will provide consistency throughout the document. One example is to use the format of the EBAA Medical Standards document, i.e. A1.000.
2. Eye banks shall utilize ICCBBA nomenclature to describe ocular tissue classes and attributes.	2. ISBT provides a common terminology and identification method that is designed to improve communication.
3. Develop a policy statement corresponding with each section of the EBAA Medical Standards document. Include relevant state and federal guidelines.	3. To be current with each guideline set by EBAA Medical Standards, develop a corresponding policy applicable to the Eye Bank's specific policies. Avoid putting administrative policies in the technical manual.
4. Along with developing a policy for each section, detail a procedure for each, where applicable.	4. Any policy that requires action by the laboratory staff will require a written procedure.
5. There are at least two elements to a procedure. A. Materials Needed: Under a heading, list the materials needed, specifying sterile supplies and non-sterile supplies, where applicable. B. Method: Number steps in sequence to be performed according to the chosen format. Avoid lengthy paragraphs. Also may include rationale or underlying principles for the outlined steps, definition of terms, references, etc.	

6. Insert forms and reference material in the appendix. Appropriately reference the location of this material throughout the document, e.g., See Appendix A.
7. Insert a header to identify the document, e.g., Corneal Laboratory Policy and Procedure Manual. Insert a footer to identify the institutional name, along with the month and year. Provide enough space on the first page of each procedure to document the date of approval, subsequent revision dates and the signatures of the medical director and the director of the eye bank.
8. Number all pages. Create a Table of Contents.
9. Proofread the document for grammatical and typographical errors.
10. Each policy and procedure is initially approved by the medical director and director of the eye bank by signing and dating the section. Any updates to the manual are approved in the same manner. Universal, single page sign-off for the entire manual is not appropriate.
11. Each policy and procedure must be readily available, either in print or electronically, to the personnel responsible for the completion of the task. These policies and procedures maybe maintained in a nearby or adjacent area, if access in the immediate area is impractical.
12. Review the manual at least annually to identify any needed updates.
13. Before printing an updated version of the manual, insert the current date where applicable.
14. Print a hard copy of the initial document and any subsequent changes and submit them to the laboratory staff for review.
15. Archive the previous copies of the manual, including the appendices, outdated policies and/or procedures and review statements from the laboratory staff, for reference. Only current version of manual will be available to staff.
7. Documents the dates of implementation, reviews and updates. See EBAA Medical Standards section C3.400.
8. It will make referencing a section easier.
10. See EBAA Medical Standards section C3.400.
11. Promotes visibility and availability of pertinent policies and procedures to staff. Required by FDA sec. 1271.180.
12. Maintains eye bank's practice in compliance with current standards and regulations. Required by EBAA Medical Standards C3.400.
14. To document the staff's' comprehension of the policies and procedures.
15. Outdated policies and procedures must be maintained for review but should not be made readily available to staff. See EBAA Medical Standards section C3.400.

C3.600 Infection Control and Personnel Safety

Purpose:

To minimize the risk of transmission to eye bank personnel of HIV, hepatitis, and other infectious diseases and to outline precautions that all eye bank personnel must follow.

Definition of terms:

Exposure Control Plan: Mandated by OSHA, this requires employers to identify in writing tasks and procedures as well as job classifications where occupational exposure can occur. The plan must be reviewed annually and must be accessible to employees and to OSHA.

Exposed Worker: Individual exposed, as described above, while performing eye banking responsibilities.

Human Exposure: Contact with blood or other body fluids through percutaneous inoculation or contact with open wounds, non-intact skin, or mucous membranes.

Infectious Materials: As defined by OSHA, these include semen, vaginal secretions, cerebrospinal fluid, synovial fluid, pleural fluid, pericardial fluid, peritoneal fluid, amniotic fluid, saliva in dental procedures, any body fluid visibly contaminated with blood and all body fluids in situations where it is difficult or impossible to differentiate between body fluids. It also includes any unfixed tissue or organ other than intact skin from a human (living or dead) and HIV containing cells or cultures.

Standard Precautions: Guidelines recommended by the CDC 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.

Universal Precautions: As defined by OSHA. Treating body fluids/materials as if infectious and emphasizing work practice controls, such as handwashing and needlestick precautions that are mandatory.

Regulatory:

29 CFR 1910.132 (f)(1)(i) through (v); (2), (3)(i) through (iii) and (4) Personal Protective Equipment

29 CFR 1910.1030 (g)(2)(i); (ii)(A) through (c); (iii) through (vii)(A) through (N); (viii) and (ix)(A) through (C) Bloodborne Pathogens

29 CFR 1910.1200 (h)(1), (2)(i) through (iii) and (3)(i) through (iv) Hazard Communication

Siegel JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee, 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings. <http://www.cdc.gov/ncidod/dhqp/pdf/isolation2007.pdf>

Materials needed:

Red biohazard bags and/or fluorescent orange biohazard labels
Protective eyewear (goggles or face shield)
Mask
Gloves
Protective moisture impermeable clothing
Puncture resistant sharps container
Sink with running water

CDC recommended disinfectant
Soiled linen container

Procedure	Rationale
1. All blood and body fluids including tissues are potential sources of infection.	1. Under Standard Precautions blood and body fluids of all patients are considered potentially infectious for HIV, hepatitis and other bloodborne pathogens.
2. Place blood specimens in clear plastic bags and label with biohazard stickers.	2. To minimize any transmission of infectious material to other individuals or the environment.
3. Place disposable paper products contaminated with blood or body fluids in red biohazard bags and properly dispose of.	
4. Place contaminated linens in fluid-resistant laundry bags.	
5. Wear gloves at all times while handling blood, body fluids, or tissues. This is essential, particularly when there are cuts, scratches, or dermatologic lesions on the technician's hands.	5. Cuts or lesions on hands provide an entry point for infectious pathogens.
6. Careful hand washing after removing gloves is mandatory.	6. This further reduces the opportunity for transmission of microorganisms.
7. Keep hands in good condition. Use hand lotion following handwashing to prevent skin breakdown.	
8. Use of other protective measures including protective eyewear, masks, and protective clothing, such as moisture resistant gowns, is mandatory.	8. To prevent exposure to open wounds, non-intact skin, or mucus membranes such as in the nose or eyes.
9. Shoe covers or boots shall be worn in instances when gross contamination can reasonably be anticipated.	
10. Always adhere to needle-stick precautions. Do not bend, recap or replace needles. Instead place used needles in a puncture-resistant sharps container designated for this purpose.	10. To prevent accidental needle stick injuries, which might expose a technician to infectious disease.
11. Minimal handling of blood-contaminated scalpel blades is essential. Take extra care to prevent self-injury. Used scalpel blades must be disposed of in a puncture resistant sharps container. If an appropriate disposal container is not available, use a glass jar or specimen container with a lid to transport scalpels/needles to a proper container.	11. All sharps must be carefully placed in red, biohazard-labeled sharps container.

12. Notify your supervisor immediately in the event of a needle puncture or blade injury. Complete and submit an occupational exposure report as directed by your eye bank. Document treatment and counseling with the date and time of injury. This report should be filed in the eye bank technician's personnel record and shall be available for review at the time of EBAA site visit inspection.
13. Blood and body fluid spills and instruments that come into direct contact with blood or tissues should be cleaned with a CDC recommended, EPA-registered disinfectant. Exposure time should be according to manufacturers' instructions.
14. Eating, drinking, smoking, applying cosmetics or lip balm and handling contact lenses are prohibited in work areas where there is reasonable likelihood of exposure.
15. Food and drink shall not be kept in refrigerators, shelves, and cabinets or on countertops or benchtops where blood or other potentially infectious materials are present.
16. Procedures involving blood or other potentially infectious materials shall be performed in such a manner as to minimize splashing, spraying, spattering, and generation of droplets of these substances.
17. Each eye bank shall have an Exposure Control Plan as stipulated in OSHA's final rule which shall include the offer of free hepatitis B vaccination within 10 working days of initial assignment unless the employee has previously received the complete hepatitis B vaccination series, antibody testing has revealed that the employee is immune or the vaccine is contraindicated for medical reasons. Employees who decline to accept the vaccine shall sign a statement to that effect. Post-exposure evaluation and follow-up must also be included in the plan. The plan must be reviewed and updated annually and must be available to employees.
18. Annually review all current OSHA and CDC regulations to ensure compliance. This includes providing in-service education to all eye bank technical staff on infection control and **Universal/Standard Precautions** and documenting it. This should be done for staff
12. An incident report should be completed indicating the treatment offered or action taken, as appropriate.
13. It has been determined by CDC and OSHA that 1:10 dilution of sodium hypochlorite is very effective against HIV and HBV.
18. See the Final Rule as published in the Federal Register, Vol. 56, No. 235, December 6, 1991.

identified in the exposure control plan as having the potential for accidental hazardous exposure.

C3.700 Waste Disposal

Purpose:

To properly dispose of human eye tissue remains in such a manner as to minimize hazard to eye bank personnel and the environment and to comply with local, state and federal regulations.

Definition of terms:

Decontamination: Removal of, or neutralization of, injurious agents from ground, buildings, clothing, etc.

Incinerate: Complete destruction of all organic matter by fire.

Materials needed:

- Red biohazard bag
- Pressure sensitive fluorescent orange biohazard labels
- Facility for decontamination or incineration

Set up:

Potentially biohazardous waste must be isolated and discarded appropriately. Each eye bank must have an appropriate mechanism, as defined by local, state and federal law, to properly decontaminate and/or dispose/incinerate biohazardous waste.

Procedure	Rationale
1. Wrap all tissue waste, serum, and blood in a dignified manner to obfuscate any recognizable human remains. Document ocular tissue disposal through the use of a "Disposal Log" and note tissue disposal in the donor record.	1. To minimize hazard to personnel and environment. See EBAA Medical Standards section C3.700.
2. Label all biohazardous waste with the OSHA designated biohazardous symbol and bag in red biohazard bags within a sealed, puncture resistant container for transport to a decontamination facility or incineration facility, according to your eye bank's policy and procedure, and local, state and federal regulations.	
3. Universal/Standard Precautions for healthcare workers must be strictly observed and adhered to while labeling, wrapping, bagging, and transporting biohazardous waste.	

D1.000 Donor Eligibility

Reference:

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D1.200 Documentation on Donor Information

Purpose:

To provide comprehensive uniform eye donor screening to ensure the highest quality ocular tissue for surgical use and avoid transmission of any infections or disease from donor to recipient.

Regulatory:

21 CFR 1271.265 Receipt and Distribution
21 CFR 1271.270 Records

Materials needed:

Donor/referral screening form
Pen; indelible black ink is recommended
Phone
Quiet area to obtain information or phone referral
Copy of EBAA Medical Standards

Procedure	Rationale
1. Complete a thorough screening of the donor by obtaining all available medical/social history and post mortem findings from accepted sources listing the guidelines set forth by the EBAA Medical Standards.	1. To ensure high quality human eye tissue for surgical use and avoid transmission of any infections or disease from donor to recipient. See EBAA Medical Standards section D1.100.
2. Collect all pertinent eye donor information using a controlled screening form at the time of the telephone referral and/or chart review. The source of the information shall be noted, including the name and title or position of the individual who provided the information and the eye bank technician or volunteer who recorded the information on the eye bank's form.	2. To ensure consistent recording of complete medical history on each donor within the EBAA established guidelines. See EBAA Medical Standards section D1.200.
3. A complete donor medical screening evaluation record shall include, but is not limited to, the following data:	3. A-F Baseline information needed for follow-up and to obtain additional information after donation.
A. Name of the eye bank person recording/obtaining the information.	
B. Date and time referral received	
C. Origin of referral (e.g., hospital, OPO, funeral home, etc).	
D. Name of hospital or facility where donor expired.	
E. Full name and title of person providing information.	
F. Phone number and unit/location.	
G. Name of donor. This should be verified and should match that on the consent form at the time of ocular tissue recovery.	G. To provide identification to be compared with the identification of the donor at the facility prior to recovery of ocular tissue to ensure that ocular tissue is removed from the correct decedent.
H. Age.	H. Essential donor information used to determine use of ocular tissue. See EBAA Medical

Standard D1.400.

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| I. Weight/Height. | I. Provides data to evaluate the overall physical condition of the donor and calculate plasma dilution. |
| J. Sex. | J. Provides statistical and demographic data |
| K. Race. | K. Provides statistical and demographic data |
| L. Unique Identification Number (e.g. social security number, medical record number, driver's license number, passport number, etc.). | L. Provides unique ID number to identify donor. These are acceptable for intermediate steps (e.g., sending the ocular tissue to the eye bank after recovery), but after the donor eligibility determination has been made, FDA regulations prohibit the use of an individual's name, social security number, or medical record number. (FDA 1271.55(a)). |
| M. Date of this hospital admission and admitting diagnosis. | M. Provides additional information as to the donor's medical condition prior to death. |
| N. Date and time of declaration of brain death, if applicable. | N. Time of brain death, which is the legal time of death important in solid organ donation, may be several hours before asystole. For the purpose of ocular tissue donation, the cessation of cardiac function (asystole or cross-clamp) is the more critical time. |
| O. Date and time of asystole (cessation of cardiopulmonary function) or last known alive time. | O. Essential donor information in conjunction with the time of preservation, used to determine the use of ocular tissue (see EBAA Medical Standards D1.500) |
| P. Cause of death (must never be recorded solely as cardiac arrest or cardiopulmonary arrest). | P. All deaths are a result of cessation of cardiac and pulmonary function. The actual cause of death should be a disease pathology or trauma that resulted in a cardiac arrest, (e.g., cardiac arrest secondary to congestive heart failure with congestive heart failure actually being the primary cause of death). |
| Q. Name and complete address and relationship of consenting next-of-kin. | Q. Verifies priority of next-of-kin. |
| R. Consent/permission obtained and for what tissues. | R. See procedure D1.300. |
| S. Whether donor is a medical examiner's or coroner's case. | S. Due to legal implications surrounding medical examiner or coroner cases, no ocular tissue may be removed without prior permission from the medical examiner or coroner. |
| T. Whether an autopsy will be performed. | T. Further medical information must be obtained following autopsy, including presence of infections or cancer, as well as actual cause of |

death. This information must be recorded and filed as part of the donor's record. See EBAA Medical Standards section D1.200.

U. Ventilator support: Duration in hours or days.

U. Prolonged respiratory support may increase the donor's chances of compromised defense mechanisms leading to secondary systemic infections.

As a result of administration of muscle relaxants to ventilator-supported patients, corneal tissue is at increased risk for bacterial invasion or damage. Decrease or absence of a normal blink reflexes alter the body's ability to naturally lubricate and protect the integrity of the eye.

V. Previous ocular history, (i.e., known eye disease, injury, or surgery). Name of ophthalmologist, if available.

V. Any notations of history of eye disease or injuries require thorough evaluation. Prior eye surgery or disease may have traumatized or damaged the corneal endothelium. See EBAA Medical Standards sections D1.120, #16-17.

W. Transfusion/Infusion History; Record date, time, number of units, and product type if donor was < 12 years old or had blood loss.

W. Plasma dilution associated with infusions / multiple transfusions may affect test results. See EBAA Medical Standards section G1.220. Calculation of a plasma dilution algorithm must comply with FDA approved methodology and must include both plasma volume and blood volume assessments.

X. Name and phone number of the family physician most knowledgeable about the donor's medical history.

X. Appropriate medical personnel who cared for donor should be contacted to obtain additional medical history, if needed, and all information obtained should be signed, dated, timed, and labeled with donor identification number. Development of a telephone/consult documentation form is suggested. See EBAA Medical Standards section D1.000.

Y. Past medical/social history, including past or current history of any contraindications listed in section D1.110 and D1.120 of the EBAA Medical Standards. This information must come from accepted sources such as listed in Medical Standards D1.000.

Y. Documentation that all items listed by the EBAA Medical Standards as contraindications for surgical use have been thoroughly reviewed during screening to eliminate risk of transmission of disease or infection to recipient is required. See EBAA Medical Standards sections D1.100 and D1.120.

Z. A visual head-to-toe inspection of each eye donor should be performed and recorded. Look for needle tracks, fresh tattoos that may hide parenteral drug use, and other high-risk behaviors. The forearms, webs of fingers and toes should be carefully examined, as well as the groin and behind the knees. Covered in E1.000

Z. To check for evidence of intravenous drug abuse or other known high-risk behavior for AIDS and hepatitis.

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| <p>AA. A review of all available records shall be performed by technical staff prior to recovery.</p> <ol style="list-style-type: none"> 1) Medications, including antibiotics, should be recorded. 2) Temperature or temperature range over last 48 hours, noting any variations. 3) Dates and results of lab tests, including (but not limited to) WBC, platelet count, VDRL or RPR, blood, urine and sputum cultures, chest x-rays, and other relevant serology that may have been performed such as HBsAg, liver enzymes, HIV or HCV screening. 4) Notation of the presence of eye care during hospitalization. A post-mortem eye prep for donation shall be routinely recommended and should be performed, according to your eye bank's policy. 5) Whether donor was refrigerated prior to recovery, and the time that cooling of the ocular tissue and/or refrigeration of the body had begun (includes ice pack placed on eyes). 6) Notation of the interval between death, enucleation, excision and preservation. <p>4. Document all of the above information on your eye bank's screening form. Follow your eye bank's protocol for review of data by your Medical Director or designee prior to release of ocular tissue for surgical use.</p> | <p>AA. To verify initial screening information and rule out potentially hazardous or contraindicated tissue for surgical use.</p> <ol style="list-style-type: none"> 1) Antibiotics may be an indicator that the donor had an infection. 2) Elevation of temperature or hypothermia can be related to factors associated with an infectious process or altered metabolic or neurologic function. 3) Evaluation of laboratory data provides further information in determining donor suitability. All results should be evaluated while keeping in mind total patient history and course of illness. 4) Proper postmortem donor eye maintenance is essential to preserve the integrity and quality of ocular tissue for surgical use. See procedure D1.600. 5) Refrigeration information could be important in determining transplant suitability if large time frame has elapsed between time of death and recovery. See Medical Standard D1.500. 6) See EBAA Medical Standard D1.500. <p>4. See EBAA Medical Standards section K1.000.</p> |
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D1.210 Medical Examiner/Coroner/Pathologist Documentation

Purpose:

To delineate minimum information an eye bank must record from the medical examiner, coroner, or pathologist performing an autopsy or inquest.

Materials needed:

Form for recording autopsy or inquest findings
 Pen, indelible black ink recommended

Procedure	Rationale
1. Follow procedure D1.200 to document donor information. Note whether this is a coroner or medical examiner case and/or whether an autopsy is to be performed.	1. Not all coroner's or medical examiner cases are autopsied. Also, autopsies may be performed by a pathologist other than a medical examiner or coroner.
2. Gross autopsy results should be obtained prior to release of ocular tissue for surgical use.	2. The pathologist may discover that the donor had transmissible disease or infection or was at risk for hepatitis or HIV.
3. Record the pathologist's findings, including cause of death, on the form provided by the eye bank. Sign and date this information.	3. The form may be completed and signed by the pathologist or may be a verbal report recorded by eye bank personnel.
4. Record the following minimum information:	4. Cause of death by "gross findings" will generally not include histology. Final autopsy reports should be obtained and reviewed when available.
A. Name of pathologist performing autopsy.	
B. Date of autopsy.	
C. Cause of death per autopsy findings.	
D. Any evidence of high risk for HIV, hepatitis or other infectious disease, such as needle tracks, as defined by EBAA Medical Standard D1.100.	
E. Any signs of infection or sepsis.	
F. Signature of pathologist or name, signature date and time of eye bank personnel taking verbal information.	
G. Name of person providing verbal autopsy findings.	

D1.300 Method of Consent

Purpose:

To ensure that informed consent for eye or corneal donation is obtained from the legally authorized individual (e.g. deceased, legal next-of-kin) as stipulated under local or state law prior to removal of any ocular tissue.

Regulatory:

Uniform Anatomical Gift Act of 1987 (see your own state regulations)
 47 CFR Part 482.45 Conditions of Participation
 Model Elements of Informed Consent for Organ and Tissue Donation: Joint Statement. (2000). AATB, AAO, EBAA.

Reference:

Farge, E. J. (1997). Ch. 42 Ethics and Eye Banking. In J. H. Krachmer, M. J. Mannis & E. J. Holland (Eds.), *Cornea, Fundamentals of Cornea and External Disease* (pp. 531-535). St. Louis: Mosby.

Fuller, R. L. (1997). Ch. 43 Medical Legal Issues. In J. H. Krachmer, M. J. Mannis & E. J. Holland (Eds.), *Cornea, Fundamentals of Cornea and External Disease* (pp. 537-541). St. Louis: Mosby.

Materials needed:

- Consent form
- Pen, indelible black ink is recommended
- Telephone with recording device and tape
- Quiet area to obtain information

Procedure	Rationale
1. Consent/authorization for ocular tissue donation should be obtained using one of the following five methods: A. Written: As described below: 1) Under the Uniform Anatomical Gift Act, enacted in all 50 states, a consent signed by the legal next-of-kin must be in order of priority in accordance with state law. The consent shall include, but not be limited to, the following information: Name of donor, relationship of the donor to the person signing the permission, signature of next-of-kin, witness(es), and the type of tissue donated. 2) Consent/authorization may be obtained by any individual designated by his/her employing institution to present the option of eye donation to the family. 3) Consent/authorization must be witnessed in accordance with state law. 4) Consent/authorization must clearly indicate permission for the ocular tissue donated. The next-of-kin should be informed of the various recovery options and the factors that influence	1) State law defines who may give permission for donation. Next-of-kin must be informed regarding what tissues can be recovered to avoid any misunderstanding or confusion after the donation has occurred. See EBAA Medical Standard D1.300. 2) As long as the next-of-kin is approached in a respectful, dignified, and professional manner, any individual may be designated by the hospital or eye bank to obtain consent for donation of tissues and/or organs. Requestor should receive training in accordance with 47 CFR Part 482, Conditions of Participation. 3) One or two additional witnesses may be required. Consult your state and local law. 4) Permission for ocular tissue donation should provide the prospective donor's next-of-kin sufficient understandable information and opportunity to consider whether or not to agree to such donation. It should also minimize the

which will occur.

possibility of coercion or undue influence.

- 5) Consent must clearly specify the organization authorized to recover eyes/corneas or "...to accept the eye/cornea donation."
- B. Telephone: As defined by state law.
- C. Living donor: Check your local and state regulations. Permission is usually obtained from the person who is donating. Per your state law, the next-of-kin may or may not be required to give consent as well.
- D. Implied/Medical Examiner:
- 1) In any case which falls under the medical examiner's/coroner's jurisdiction, consent from the coroner or medical examiner must be obtained prior to removal of tissue.
 - 2) Some states have coroner/medical examiner laws that permit cornea removal with coroner/medical examiner consent in the absence of expressed permission from next-of-kin. Check your state law and your eye bank's policy.
- E. Registry Consent (where applicable)
- 1) A hardcopy of registration for donation (e.g. driver's license or donation registry) may be a legal form of consent for donation according to state law(s) in your region. Refer to your state law to determine what constraints apply before using donation registry documentation as consent for removal of tissue.
2. Original signed consent form should remain with the donor's record at the institution. A copy of the consent form must be obtained by the eye bank for their records.
 2. See the OBRA of 1987, your state's required request law, and Joint Commission requirements. Each hospital must document compliance with state and national routine referral, routine inquiry or required request laws. Check with the hospital for their procedure.

D1.600 Eye Maintenance Prior to Recovery

Purpose:

To retard the deterioration of ocular tissue following cardiac asystole, prior to recovery.

Regulatory:

21 CFR 1271.260 Storage

Reference:

Breslin, C. W., & Ng, W. (1976). The endothelial function of donor corneas: Effects of delayed enucleation and refrigeration. *Investigative Ophthalmology & Visual Science*, 15(9), 732-739.

McKinnon, J. R., & Walters, G. D. (1976). Cadaver storage time. An important factor in donor cornea survival. *Archives of Ophthalmology*, 94(2), 217-220.

Ritter, E., Gotze, J., Trute, K., Strache, S., Schmidt, G., & Gliem, H. (1990). The extent of bacterial contamination of keratoplasty donor eyes post mortem. *Klinische Monatsblätter Fur Augenheilkunde*, 196(2), 70-75.

Rosenwasser, G. O. D., & Nicholson, W. J. (2003). Donor maintenance. *Introduction to Eye Banking: A Handbook and Atlas*. (1st ed.) (pp. 25-29).

Thoft, R. A., Friend, J., Freedman, H., & Dohlman, C. H. (1975). Corneal epithelial preservation. *Archives of Ophthalmology*, 93(5), 357-361.

Materials needed:

- Wet ice packs (such as rubber gloves filled with crushed ice). Note: Ice should be wet ice
- Sterile ophthalmic broad-spectrum antibiotic solution, sterile normal saline or balanced salt solution (BSS)
- Ophthalmic lubricating ointment for ventilator maintained donors
- Paper tape
- Pillow or head block

Procedure	Rationale
1. Instill sterile ophthalmic antibiotic solution (minimum of two drops per eye), or rinse with sterile saline or balanced salt solution prior to recovery of ocular tissue.	1. Provides lubrication and moistening of corneal tissue. Antibiotic solution retards microbial growth prior to enucleation or in situ cornea removal.
2. Close eyelids completely and gently. Lightly apply paper tape if indicated in local eye bank's procedures. Alternatively, apply 4X4 gauze moistened with saline or BSS over closed eyelids.	2. Decreases exposure of corneal epithelium to air, resulting in damage to eye tissue. Paper tape prevents natural opening of lids due to decreased muscle tone and post mortem relaxation of eye lids. Paper tape will prevent tape burns to lids and reduce chances of removing eyelashes.
3. Refrigerate the donor's body if possible or lightly apply wet ice packs over eyes, securing gently in place.	3. A cool environment decreases the effects of metabolic byproducts (toxins) on eye tissue, which occur naturally within the body after death.
4. Elevate the donor's head.	4. Prevents pooling of blood in head to decrease incidence of bleeding and swelling in eye region following recovery.
5. Record whether these procedures were carried out on your eye bank's donor screening form or	5. This information should be used to evaluate the suitability of the corneal tissue for surgical use.

recovery paperwork and note the time that cooling of the ocular tissue began.

E1.000 Recovery, Open-Container Processing and Preservation

Reference:

- Croasdale, C. R., Schwartz, G. S., Malling, J. V., & Holland, E. J. (1999). Keratolimbal allograft: Recommendations for tissue procurement and preparation by eye banks, and standard surgical technique. *Cornea*, 18(1), 52-58.
- Lindquist, T. D., Miller, T. D., Elsen, J. L., & Lignoski, P. J. (2009). Minimizing the Risk of Disease Transmission During Corneal Tissue Processing. *Cornea*, 28(5), 481-484.
- Oiland, D. (1997). Ch. 37 tissue removal. In J. H. Krachmer, M. J. Mannis & E. J. Holland (Eds.), *Cornea, fundamentals of cornea and external disease* (pp. 493-500). St. Louis: Mosby
- Rosenwasser, G. O. D., & Nicholson, W. J. (2003). Surgical processing techniques in eye banking. *Introduction to eye banking: a handbook and atlas*. (1st ed.) (pp. 17-24).
- Soper, M. C., & Lisitza, M. A. (1999). Ch. 103 tissue removal. In F. S. Brightbill (Ed.), *Corneal surgery: Theory, technique & tissue* (3rd ed.) (pp. 882-887). St. Louis: Mosby.

E1.100 Recovery

E1.110 Pre-ocular Tissue Recovery and Donor Preparatory Procedures

Purpose:

To delineate standardized procedures for preparation of the donor and activities to be completed before the removal of the ocular tissue by enucleation or in situ corneal excision.

These procedures include the following:

- Ensure appropriate supplies before traveling to donor site
- Verify consent for ocular tissue removal
- Check the donor's history and medical record Identification of the donor
- Don personal protective equipment
- Perform physical examination/inspection of the donor and penlight examination
- Draw blood sample
- Evaluate recovery site
- Prepare the work site
- Donor preparation: Irrigation and prep of the operative site
- Set up of the sterile field
- Draping of the donor
- Penlight Examination

Reference:

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Materials Needed:

1. Sterile Supplies:

- Sterile ophthalmic irrigating solution; e.g. normal saline or balanced salt solution
- Sterile povidone-iodine or antibiotic solution (for in situ excision)
- Sterile gloves
- Sterile gown or sterile sleeves
- Sterile supplies used in whole eye enucleation and in situ corneal excision. See procedure E1.100 and E1.200.
- Povidone-iodine antiseptic swabs or sterile preoperative skin prep tray
- Alcohol swabs
- Syringe needle or a vacutainer apparatus to draw blood
- Moisture impermeable table drape and antiseptic solution to clean work table
- Sterile scrub brush for hands (with antimicrobial hand soap)

2. Non-Sterile Supplies:

- Forms (Screening form, enucleation/excision form, donor information form per your eye bank's policy)
- Non-sterile gloves
- Protective moisture impermeable clothing
- Protective eyewear (goggles or face shield)
- Mask
- Cap to cover hair
- Non-sterile supplies used in whole eye enucleation and in situ corneal excision
- Penlight

Procedure	Rationale
<p>1. Ensure appropriate supply before traveling to donor site.</p> <p>Check expiration dates and integrity of sterile instrument kits and sterile equipment before leaving the eye bank laboratory. Pack necessary instruments kit(s), as well as all necessary supplies, and transport in clean bag or case to donor site. The eye bank must have a specific policy and procedure for back up instruments which may be missing from the kit or which become contaminated. This may be accomplished by taking an extra instrument kit and supplies.</p>	<p>1. To assure sterility of instruments and supplies.</p>
<p>2. Verify consent for ocular tissue removal.</p> <p>Obtain and review the consent/authorization form. Confirm that it has been completed fully and has signatures of consenting legal next-of-kin. Leave original in the donor's chart and take a photocopy for the eye bank's record. See procedure D1.300. If your eye bank uses a means of obtaining</p>	<p>2. To verify whether consent is for whole eyes or corneas only and that consent is valid prior to removal of any ocular tissue.</p>

consent other than written consent it is essential that the consent procedure conforms to state law and that documentation of the consent/authorization is retained.

3. Check the donor's history and medical record.

Review the donor's medical history by means of chart review or interviews with knowledgeable medical staff.

4. Identify the donor.

Match the name on the consent form to the name on the donor's ID tag, e.g., toe tag or bracelet. Never assume the identity of the donor in the absence of checking appropriate sources on the body.

5. Don personal protective equipment.

Follow all eye bank procedures related to Standard Precautions.

Put on protective apparel, including gloves, mask, cap to cover hair, protective eye wear such as goggles, safety glasses or face shield, and moisture impermeable protective clothing.

6. Perform physical examination/inspection of the donor and penlight examination of the donor's eyes.

Perform gross inspection of the donor. Examine the entire body of the donor for evidence of needle tracks, recent homemade tattoos, male-to-male sexual contact or physical signs of HIV, hepatitis, or evidence of sexually transmitted diseases. If an in-situ cornea recovery is to be performed, use a penlight to grossly examine the eyes for signs of infection, corneal damage, embedded foreign bodies, iris abnormalities, or previous surgery. Examination of the entire body may require assistance to remove clothing and turn the body. Also see procedure D1.200 (Y).

7. Draw a blood sample.

3. To verify the accuracy of all reported information.

4. To verify the accuracy of all reported information.

5. To protect the eye bank technician from potential exposure to infectious disease.

6. To provide and record further evidence that the donor is in physically acceptable condition and free of signs of high risk for HIV, hepatitis or other infection. See EBAA Medical Standard D1.000 Donor Eligibility Determination. Medico-legal restrictions to distinct areas of the body, as may occur in a medical examiner or Coroner's case, may warrant attainment of exam info pertaining to these specific areas by a third party. Additionally, a recent ante-mortem physical exam or a post-mortem physical exam performed by another agency (e.g. OPO) may be used to supplement an eye bank post-mortem physical when circumstances prevent a complete examination of the body (e.g. organ donor or morbidly obese donor). Document the use of any information obtained from sources other than eye bank personnel accordingly.

7. To obtain the serum necessary for EBAA

and FDA required serology testing.

See procedure E1.700. Be sure to verify the donor's infusion/transfusion history and whether a pre-infusion/transfusion sample is required. Always strictly adhere to **Standard Precautions** when drawing a blood sample. Immediately label every sample with the donor's identification number and date and time of draw. The sample may be drawn before or after the ocular tissue has been recovered, per your eye bank's policy.

8. Evaluate the recovery site.

The recovery site must be qualified prior to the recovery to prevent contamination and cross contamination during the recovery process. The site should be in a good state of repair; be of appropriate size and location to permit aseptic procedures; and have adequate ventilation, airflow, and lighting.

9. Prepare the work site.

Identify a suitable worktable, Mayo stand, or counter space near the donor on which to set up your sterile field. Clean this area with a disinfectant and cover the surface with a moisture impermeable barrier drape. The sterile field will be set up on this area.

10. Prepare the donor.

- A. Elevate the donor's head if this has not already been done.
- B. Gently open each eye-lid and thoroughly irrigate the corneal and conjunctival sac of each eye following the procedure approved by the eye bank medical director. The procedure must include rinses of each eye with a sterile ophthalmic solution such as a normal saline or balanced salt solution. Additional rinses with ophthalmic povidone- iodine solutions may also be included. Irrigation of the eyes with a broad-spectrum ophthalmic antibiotic such as gentamicin or polymyxin B may also be included in the irrigation procedure. Care

- 8. To prevent the introduction, transmission, and spread of communicable disease. See FDA sec. 1271.190.

9. To ensure a clean area for set up of the sterile field.

- A. To prevent pooling of blood in the orbital area which could lead to excessive bleeding, swelling, and bruising post ocular tissue removal.
- B. To remove debris, microorganisms and other sources of contamination from the donor's eye. Antibiotic solution retards and prevents microbial growth. Povidone-iodine solutions must be carefully removed from ocular surfaces to prevent corneal toxicity. Per EBAA medical standards, Povidone Iodine shall contact any ocular tissue intended for transplantation at least once between the time of the donor's death and tissue preservation. The concentration (i.e. 1-10%), volume of solution, and the duration of ocu-

should be given to rinse povidone-iodine solutions and antibiotics from each eye with sterile ophthalmic solutions such as sterile saline within reasonable time limits.

- C. Clean the orbital area and surrounding skin, using alcohol or gauze moistened with water.
- D. Perform a prep of the operative area (the operative site) using povidone-iodine solution. Do not use antiseptic products like Hibiclens or PhisoHex, as this has been shown to be toxic to the cornea. The technique used to perform the prep should be a standard pre-operative skin prep. (See Berry and Kohn's or other surgical textbook for illustrations and in depth discussion.) The prep should start at the medial canthus of the upper closed eyelid and move out, around and below the lid, over the bridge of the nose, in an ever-widening circular pattern. Do not go over the same area twice. Cleanse each orbital area in this manner at least twice.

Following this, a povidone-iodine paint may be applied, per your eye bank's protocol.

Avoid getting any povidone-iodine solution or paint into the eye during this prep. Any povidone-iodine product applied to the eye at this point must be promptly rinsed to avoid toxicity to the cornea.

- E. Remove your prep gloves and dispose of them in a biohazard bag.

11. Prepare the sterile field

- A. Prepare the sterile field by first placing the sterile instrument tray on your prepared work surface. Remove the plastic dust cover if one has been applied. Verify that the instrument tray is sterile by checking the expiration date and the integrity of the wrap. Carefully open the inner wraps. Open additional sterile supplies or equipment, such as cotton-tipped applicators, 4 x 4 gauze, and eye jars by carefully peeling the bags and flipping the items onto the sterile field. If performing an in situ ex-

lar surface exposure (e.g. 3 mins.) to the solution shall be specified in the eye bank's operating procedures and determined by the Medical Director.

- C. To remove gross blood, dirt, or debris from the donor's skin.
- D. The use of friction mechanically removes microorganisms. This is combined with an antiseptic solution to further kill organisms and reduce the microbial population to the minimum possible.

- A. Develop a sterile conscience to protect the sterile field from inadvertent contamination.

cision, set up the vials or chambers containing corneal preservation medium adjacent to your sterile field, but not touching the field.

B. Open the outside package(s) of sterile gloves and sterile gown or sleeves. Scrub hands and forearms from fingertips to elbows, using an antiseptic scrub brush or solution such as Hibiclens, Avagard, povidone-iodine, or other approved preoperative surgical hand antisepsis product. Scrub for three to five minutes using standard surgical hand antisepsis technique or follow the manufacturer's instructions. Rinse thoroughly and dry with a sterile towel, drying from fingertips to elbows (if applicable).

C. Don sterile sleeves using aseptic technique. Double glove if this is your eye bank's policy. Powdered gloves should not be used.

D. Don sterile sleeves by slipping on and over gloved hands.

E. If using a sterile gown, aseptically don sterile gown, then don sterile gloves. If double gloving, don second pair after donning the first pair.

12. Drape the donor

Drape the donor with sterile drapes according to your eye bank's policy. Place a fenestrated sterile eye drape over each eye so that both eyes can be visualized. Once in place, do not move the drape(s) around. At this point consider only the inner area of the drape to be sterile.

B. See OR textbook (Berry and Kohn or MMWR October 25, 2002 / 51(RR16); 1-44) for a more detailed and illustrated guide on scrubbing. If a sterile gown is not used, sterile sleeves may be substituted.

C. Glove powder contaminants may appear reflective during slit lamp examination and as foreign bodies and may contribute to post-operative complications. See EBAA Informational Alert from March 16, 2012 regarding the *Potential Consequences of Use of Powdered Gloves*.

D. If double gloving, the second pair of gloves is donned after the sterile gown or sleeves.

12. The drape(s) provides the technician with a sterile surface around each eye on which to work.

In order to avoid contaminating the second eye, both eyes should be draped at once with a fenestrated drape to expose each eye. One drape for each eye may be used as long as a portion of one drape does not overlap the opposite eye.

E1.120 Enucleation

Purpose:

To provide a standardized method for the aseptic removal of human eye tissue.

This procedure describes the basic technique for performing an eye enucleation according to EBAA standards. Certain portions of the procedure are at the discretion and direction of your eye bank's medical director. Please refer to your eye bank's procedures manual as directed.

Regulatory:

21 CFR 1271.145 Prevention of the introduction, transmission, or spread of communicable diseases

Reference:

Rosenwasser, G. O. D., & Nicholson, W. J. (2003). Enucleation technique. *Introduction to eye banking: a handbook and atlas*. (1st ed.) (pp. 31-40).

Materials needed:

1. Sterile Supplies:

A sterile instrument tray: (The tray may either be irradiated, or steam or gas sterilized, appropriately wrapped, labeled with expiration date, and stored in plastic according to your eye bank's policy.)

- 1 Small curved scissors
- 1 Large curved enucleation scissors
- 1 Small (mosquito) curved hemostat
- 1 Small muscle hook (retractor)
- 1 Small toothed forceps
- 1 Eyelid speculum
- 2 Fenestrated eye drapes or 1 double-fenestrated drape
- 2 Plain drapes (optional, if the fenestrated drapes are moisture impermeable)
- 1 Hemostat for handling ophthalmic irrigating solution
- 2 x 2 gauze sponges
- Cotton balls
- Sterile cotton-tipped applicators
- Sterile eye jars, either glass or plastic. The eye jars may be sterilized within your instrument tray or separately. They should contain dental roll, gauze, or metal cage to hold the eye.
- Sterile gloves (at least 2 pair)
- Sterile gown or sleeves

2. Non-sterile Supplies:

Styrofoam container for transporting the eyes
Personal protective equipment.

Procedure

Rationale

- 1 All donor preparatory and pre ocular tissue recovery procedures should be performed according to procedure E1.110.
 - 2 Set up the sterile right and left eye jars. Check instruments to be sure none are missing or damaged.
 - 3 According to your eye bank's policy, begin with the left or right eye. Using 2 x 2 gauze or cotton tipped applicator, gently open the upper eyelid by pulling towards the top of the head, insert the closed lid speculum under the upper and lower eyelids near the nose. Slowly open the speculum while moving toward the middle of the eye. Be very careful not to touch the cornea with the speculum.
 - 4 Grasp the conjunctiva with the forceps, near the lateral edge of the cornea at the limbus. Cut the conjunctiva with the small, round tip scissors pointed away from the cornea. Continue this 360° around the cornea.
 - 5 Insert the closed scissors under the conjunctiva and perform a blunt dissection.
 - 6 Using a muscle hook and small scissors elevate and sever ocular muscles. A hemostat may be applied to clamp either the lateral or medial rectus muscle prior to cutting to provide a safe "handle" for the eye.
 7. With the globe still rotated laterally, insert the closed blades of the large enucleation scissors behind the back of the eye. Open the blades slightly and position the optic nerve between the blades. Push the scissors towards the back of the orbit and cut the optic nerve, leaving 5- 10mm stump.
 8. Use the hemostat, which is clamped to the medial rectus muscle, to gently lift the globe from the socket. Carefully cut any remaining connective tissue.
 9. Secure the eye in a sterile eye jar that can be sealed from the environment. Using a dental
1. Ensure all appropriate steps were taken for recovery of the ocular tissue from the correct donor and that tissue has been sufficiently prepared.
 2. Ensure all necessary supplies/instruments are present prior to beginning the aseptic recovery
 3. This provides access to the eye during the enucleation procedure.
 4. Cutting the conjunctiva provides the enucleator access to the ocular muscles and optic nerve and removes a membrane that may be contaminated with bacteria.
 5. To facilitate access to the ocular muscles.
 6. This description of cutting the ocular muscles is one of several ways to remove the eye. Please refer to your local eye bank's procedure manual for any variation. All 6 ocular muscles must be isolated and severed; however, the order and technique may differ. Be careful not to puncture the globe while severing of the muscles. The sclera is thinnest underneath the insertion sites of the ocular muscles. Do not traumatize the cornea during this procedure.
 7. A 5-10mm optic nerve stump will assure that it is not cut too close to the posterior so as to risk puncture and collapse of the globe. A generous stump also allows for sufficient length to anchor the eye in the cage, if used, by pulling the stump through the bottom.
 8. The globe will be completely removed from the socket after this step.
- roll, gauze, cotton ball or metal cage, orient the eye to prevent trauma to the cornea. If using a

metal cage, place the optic nerve through the hole and either clamp or pin the nerve in place. If using gauze or dental roll, ensure that the epithelium is not contacted by the material for the duration of the shipment.

10. Pour a **small amount** or approximately 5 ml of balanced salt, antibiotic solution, or other sterile ophthalmic irrigating solution over the eye (just enough to moisten the gauze, dental roll or cotton in the bottom of the jar).
11. Reglove or remove outer glove. Repeat steps (1-13) above for the other eye. The second eye should already be draped.
12. Donor Reconstruction
 - A. Remove drapes
 - B. Place a folded piece of gauze or a cotton ball in the socket and insert eye caps per your eye bank's policy. Close the eyelids and gently wipe off the povidone-iodine or other solution by patting with moist gauze.
 - C. If necessary, control excessive bleeding. Check with your local funeral directors and follow your eye bank's protocol. Trocar buttons, local cauterizing agents, gel foam, and other techniques may be used.
 - D. Leave the donor's head elevated.
 - E. Remove surgical gloves, don clean gloves, and place the lids on both jars, being careful NOT to touch the inside of the jar or lid.
 - F. Label each eye jar (see procedure J1.000) and place both jars in transport container with frozen water beginning to melt to maintain the temperature between 2-8o C. (Label non-surgical tissue according to H1.000
 - G. Record information about the enucleation in the donor's medical record according to your eye bank's policy.
9. Although pins have been used to secure the eye in the cage, they introduce increased risk of puncture to the ocular tissue and the eye bank technician. They may also be difficult to remove.
10. The addition of the solution maintains a moist chamber effect to avoid desiccation of the globe. Overfilling the moist chamber such that the cornea is submerged in hypertonic solution may cause irreversible damage to the cornea.
 - A. Gently remove drapes so as not to damage the donor's skin or accidentally remove eyebrow or eyelashes.
 - B. To restore the appearance of the donor. Minimal or gentle manipulation of the eyelids will help decrease post-mortem discoloration and swelling.
 - C. These procedures may be developed in consultation with your local funeral directors, hospitals, and skin or tissue bank(s).
 - D. Promotes blood and fluid to drain away from the face to reduce bleeding and swelling.
 - E. Surgical gloves should be removed so that the exterior of the jars are not contaminated with eye tissue or body fluid, avoiding the creation of a potential biohazard.
 - F. The non-sterile labels are added to the jars after sterile handling of the exterior is completed.
 - G. To fulfill The Joint Commission requirements on documentation of tissue and organ removal. TS.03.02.01 requires documentation of dates, times, and staff involved when tissue is accepted, prepared, and issued.

- H. Complete the eye bank's enucleation form, as required.
 - I. Leave a form or attach a tag to the body informing the funeral director that the eyes have been removed and to keep the head elevated. Also give the eye bank's name, location, and phone number with instructions to notify the eye bank if there are any questions or problems.
 - J. Don nonsterile gloves and rewrap the donor in the body bag or shroud and return to the storage location from which it was removed.
 - K. Clean the work area. Discard all used disposables in a biohazard bag and all sharps in a sharps container.
 - L. Rewrap any non-disposable instruments for return to the eye bank or for cleaning and sterilization by the facility if necessary.
 - M. Transport the eyes to the eye bank as soon as possible.
- I. These procedures may be developed in consultation with your local funeral directors, hospitals, and skin or tissue bank(s).
- K. Disposable instruments should be discarded as sharps in a sharps container.
- L. Be sure that used non-disposable instruments are marked as biohazardous during transport.

E1.130 In Situ Cornea Excision

Purpose:

To provide a standardized method for the aseptic in situ removal of corneal tissue for surgical use that will minimize endothelial cell loss and contamination, and maximize the number and quality of cells that are ultimately grafted.

Reference:

Rosenwasser, G. O. D., & Nicholson, W. J. (2003). In-situ excision. *Introduction to eye banking: a handbook and atlas*. (1st ed.) (pp. 57-63).

Regulatory:

21 CFR 1271.145 Prevention of the introduction, transmission, or spread of communicable diseases 21
CFR 1271.220 Process Controls

Materials needed:

Skin prep tray, povidone-iodine or other microbicidal solution and sterile 4 x 4's or Sterile ophthalmic irrigant solution, such as sterile saline

Sterilized, appropriately wrapped instrument tray to include the following:

- 1 Lid speculum
- 2 Forceps with teeth
- 2 Pair of iris or tenotomy scissors
- 2 #11 or #15 blades
- 1 Corneal section scissors, Castroviejo scissors, or Aebli Scissors
- 1 Pair of forceps to handle lids of medium (optional)

2 sterile corneal storage containers (e.g. corneal viewing chambers) 2

vials of corneal tissue culture preservation medium

Two single fenestrated drapes or one double fenestrated drape, or sterile towels

Culturettes or other items specified by your eye bank if culturing of the corneoscleral rim at time of removal is desired.

Procedure	Rationale
<ol style="list-style-type: none">1. All donor preparatory procedures prior to ocular tissue recovery should be performed according to procedure E1.110. As noted in step 10D, in situ excision is a tissue preservation procedure requiring application of povidone-iodine, followed by a normal saline or balanced salt solution rinse. The povidone-iodine solution concentration should conform to your eye bank's standard operating procedure, generally between 1% and 10%.	<ol style="list-style-type: none">1. Application of povidone-iodine to the corneal surface prior to preservation of the cornea for transplant is a required precaution to reduce the bioburden of the exterior corneal surface. Medical Standard E1.110 dictates that povidone-iodine shall contact the surface of the ocular tissue intended for transplant at least once between the time of the donor's death and tissue preservation.

2. Some eye banks may perform a culture at the time of procurement. Please refer to section G1.200 and your eye bank's policy for specific direction about cultures.
 3. Label the corneal storage containers, loosen the caps to the top thread, and place the containers adjacent to a top corner of the sterile field. If sterile containers are dropped onto the sterile field the containers are labeled as soon as possible at the end of the procedure.
 4. If required by the coroner or medical examiner, label test tubes for blood and vitreous samples and position near the sterile field along with the syringe, needle, and cosmetic restoration materials.
 5. Open the eyelid using a sterile cotton tipped applicator and insert a solid blade eye speculum.
 6. Lift and cut the conjunctiva at the limbus 360o around the cornea using small-toothed forceps and iris or tenotomy scissors. Any adhesions between the conjunctiva and the anterior globe are separated so that the conjunctiva is not in contact with the anterior globe to within 5 mm of the limbus. Remove any remaining conjunctiva by carefully scraping from the limbus with a scalpel blade. If the tissue is being recovered for cadaveric limbal allograft, leave approximately a two-millimeter skirt of conjunctiva around the corneal limbus.
 7. Isolate the instruments used to manipulate the exterior surfaces of the eye, including those instruments used in the removal of conjunctiva (if performed), from the other instruments on the sterile field. Use these only for the same purpose on the opposite eye.
2. Performing a procurement culture is at the discretion of the eye bank's medical director.
 3. Take care in the positioning of the storage medium vials to avoid accidentally knocking over the vials while reaching for instruments if they are at the bottom of the field or contaminating the field by reaching over if they are at the top of the field.
 5. Take care not to touch cornea with the solid blade eye speculum when placing it under the eyelid.
 6. Removing the conjunctiva close to the limbus prevents slippage of the rim while it is mounted on an artificial anterior chamber. Slippage can cause damage to the cornea during the lamellar keratectomy pass of the microkeratome rendering the cornea unusable. Additionally, the conjunctival tissue can increase the burden of microorganisms that travel with the donor tissue, increasing the potential for contamination during transplantation. Leaving 2mm of conjunctiva will help ensure that tissue may be suitable for surgeries for patients in need of limbal stem cells. Any grossly contaminated or jaundiced conjunctiva should be removed completely without damaging the limbus to reduce the introduction of contaminants to the preservation media.
 7. Exterior surfaces of the eye have been exposed to environmental contaminants. Avoid mechanical introduction of microorganisms to the interior surfaces of the cornea by keeping instruments used for the different parts of the procedure appropriately separated.

8. Make an incision through the sclera 2 mm - 4 mm from the limbus and parallel to the limbus. Carefully cut all the way through the sclera without perforating the choroid.

9. Extend the scleral incision 360° around the cornea using corneal section scissors (Castroviejo or Aebli). Avoid perforating the choroid, breaking into the anterior chamber, or causing any deformation of the cornea's normal curvature.

The scissor blades should not be visible in the anterior chamber.

Keep the incision parallel to the limbus to produce an even scleral rim between 3 mm - 4 mm in width (with 2 mm of intact conjunctiva if recovery is being performed for limbal allografts).

10. Inspect the incision to ensure it is complete and that the anterior chamber is intact. If the incision has been made properly, the corneoscleral disc should be attached to the uvea (ciliary body-choroid) only at the scleral spur.

11. Cultures of the incision site may be taken at this time, per your eye bank's policy.

12. Complete the corneal removal using one pair of small forceps to hold the scleral rim stationary and a second set of small forceps, an iris spatula, or similar technique to push the ciliary body-choroid downward and away from the corneoscleral disc.

8. Perforation of the choroid causes vitreous leakage, which may collapse the globe including the anterior chamber and compromise the corneal endothelium. Additionally, vitreous leakage would make cosmetic restoration more difficult.

9. Trauma to the cornea during excision due to bending, loss of the anterior chamber, or collapse of the globe through vitreous loss may compromise its suitability for surgical use.

This indicates that the anterior chamber has been inadvertently entered, which may damage the corneal endothelium.

Scleral rim width is important because some surgical corneal holding devices require a minimum of 3 mm rim while other such devices require a rim no wider than 4 mm. Also, cutting a rim less than 3 mm wide greatly increases the chance of entering the anterior chamber while performing the peripheral scleral dissection. Use of a scoring trephine may help to achieve consistent rim sizes.

10. The risk of endothelial trauma or corneal contamination is greatest at this stage of the excision process.

11. Culturing is performed at the discretion of the eye bank medical director.

12. Aqueous fluid should escape from the anterior chamber at this point assuring that the anterior chamber was indeed intact.

13. Gently separate remaining adhesions away from the corneoscleral disc working side to side and taking great care to avoid pulling on the cornea and creating folds. The corneoscleral rim should never be allowed to drop back down while making this separation. The corneoscleral disc must never be pulled in such a way as to cause cross-corneal tension.

Care must also be taken to prevent the cornea from contacting the eyelids or other facial skin while removing it from the eye.

14. Continue to hold the cornea by the scleral rim with the small-toothed forceps, transfer it to a labeled storage medium container. The pre-loosened cap is lifted off the vial using sterile forceps immediately prior to placing the cornea in the medium and replaced immediately afterward. If forceps are not used, reglove before starting on the next cornea.

15. Examine the posterior chamber for a crystalline lens.

16. Repeat the excision on the second eye (Steps 1- 15). After the second cornea is placed in storage medium, both container caps are tightened and appropriately labeled.

17. Completion

- A. Dispose of sharps in a sharps container.
- B. Remove drapes. Insert eye caps. Close the eyelids and remove all remaining prep solution with gauze and water or alcohol.
- C. Leave the donor's head elevated.
- D. Record information about the excision in the donor's medical record according to your eye bank's policy.

13. To avoid stretching or folds leading to potential loss of endothelial cells.

To avoid contamination of the ocular tissue.

14. Removing the vial cap at the time the cornea is placed in the storage medium minimizes the medium's exposure to airborne contaminants.

15. To inspect for signs of previous cataract surgery that would possibly contraindicate use of the ocular tissue for penetrating keratoplasty per EBAA Medical Standards section D1.110, depending on your eye bank's policy.

- A. Sharps are disposed as soon as possible to decrease the risk of exposure to contaminated sharps.
- B. To restore the appearance of the donor. Use care when removing the drapes from the face to minimize the chance of damage to the skin or accidentally removing eyebrow or eyelid hair.
- C. Promotes blood and fluid to drain away from the face to reduce bleeding and swelling.
- D. To fulfill The Joint Commission requirements on documentation of tissue and organ removal.

- E. Complete the eye bank's excision form, as required.
 - F. Leave a form or attach a tag to the body informing the funeral director that the corneas have been removed and to keep the head elevated. Also give the eye bank's name, location, and phone number with instructions to notify the eye bank if there are any questions or problems.
 - G. Don non-sterile gloves and rewrap the donor in the body bag or shroud and return to the storage location from which it was removed.
 - H. Clean the work area. Discard all used disposables in a biohazard bag.
 - I. Rewrap non-disposable instruments for return to the eye bank or for cleaning and sterilization by the facility if necessary.
 - J. Transport the corneas to the eye bank as soon as possible.
- F. As a courtesy to the local funeral director. Also, hopefully, the funeral director will notify the eye bank before discussing problems related to the eye removal with the family.
 - H. Disposable instruments should be discarded as sharps in a sharps container.
 - I. Be sure that used non-disposable instruments are marked as biohazardous during transport.

E1.140 Blood Drawing

Purpose:

To describe the procedure for obtaining a blood sample from a donor for the purpose of serologic testing.

Reference:

Langer, C., Francke, A., Duncker, G. I., & Bredehorn, T. (2002). Procedures for blood-taking from cadaveric cornea donors. *Transplantation Proceedings*, 34(6), 2334.

Materials needed:

Sterile Supplies:

- 10cc syringe
- Sterile povidone-iodine or alcohol swab to prep the skin
- 16 or 18 gauge needle or vacutainer needle and holder
- 10cc red top vacutainer tube purple tops or any other vacutainer tubes required by SOP or testing facility

Non-Sterile Supplies

- Exam gloves
- Moisture impermeable protective clothing
- Mask
- Protective eyewear Biohazard labels
- Plastic bag with closure device
- Blood specimen transportation box/container*

Procedure	Rationale
1. Verify the IV infusion/transfusion status of the donor. Seek a pre-infusion specimen per EBAA Standard D1.200, if appropriate.	1. See EBAA Medical Standards section D1.200. Plasma dilution from blood products, colloids and crystalloids may affect test results and make detection of HIV 1/2 antibodies difficult leading to false negative results. Check with your local blood bank for specific volumes of each blood product administered.
2. Set up supplies near the donor.	
3. Select the blood draw site. The major vessels such as the subclavian vein and the femoral artery are the easiest. A blood sample may also be drawn from the heart.	3. Decision may be influenced by coroner or medical examiner preference, if this is a coroner or medical examiner case.
4. Put on gloves and other protective apparel.	4. Adherence to <i>Standard Precautions</i> is mandatory.
5. Cleanse skin with alcohol or povidone-iodine at the site from which you wish to draw.	5. To avoid contaminating the needle and therefore the blood sample with skin contaminants that may affect the results.

6. Locate the appropriate anatomic landmarks that overlay the chosen vessel. For example, to obtain a blood sample from the subclavian vein, the needle should be inserted through the skin, above the right clavicle (collar bone) at a 30° angle, towards the throat and parallel to the clavicle.
7. Insert needle full length to hub of syringe and pull back plunger. Blood will enter the needle when the vessel has been entered or, if using a vacutainer system, insert needle and connect the red top vacuum tube.
8. If blood does not enter syringe, pull back slightly and angle needle differently until you enter the vessel and see a blood return.
9. Draw a sufficient amount of blood needed to complete the required infectious disease testing.
10. Carefully and slowly inject blood into red top tube, taking extreme care to avoid a needlestick.
11. Use **Standard Precautions**. Do not recap needle. Discard into appropriate sharps container.
12. Apply pressure over puncture site and gently rub skin to close puncture and stop bleeding.
13. Label tube with date and time of draw, name of donor, a donor identification number, and initials of the technician.
14. Avoid freezing the blood sample while storing or transporting.
15. Transport specimen to laboratory
10. Inject or transfer blood slowly and carefully into tube to prevent hemolysis.
11. See procedure C3.600.
14. Freezing will hemolyze the cells and make it virtually impossible to obtain serum.
15. Ship blood and tissue according to your state and federal guidelines.
16. To provide a cleaner non-hemolyzed serum sample, the blood may be spun down in a centrifuge. Pipette the serum from the top and transfer to a clean tube and label. Extra serum may be archived in the eye bank laboratory freezer, if directed by your eye bank's policy and procedure manual.

See EBAA Medical Standards sections D1.210 – D1.230.

Avoid or minimize hemolysis by using a large bore needle. Also, wait until blood is fully clotted before centrifugation.

17. Record results of serologic testing on the donor ocular tissue record prior to release of tissue for surgical use. ***Tissue must not be shipped prior to receipt and recording of non-reactive (negative) results from a hardcopy report.***
18. Attach copy of laboratory results in printed form to the donor record.
17. To avoid the possibility that tissue will be surgically implanted prior to receipt of required serology results.

E1.200 Open-Container Processing

Purpose:

To outline the different non-recovery methods of ocular tissue handling and processing.

Procedure	Rationale
1. Open container processing must be performed in: a) a laminar flow hood or biosafety 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 90mm settle plate per one hour exposure.	1. To ensure the environment to which the ocular tissue is exposed is sufficiently aseptic as to not contaminate the tissue.

E1.210 Whole Eye Storage for Surgical Use

Purpose:

To delineate the methods used for storage of whole globes for surgical use.

Definition of terms:

Moist chamber: A closed container with cotton gauze moistened with sterile saline or other sterile ophthalmic solution to provide a moist environment. The container is never completely filled with liquid so that the entire eye is immersed.

Decontamination: To reduce surface contamination by antimicrobial action.

Regulatory:

21 CFR 1271.145 Prevention of the introduction, transmission, or spread of communicable diseases
21 CFR 1271.210 Supplies and Reagents

Materials needed:

Sterile Supplies

A sterile instrument tray:

2 Large toothed forceps

1 Hemostat

2 Sterile eye jars or medicine cups for soaking eyes

2 Sterile eye jars containing gauze

2 Cotton tipped applicators

1 Sterile ophthalmic irrigating solution, e.g., normal saline, balanced salt solution or antibiotic solution

1 Sterile ophthalmic broad-spectrum antibiotic solution or povidone-iodine irrigating solution Sterile impermeable barrier drape (optional)

Sterile gloves

Sterile gown or sleeves

Sterile Instrument pack or tray containing the following:

Sterile scrub brush for hands

Jars containing donor eyes

Non-sterile Supplies:

Prep gloves

Moisture impermeable protective clothing

Mask

Cap to cover hair

Protective eyewear (goggles or face shield)

ISO Class 5 Hood or Biosafety Cabinet or

approved processing room

Refrigerator and/or freezer and/or liquid nitrogen container

CDC recommended disinfectant

Sealing material e.g. shrink wrap

Procedure	Rationale
1. Turn on laminar airflow of the hood or biosafety cabinet and allow to run according to manufacturers' instructions prior to use. If a laminar airflow hood or biosafety cabinet is not being used, another environment documented annually to have less than 25 colony forming units per 90mm settle plate per one hour exposure may be used.	
2. Clean the laminar flow hood, biosafety cabinet or processing room according to the procedure established by your eye bank. Cleaning is required before and after each use.	
3. Place jars containing eyes and all sterile instruments and supplies on work surface of hood or biosafety cabinet or work table in the open container processing room.	
4. Don appropriate protective apparel, per procedure E1.110.	
5. Position the eye jars so that they are immediately adjacent to the edge of the sterile field formed when the sterile instrument pack is opened. The eye jar lids are removed and placed with inner side up next to their respective jars. Position eye jars to ensure that left and right specimen bottles are clearly and readily identified.	
6. Uncap a 10 cc bottle of broad range sterile ophthalmic antibiotic solution or a povidone-iodine solution and place near the eye jars according to your eye bank's policy.	6. Antibiotic or antiseptic application to the whole eye prior to corneal excision reduces the microbial population and potential contamination.

7. Set up the sterile field by opening wraps of the sterile instrument tray. Alternatively, a sterile moisture impermeable barrier drape may be opened and placed on the work surface of the hood, biosafety cabinet or processing room worktable followed by opening sterile instruments in peel packs and dropping them on. Avoid contaminating the sterile field created by touching or reaching over the field. Open individually wrapped sterile items, such as gauze or sterile cotton-tipped applicators and flip onto the sterile field with the surgical instruments.
8. Perform surgical hand antisepsis, and dry hands with a sterile towel. Don sterile gown/sleeves and gloves.
9. Lift the eye and the eye cage, if one is used, from the eye jar with sterile forceps (or the cage with a sterile cotton-tipped applicator.) Remove the fastener, if one is in place, from the optic nerve with a hemostat.

Remove the eye from the cage using forceps to grasp a rectus muscle.

10. Soak or irrigate the eye using a povidone-iodine or antibiotic solution for 3 to 5 minutes in a sterile medicine cup according to your eye bank's procedure. Avoid contaminating the sterile field by wetting of a cloth drape, if one is used. Irrigation should be performed over a metal instrument pan or a moisture impermeable drape.
10. Studies have shown that whole eye immersion is superior to irrigation for removal of microbes (see reference list.)
11. Transfer the whole eye with sterile forceps from antibiotic/antiseptic soaking solution to sterile eye jars for storage.
12. Label all storage containers with appropriate identification as follows:
 - a. Source eye bank name
 - b. ISBT 128 tissue identifier (DIN, Product Code, and Fin(P)).
 - c. Type of ocular tissue
 - d. Type of storage solution
 - e. Date/Time of death
 - f. Date/Time of preservation
 - g. Expiration date of tissue
 - h. Statement that ocular tissue is for single patient use and not considered sterile.
 - i. 2-D data matrix symbol if distributed internationally (effective 1/1/2017).
12. All ocular tissue must be labeled with a unique eye bank identification record number for proper quality control assurance. Proper labeling is required according to EBAA Medical Standards. See procedure J1.000.

13. Seal and store whole eyes for penetrating keratoplasty (PK) in a moist chamber at 2–8°C for 24-48 hours, or as instructed by your eye bank medical director.
 14. Store whole eyes for lamellar keratoplasty (LK) either in a moist chamber at 2–8°C or frozen at 0° C. The temperature and length of storage are determined by the medical director and must be recorded in your eye bank's procedure manual.
 15. Record the method and date of storage on the tissue report form.
 16. Wipe down the work surface with a CDC recommended disinfectant solution immediately after use and allow it to air dry. Document these cleaning procedures according to your eye bank's Policies and Procedures.
13. This environment provides for short-term preservation of the cornea.
 14. Ocular tissue used for LK does not require an intact endothelium.

E1.221 Excision of the Corneoscleral Disc from Enucleated Whole Eyes

Purpose:

To provide a standardized method for the aseptic preservation of corneal tissue in the laboratory that will minimize endothelial cell loss and contamination and maximize the number and quality of cells that are ultimately grafted.

Regulatory:

21 CFR 1271.145 Prevention of the introduction, transmission, or spread of communicable diseases
 21 CFR 1271.220 Process Controls

Reference:

Rosenwasser, G. O. D., & Nicholson, W. J. (2003). Corneal excision. *Introduction to eye banking: a handbook and atlas*. (1st ed.) (pp. 47-55).

Materials needed:

Sterile Supplies

- Sterile gown or sleeves
- Sterile gloves
- Sterile scrub brush for scrubbing hands
- 1 sterile towel
- Sterile ophthalmic irrigating solution

Sterile ophthalmic broad-spectrum antibiotic or antimicrobial solution
 2 vials corneal storage medium
 2 sterile corneal containers (e.g. corneal viewing chambers)
 2 mini tipped culettes (if cultures are performed by the eye bank)
 Sterile cotton-tipped applicators
 Sterile gauze
 Jars containing whole eyes
 Appropriately wrapped sterilized instrument tray containing the following:

- 2 Small toothed forceps
- 2 Scalpel handles
- 2 #11 or #15 blades
- 1 Corneal section scissors, or Castroviejo or Aebli scissors
- 2 Tenotomy or iris scissors
- 1 Hemostat
- 1 Forceps to handle cages and/or solution bottles
- 2 Medicine cups or other small 30 cc glass/steel container

Non-Sterile Supplies

ISO Class 5 Hood Biosafety Cabinet or an open container processing room (as described in Section E1.200)
 Moisture impermeable protective clothing
 Mask
 Cap to cover hair
 Protective eyewear (goggles or face shield)
 Slit Lamp
 Evaluation Form
 CDC recommended disinfectant solution

Procedure	Rationale
<p>1. Slit lamp globes. Perform the corneal removal (excision) in the laboratory in an ISO Class 5 Hood or Biosafety Cabinet or open container processing room following a whole eye enucleation. Wipe down and air-dry the work surface of the hood, cabinet, or work surface with a disinfectant solution immediately prior to use. Turn on laminar airflow of hood and allow to run at least fifteen minutes or according to manufacturers' instructions prior to use, if utilizing a hood or cabinet. Document cleaning of the hood according to each eye bank's policies and procedures.</p>	<p>1. Minimizes the risk of contamination by providing a decontaminated work surface. Allows laminar flow to be established.</p>
<p>2. Don appropriate protective apparel consistent with the biological safety cabinet being used.</p> <p>If using an open container processing room for this procedure, an operating room head cover, mask, eye protection, shoe covers, sterile gown, and at least one pair of sterile gloves shall be worn.</p>	<p>2. Use of a biosafety cabinet with a glass or plastic shield protects the technician and tissue. Therefore, protective eye wear and mask in particular may not be necessary. However, if tissue is opened outside of the hood, e.g., while slit lamping the whole globe, full protective apparel is still required.</p>

3. Place sterile instrument pack, eye jars, antibiotic or antimicrobial solution, and corneal storage medium containers on the prepared surface of the laminar airflow work surface. If sterile corneal storage containers are dropped onto the sterile field, the containers are labeled as soon as possible at the end of the procedure.
4. Position the eye jars so that they are immediately adjacent to the edge of the sterile field formed when the sterile instrument pack is opened. The eye jar lids are removed and placed with inner side up next to their respective jars. The labeled storage medium vials are positioned so that they also will be adjacent to the sterile field. Remove the caps of the vials. Position eye jars and medium vials to ensure that left and right specimen bottles are clearly and readily identified.
5. Uncap a 10 cc bottle of broad range sterile ophthalmic antibiotic solution or a povidone-iodine solution container and place near the eye jars and medium vials, according to your eye bank's policy.
6. Using aseptic technique set up the sterile field by opening the wraps of the sterile instrument tray. Alternatively, a sterile moisture impermeable barrier drape may be opened and placed on the work surface of the laminar airflow hood, cabinet, or work surface followed by opening sterile instruments in peel packs and dropping them onto it. Avoid contaminating the sterile field created by touching or reaching over the field. Using aseptic technique, open individually wrapped sterile items, such as gauze or sterile cotton-tipped applicators and flip onto the sterile field with the surgical instruments.
7. Perform surgical hand antisepsis according to eye bank procedure. Dry hands with a sterile towel. Using aseptic technique don sterile gloves and gown or sleeves. Double glove if this is your eye bank's policy.
8. Fold a sterile 4 x 4 gauze sponge to form a long strip.
9. Lift the eye and the eye cage, if one is used, from the eye jar with sterile forceps (or the cage with a sterile cotton-tipped applicator.) Remove the pin if one is in place from the optic nerve with a hemostat.
5. Antibiotic or antiseptic application to the whole eye prior to corneal excision reduces the microbial population. Refer to EBAA Medical Standard E1.110 regarding the necessity of a povidone-iodine preparation of ocular tissue "at least once between the time of the donor's death and tissue preservation."
8. This is used to hold the eye during the corneal removal.

Remove the eye from the cage using forceps to grasp a rectus muscle.

10. Soak or irrigate the eye using an antibiotic solution according to your eye bank's policies and procedures. Avoid contaminating the sterile field by wetting of a cloth drape, if one is used. Irrigation should be performed over a metal instrument pan or a moisture impermeable drape.
 11. Wrap the eye securely with the gauze strip several times around the equator.
 12. Lift and cut any remaining conjunctiva at the limbus and extending out 5 mm from the limbus using small toothed forceps and iris or tenotomy scissors. The exposed sclera may be carefully scraped from the limbus outward with a scalpel blade to remove all remaining conjunctival tissue. If recovering the tissue for limbal allograft purposes, lift and cut the conjunctiva at the limbus 360° around the cornea using small-toothed forceps and iris or tenotomy scissors, leaving about 2mm of conjunctiva evenly around the cornea.
 13. Isolate the instruments and scalpel blade (if used) used to remove the conjunctiva from the other instruments on the sterile field. Use these only for the same purpose on the opposite eye.
 14. Pick up the gauze-wrapped globe and hold with one hand.
 15. Make an incision through the sclera 3 mm - 4 mm from the limbus and parallel to the limbus. Carefully cut all the way through the sclera without perforating the choroid.
 16. Extend the scleral incision 360° around the cornea using corneal section scissors (Castroviejo or Aebli). Avoid perforating the choroid, breaking into the anterior chamber, or causing any deformation of the cornea's normal curvature. The scissor blades should not be visible in the anterior chamber.
 17. Keep the incision parallel to the limbus to
10. Studies have shown that whole globe immersion is superior to irrigation for removal of microbes (see reference list.)
 12. Removing the conjunctiva close to the limbus prevents slippage of the rim while it is mounted on an artificial anterior chamber. Slippage can cause damage to the cornea during the lamellar keratectomy pass of the microkeratome rendering the cornea unusable. Additionally, the conjunctival tissue can increase the burden of microorganisms that travel with the donor tissue, increasing the potential for contamination during transplantation. Leaving 2mm of conjunctiva will help ensure that tissue may be suitable for surgeries for patients in need of limbal stem cells. Any grossly contaminated or jaundiced conjunctiva should be removed completely without damaging the limbus to reduce the introduction of contaminants to the preservation media.
 13. Exterior surfaces of the eye have been exposed to environmental contaminants. Avoid mechanical introduction of microorganisms to the interior surfaces of the cornea by keeping instruments used for the different parts of the procedure appropriately separated.
 15. Perforation of the choroid causes vitreous leakage, which may collapse the globe including the anterior chamber. This would compromise the corneal endothelium.
 16. Trauma to the cornea during cutting due to bending, loss of the anterior chamber, or collapse of the globe through vitreous loss would severely compromise its suitability for surgical use.
 17. Scleral rim width is important because some

produce an even scleral rim between 3 mm and 4 mm in width. If the tissue is recovered for limbal allograft use, maintain 2mm of intact conjunctiva.

18. Inspect to be certain the incision is complete and that the anterior chamber is intact. If the incision has been made properly, the corneoscleral button should be attached to the ciliary body-choroid only at the scleral spur.
 19. A culture of the incision site may be performed at this time, per your eye bank's policy.
 20. Set the wrapped eye down near the center of the sterile field that may be stabilized by attaching a sterile hemostat. Complete the corneal removal using one pair of the small forceps to hold the scleral rim stationary and a second set of small forceps, an iris spatula or similar technique to push the ciliary body-choroid downward and away from the corneoscleral button. Gently separate remaining adhesions from the corneoscleral button working side to side. The corneoscleral rim must never be pulled in such a way as to cause cross-corneal tension. The corneoscleral rim should never be allowed to drop back down onto the anterior chamber.
 21. Continue to hold the cornea by the scleral rim with the small-toothed forceps and transfer it to a labeled corneal storage container from which the caps have already been removed.
 22. Examine the posterior chamber for crystalline lens.
 23. Carefully unwrap and return the remaining posterior segment to its respective eye jar. Avoid contaminating the posterior segment, instruments, or surgical gloves.
 24. Repeat the procedure on the second eye.
 25. After the second cornea is placed in storage medium, replace both container caps and tighten. Replace the lids on the eye jars. The containers with the ocular tissue are immediately labeled and sealed and the tissue refrigerated
18. The risk of endothelial trauma and cell damage is greatest at this stage of the excision process.
 19. Culturing is performed at the discretion of the eye bank medical director.
 20. To avoid pulling on the cornea and creating folds. Aqueous fluid should escape from the anterior chamber at this point assuring that the anterior chamber was indeed intact.

Never allow the cornea to drop back down once the removal has started. Doing so may cause endothelial cell damage if the cells come in contact with the iris.
 21. The vials may remain open under the laminar airflow hood, biosafety cabinet, or on an open container room work surface for a period of 1 hour, which is acceptable operating room practice.
 22. Inspect for signs of previous cataract surgery, which would possibly contraindicate use of the corneal tissue for penetrating keratoplasty, depending on your eye bank's policy (See EBAA Medical Standards (D1.110)).
 25. See procedures I1.000 and J1.000.

according to each eye bank's policies and procedures.

26. Dispose of sharps in a sharps container. Non-disposable instruments and eye jars are immediately cleaned according to your eye bank's policy and procedure. Discard all disposables in a biohazard receptacle.
26. Sharps are disposed as soon as possible to decrease the risk of exposure to contaminated sharps. See procedure C3.300 for care of instruments. Disposable instruments should be discarded as sharps in a sharps container.
27. Immediately after use, wipe down the work surface of the hood, cabinet, or open container room surface with a disinfectant and allow to air dry. Document these cleaning procedures according to your eye bank's policies and procedures.
27. See EBAA Medical Standards C3.300.

E1.222 Laboratory Microkeratome Anterior or Endothelial Lamellar Processing

Purpose:

To provide a standardized method for the aseptic processing of corneal tissue for anterior or posterior lamellar keratoplasty with a microkeratome that will minimize cross-contamination and maximize the quality of tissue for the intended use.

Reference:

- Gorovoy, M.S. & Locke, G.D. (2009). Ch 13 use of eye bank precut vs. surgeon-dissected donor tissue for EK. In F.W. Price & M.O. Price (Eds.) DSEK, what you need to know about endothelial keratoplasty (pp. 171-176). Thorofare: Slack.
- Kitzmann, A.S., Goins, K.M., Reed, C., Padnick-Silver, L., Macsai, M.S., & Sutphin, J.E. (2008). Eye bank survey of surgeons using precut donor tissue for Descemet stripping automated endothelial keratoplasty. *Cornea* 27(6), 634-639,
- Price, M.O., Baig, K.M., Brubaker, J.W., & Price, F.W. (2008). Randomized, prospective comparison of precut vs. surgeon-dissected grafts from Descemet stripping automated endothelial keratoplasty. *American Journal of Ophthalmology*, 146(1), 36-41.
- Rose, L., Briceno, C.A., Stark, W.J., Gloria, D.G., & Jun, A.S. (2008). Assessment of eye bank-prepared posterior lamellar corneal tissue for endothelial keratoplasty. *Ophthalmology* 115(2), 279-286.
- Takeshi, I., Yoo, S.H., Kymionis, G.D., Perez, V.L., Goldman, J.M., & O'Brien, T.P. (2008). Descemet-stripping automated endothelial keratoplasty (DSAEK): Effect of nontoxic gentian violet marking pen on DSAEK donor tissue viability by using vital dye assay. *Cornea*, 27(5), 562-564.
- Terry, M.A. (2009). Endothelial Keratoplasty: A comparison of complication rates and endothelial survival between precut tissue and surgeon-cut tissue by a single DSAEK surgeon. *Transactions of the American Ophthalmological Society*, 107, 184-191.

Regulatory:

- 21 CFR 1271.145 Prevention of the introduction, transmission, or spread of communicable diseases
- 21 CFR 1271.220 Processing and Process Controls

Materials needed:

Corneas or whole globes

Sterile Supplies

- 1 sterile gown or (2) sleeves
- 1 pair sterile gloves
- 1 sterile surgical scrub brush
- 1 sterile towel
- 2 vial corneal storage medium
- 2 sterile corneal containers (e.g. corneal viewing chambers)
- Sterile surgical spears
- Sterile serrated forceps
- Microkeratome system
- Artificial anterior chamber

Non-Sterile Supplies

- ISO Class 5 Hood or Biosafety Cabinet or suitable environment
- Moisture impermeable protective clothing
- Mask
- Cap to cover hair
- Protective eyewear (goggles or face shield)
- Device for determining pachymetry
- Device for measuring stromal bed
- Tissue thickness nomogram
- Evaluation form
- CDC recommended disinfectant solution

Procedure

Rationale

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|---|--|
| <p>1. Establish guidelines which deem outcomes from processing as acceptable or not-acceptable, including, but not limited to:</p> <ul style="list-style-type: none">a. Target and/or minimum/maximum stromal bed thickness.b. Post-processing endothelial cell count.c. Uniformity of cut.d. Absence of perforation. <p>2. Select appropriate donor tissue (cornea or whole globe).</p> | <ul style="list-style-type: none">a. To identify desired thickness post-cut.b. To ensure adequate cell viability following surgery.c. To ensure transplant adheres properly.d. Perforated cornea would indicate traumatized tissue. <p>2. To ensure suitable tissue is identified and used.</p> |
|---|--|

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|--|--|
| <p>3. Clean work area with a disinfectant where processing will occur and document cleaning.</p> | <p>3. To minimize the risk of contamination by providing a decontaminated work surface.</p> |
| <p>4. If using lamellar flow hood or biosafety cabinet, turn airflow on for at least 15 minutes prior to use or according to manufacturer's recommendation.</p> | <p>4. To establish laminar flow to provide a clean air environment for processing.</p> |
| <p>5. Don appropriate personal protective apparel consistent with processing environment used (eg. biological safety cabinet).</p> | <p>5. To prevent exposure to open wounds, non-intact skin, or mucus membranes such as in the nose or eyes.</p> |
| <p>6. Using aseptic technique, establish sterile field. Drop sterile items on the field as needed for the procedure.</p> | |
| <p>7. Prepare sterile field (i.e. clean laminar flow hood or other appropriate work site).</p> | <p>7. To minimize the risk of contamination by providing a decontaminated work surface.</p> |
| <p>8. Perform 3-5 minute surgical scrub according to eye bank policy. Dry hands with a sterile towel. Use aseptic technique to don sterile gloves and gown or sleeves.</p> | <p>8. See AORN Standards for information on scrubbing and alternative scrub methods to achieve an aseptic environment.</p> |
| <p>9. Set up sterile field. Arrange instruments appropriately on the sterile field and transfer donor tissue.</p> | |
| <p>10. Set up microkeratome system and run appropriate system checks according to manufacturer's recommendations.</p> | <p>10. To ensure equipment functions properly prior to use.</p> |
| <p>11. Prior to cutting tissue, assess initial corneal thickness via pachymetry (this may be performed once tissue is mounted (see step below) or prior to introduction to the sterile field using a non-contact pachymeter.</p> | <p>11. To determine initial corneal measurements.</p> |
| <p>12. For corneal tissue, use an anterior chamber:</p> <p style="margin-left: 20px;">a. Place cornea on artificial chamber, taking care not to fold cornea, induce stress lines, or traumatize the endothelium.</p> <p style="margin-left: 20px;">b. Center tissue.</p> | <p>12.</p> <p style="margin-left: 20px;">a. The risk of endothelial trauma and cell damage is greatest at this stage (and step "1" below) of the lamellar processing.</p> <p style="margin-left: 20px;">b. To ensure cut is central to help promote an</p> |

- c. Secure helmet.
 - d. Pressurize the chamber.
 - e. Verify desired pressure is achieved (i.e. tonometer or other validated method).
 - f. Mark tissue with a sterile marker, if desired.
 - g. Use nomogram to determine depth of cut (eg. size of cutting head).
 - h. Cut tissue, taking care to have a consistent pass over the cornea.
 - i. Remove cap from cutting apparatus.
 - j. Perform measurements (these may also be performed after processing, using non-contact methods):
 - i. Measure appropriately to determine residual stromal bed and anterior cap thickness (eg. pachymeter).
 - ii. Determine stromal bed diameter.
 - k. Replace and center the cap. Ensure cap is secure.
 - l. Remove cornea, taking care not to fold cornea or allow the chamber to collapse, induce stress lines, or traumatize the endothelium.
13. Place cornea into sterile media solution and container.
14. Label container.
15. Perform above procedure for mate tissue, if desired.
- even post-cut endothelial thickness.
- c. To ensure corneal stays in place during the procedure.
 - d. Determined by your manufacturer's instructions and/or your SOP's.
 - e. Pressure must be determined in a manner that is accurate and reproducible.
 - f. Mark cornea as per surgeons' request. Beware the potential toxicity of ink (e.g. gentian violet) on the endothelium.
 - i. To take care not to damage cap and to inspect for damage. Very important if cap is being used for anterior lamellar keratoplasty.
 - i. To verify the target stromal bed thickness was achieved. (See Step 1 and 14.a).
 - k. Replacing the cap limits the exposure of stromal lamellae to storage media, slowing edema.
 - l. The risk of endothelial trauma and cell damage is greatest at this stage of lamellar processing.
15. Tissue from only the same donor may be processed on the same sterile field and only after the first tissue has been removed from the field. Caution should be taken not to confuse one tissue with the other tissue.

16. Perform a post-processing slit lamp and specular microscopy evaluation of the tissue.

16. It is necessary to inspect the tissue for suitability after processing.

17. Prepare Tissue Report Form in accordance to EBAA Medical Standards L1.100, including:

- a. Estimate of stromal bed thickness.
- b. Diameter of cut.
- c. Pre and post-cut slit lamp and specular microscopy reports.

E1.224 Transfer of Corneal Tissue

Purpose:

To describe an accepted method for the transfer of corneal tissue to different medium or storage chamber.

Regulatory:

21 CFR 1271.145 Prevention of the introduction, transmission, or spread of communicable diseases

Materials needed:

Sterile Supplies

Sterile forceps 2X3
ISO Class 5 Hood or Biosafety Cabinet or suitable environment
Tissue in medium
Vial of sterile corneal tissue preservation medium or chamber
Sterile moisture impermeable drape
Sterile scrub brush for hands
Sterile towel to dry hands
Sterile gown or sterile sleeves
Sterile gloves

Non-Sterile Supplies

Shrink seal
Label
Mask
Cap to cover hair
Protective eyewear
CDC recommended disinfectant

Procedure

Rationale

1. Turn on laminar airflow of hood or biosafety cabinet and allow to run according to

manufacturers' specifications prior to use. If using a work surface in an open container processing room, proceed with the steps listed below.

2. Wipe down work surface of hood, cabinet, or open container processing room with disinfectant and allow to air dry per procedure E1.220. Document the cleaning in the appropriate log as per eye bank policy.
 3. Open sterile moisture impermeable drape on work surface of hood, cabinet, or open container processing room surface.
 4. Remove tissue stored in medium from refrigerator and set under hood or on open container processing room work surface next adjacent to sterile field. Place next to this either a fresh unused open vial of medium or drop a sterile chamber onto sterile field.
 5. If transferring to different medium, also drop sterile forceps onto sterile field.
 6. Don mask protective eyewear and cap to cover hair, Perform surgical hand antisepsis and don appropriate sterile attire for work surface being used.
 7. Using forceps, carefully and gently grasp the cornea by the scleral rim and transfer to fresh vial containing medium. Culture the tissue and/or old medium if this is your eye bank's policy or gently pour in a single motion, the tissue and medium from existing vial to sterile corneal viewing chamber (CVC). Be sure to keep the endothelial side up.
 8. Record the transfer date, time, technician's initials, and type of medium transferring from and to on your eye bank's form as indicated.
 9. Wipe down the work surface of the hood, cabinet, or open container processing room with a CDC recommended disinfectant solution immediately after use and allow it to air dry. Document these cleaning procedures according to your eye bank's Policies and Procedures.
3. To set up a sterile field.
 7. Avoid contamination of tissue or damage to the corneal endothelium during this step.
 8. This is particularly important if transferring from Optisol to MK, etc., which is essential information for tissue used for refractive keratoplasty (epikeratoplasty.)

E1.225 Femtosecond Laser Processing of Donor Cornea

Purpose:

To provide a standardized method for the aseptic processing of corneal tissue with a femtosecond laser for anterior, posterior, or penetrating keratoplasty that will minimize cross-contamination and maximize the quality of tissue for the intended use.

Regulatory:

21 CFR 1271.145 Prevention of the introduction, transmission, or spread of communicable diseases
21 CFR 1271.220 Processing and Process Controls

Materials needed:

Donor corneas or whole globes

Sterile Supplies

- 1 sterile gown or (2) sleeves
- 1 pair sterile gloves
- 1 sterile surgical scrub brush
- 1 sterile towel
- 1-2 vial corneal storage medium
- 1-2 sterile corneal containers (e.g. corneal viewing chambers)
- Sterile surgical spears
- Sterile serrated forceps
- Artificial anterior chamber

Non-Sterile Supplies

- Suitable processing environment
- Moisture impermeable protective clothing
- Mask
- Cap to cover hair
- Protective eyewear (goggles or face shield)
- Device for determining pachymetry (if necessary)
- Evaluation form
- CDC recommended disinfectant solution
- Femtosecond Laser

Procedure

1. Ensure that the surgical environment where femtosecond laser processing of cornea will occur is in accordance with policy E1.200: Open-Container Processing.
2. Select appropriate donor tissue (cornea or whole globe).

Rationale

1. Surgical environment should be an accredited operating room or in another environment documented annually to have less than 25 colony forming units per 90mm settle plate per one hour exposure.
2. To ensure suitable tissue is identified and used.

3. Turn on femtosecond laser and perform appropriate warm up procedure.
 4. Don appropriate attire and personal protective equipment consistent with surgical environment (e.g. operating room).
 5. Carefully check and confirm the laser parameters and settings desired by the transplanting surgeon for the corneal tissue. Set laser according to these parameters.
 6. With approved decontaminant, clean work area and surfaces where processing will occur and document.
 7. Using aseptic technique, establish sterile field(s). Aseptically present all sterile items to the field as needed for the procedure.
 8. Perform surgical scrub according to eye bank policy. Dry hands with a sterile towel, if applicable. Use aseptic technique to don sterile gloves and gown or sleeves.
 9. Set up sterile field. Arrange instruments appropriately on the sterile field and transfer donor tissue.
 10. Prior to cutting tissue, if needed, assess initial corneal thickness via pachymetry (this may be performed once tissue is mounted or prior to introduction to the sterile field using a non-contact pachymeter).
 11. For corneal tissue, use an artificial anterior chamber:
 - a. Place cornea on artificial chamber, taking care not to fold cornea, induce stress lines, or traumatize the endothelium.
 - b. Center tissue.
 - c. Secure helmet.
 - d. Tighten cornea into place.
 - e. Pressurize the chamber.
3. Perform in accordance with laser manufacturer's recommendation, to ensure equipment functions properly prior to use.
 4. To prevent exposure to open wounds, non-intact skin, or mucus membranes such as in the nose or eyes.
 5. Depth and shape of vertical and horizontal dissection is dependent on the type of surgery the tissue is to be used for (e.g. EK, ALK, PK).
 6. To minimize the risk of contamination by providing a decontaminated work surface.
 7. To ensure all necessary supplies are delivered to the sterile field in an aseptic manner.
 8. See AORN Standards for information on scrubbing and alternative scrub methods to achieve an aseptic environment.
 9. Have all necessary supplies ready for processing to minimize the length of time the cornea is out of the container and exposed.
 10. To determine initial corneal measurements.
 11.
 - a. High risk of endothelial trauma and cell damage at this stage.
 - b. To ensure dissection is central to help promote a uniform graft thickness.
 - c. To keep cornea in place during processing.
 - d. To ensure cornea is securely positioned between piston and helmet.
 - e. Pressure must be adequate to maintain the corneas integrity once applanated. Method of pressurization/infusion of artificial chamber is determined by eye bank SOP and must be validated, accurate, and reproducible.

- f. Mark tissue, with sterile marker if desired.
 - g. Lower the laser head and appanate sterile contact lens onto the cornea.
 - h. Emit the laser.
 - i. Using fine forceps and a fine blunt instrument perform detachment of cleavage plane to loosen stromal adhesions and tissue bridges.
 - j. If needed, perform depth and diameter measurements of anterior cap and/or posterior stroma.
 - k. If needed, replace and center the cap. Ensure cap is secure.
 - l. Remove cornea-scleral button or graft, taking care not to fold cornea or allow the chamber to collapse, induce stress lines, or traumatize the endothelium.
12. Place corneal tissue into sterile media solution and container.
 13. Label container.
 14. Perform above procedure for mate tissue, if desired.
 15. Perform a post-processing slit lamp and specular microscopy (if required) evaluation of the tissue.
- f. Mark cornea as per surgeon's request. Beware the potential toxicity ink (e.g. gentian violet) on the endothelium.
 - g. Ensure that appanation is complete and centered onto the cornea.
 - h. Allow laser to run its full cycle. Take care not to move laser or surgical table during emission.
 - i. Take care not to damage cap/button and to inspect for damage tissue.
 - j. To verify the target stromal bed/cornea button thickness and the target diameter of the graft was achieved.
 - k. Replacing the cap limits the exposure of stromal lamellae to storage media, slowing edema.
 - l. High risk of endothelial trauma and cell damage is greatest at this stage of processing.
12. To maintain tissue viability and to provide storage of the tissue.
 13. Ensure tissue is appropriately identifiable.
 14. Tissue from only the same donor may be processed on the same sterile field and only after the first tissue has been removed from the field. Caution should be taken not to confuse one tissue with the other tissue.
 15. It is necessary to inspect the tissue for suitability after processing.

E1.226 Laboratory Processing of Donor Tissue for Descemet's Membrane (Automated) Endothelial Keratoplasty (DMAEK/DMEK)

Purpose:

To provide a standardized method for the aseptic processing of corneal tissue intended for DMAEK/DMEK in a laboratory setting that will minimize cross-contamination and maximize the quality of tissue for the intended use.

Regulatory:

21 CFR 1271.145 Prevention of the introduction, transmission, or spread of communicable diseases 21
CFR 1271.220 Processing and Process Controls
21 CFR 1271.225 Process Changes
21 CFR 1271.230 Process Validation
EBAA Medical Standard E1.200 EBAA
Medical Standard F1.100 EBAA Medi-
cal Standard F1.200 EBAA Medical
Standard L1.100

Reference:

- Busin M, Scorcia V, Patel A, et al. (2010). Pneumatic Dissection and Storage of Donor Endothelial Tissue for Descemet's Membrane Endothelial Keratoplasty. *Ophthalmology*;117(12):1517-1520.
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- Groeneveld-van Beek E.A., Lie J.T., van der Wees J., Bruinsma M., Melles G.R. (2012) Standardized 'no-touch' donor tissue preparation for DALK and DMEK: harvesting undamaged anterior and posterior transplants from the same donor cornea. *Acta Ophthalmologica*, epub ahead of print.
- Krabcova I, Studeny P, Jirsova K. (2012). Endothelial Quality of Pre-cut Posterior Corneal Lamellae for Descemet Membrane Endothelial Keratoplasty with a Stromal Rim (DMEK-S): Two-year Outcome of Manual Preparation in an Ocular Tissue Bank. *Cell Tissue Bank*, epub ahead of print
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- Pereira C, Guerra F, Price F, et al. (2011). Descemet Membrane Automated Endothelial Keratoplasty (DMAEK): Visual Outcomes and Visual Quality. *Br J Ophthalmol*;95(7):951-954.
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- Terry M.A.(2012). Endothelial Keratoplasty: Why Aren't We All Doing Descemet Membrane Endothelial Keratoplasty?. *Cornea*, 31(5), 469-471.

Yoeruek E, Bayyoud T, Hofmann J, et al. (2012). Comparison of Pneumatic Dissection and Forceps Dissection in Descemet Membrane Endothelial Keratoplasty: Histological and Ultrastructural Findings. *Cornea*; 31(8):920-5.

Materials needed:

Cornea(s)

Sterile Supplies

- 1 sterile gown or (2) sleeves
- 1 pair sterile gloves
- 1 sterile surgical scrub brush
- 1 sterile towel
- 1-2 vial corneal storage medium
- 1-2 sterile corneal containers (e.g. corneal viewing chambers)
- Sterile surgical spears
- Sterile serrated forceps
- Microkeratome system or femtosecond laser
- Artificial anterior chamber
- 1 15-degree angle blade
- 0.06% Trypan Blue Viscoelastic
- 5 or 10cc sterile syringe
- 1 Anwar scissor
- 1 Sinsky Hook
- Additional items needed for Step 13 (Pneumatic dissection)*
 - 27-30g needle Caliper
- Additional items for Step 14 (Peeling dissection)*
 - Cornea suction block (optional)
 - Needle or hook for scoring

Non-serrated tying style forceps

Non-Sterile Supplies/Equipment

- ISO Class 5 Hood or Biosafety Cabinet or suitable environment for processing
- Magnification sufficient for viewing the Descemet Membrane
- Moisture impermeable protective clothing
- Mask
- Cap to cover hair
- Protective eyewear (goggles or face shield)
- Device for determining pachymetry Evaluation form
- CDC recommended disinfectant solution
- Additional items for Step 11*
 - Device for determining pachymetry

Procedure

Rationale

1. Establish guidelines which deem outcomes from processing as acceptable or not- acceptable, including, but not limited to:
 - a. Post-processing endothelial cell count.
 - a. To ensure adequate cell viability following surgery.
 - b. Uniformity of graft.
 - b. To ensure transplant adheres properly.
 - c. Descemet's membrane is intact and absent of perforation or significant tears.
 - c. Perforated cornea would indicate traumatized tissue.
 - d. Target and/or minimum/maximum bubble size.
 - d. Air injection may generate a central bubble too small, too large or peripheral (off center)
 - e. Target and/or minimum/maximum size for DM-endothelium only diameter.
 - e. Trimmed area needs to provide at least a central zone of DM-endo only.

2. Select appropriate donor tissue.
 2. To ensure suitable tissue is identified and used.

3. Clean work area with a disinfectant where processing will occur and document cleaning. Adjust operating scope or other magnification to suit the operator.
 3. To minimize the risk of contamination by providing a decontaminated work surface. Proper use of magnification will aid the operator.

4. If using lamellar flow hood or biosafety cabinet, turn airflow on for at least 15 minutes prior to use or according to manufacturer's recommendation.
 4. To establish laminar flow to provide a clean air environment for processing.

5. Don appropriate personal protective apparel consistent with processing environment used (e.g. biological safety cabinet).
 5. To prevent exposure to open wounds, non-intact skin, or mucus membranes such as in the nose or eyes.

6. Using aseptic technique, establish sterile field. Drop sterile items on the field as needed for the procedure.

7. Prepare sterile field (i.e. clean laminar flowhood or other appropriate work site).
 7. To minimize the risk of contamination by providing a decontaminated work surface.

8. Perform 3-5 minute surgical scrub according to eye bank policy. Dry hands with a sterile towel. Use aseptic technique to don sterile gloves and gown or sleeves.
 8. See AORN Standards for information on scrubbing and alternative scrub methods to achieve an aseptic environment.

9. Set up sterile field. Arrange instruments appropriately on the sterile field and transfer donor tissue.

A. Continue to the following steps according to method selected:

- Femtosecond/microkeratome – Step 11-12
- Pneumatic dissection – Step 13
- Peeling dissection – Step 14

B. Perform an anterior lamellar resection with either a microkeratome or femtosecond laser.

C. Begin preparing Descemet's Membrane graft.

- a. Anterior cap should remain detached.
- b. Inject air in to posterior stroma to detach Descemet's Membrane and obtain approximately a 6-8 mm central bubble for DMAEK tissue.
- c. Coat endothelium with viscoelastic.
- d. Use 15 degree blade and Anwar scissor to cut and remove posterior stroma.
- e. Use air to elevated Descemet's Membrane and re-attach anterior stromal cap.

A. Different methods may be utilized to obtain the graft. The pneumatic and peeling dissection technique does not utilize microkeratome or femtosecond laser.

B. Refer to E1.222 if utilizing a microkeratome and E1.225 if utilizing a femtosecond laser.

- a. Allows for access to posterior stroma.
- b. Separates Descemet's Membrane from posterior stroma. A bubble which is too large or one with peripheral separation will result in DMEK tissue.
- c. Protects endothelial cells during manipulation of tissue.
- d. This step is not performed if tissue is a DMEK graft. Use of trypan blue assists in visualization during processing.
- e. Stabilizes shape and integrity of graft when adhered to stroma.

13. Pneumatic dissection (DMEK)

- a. Insert 27-30g needle (or other preferred cannula) attached to a 10mL syringe into the stroma at the limbus such that the Descemet membrane is not ruptured.
 - b. Once the needle is approximately 2mm from the limbus and properly positioned, inject air.
 - c. Once the bubble is achieved, do not push air vigorously. The bubble may be expanded with gentle pressure.
 - d. Once the bubble has been achieved, measure the size with a caliper in order to ensure adequate graft size.
 - e. Deflate the bubble by piercing the anterior stroma with scissors or a sharp blade.
 - f. Optional step. Stain DM with trypan blue and rinse with BSS.
- a. Angling the bevel away from the DM will help to protect the delicate membrane from rupture which will ruin the ability to get a bubble.
 - b. It is not unusual to see air leaking from the limbal area prior to achievement of the big bubble. Keep pushing air until the bubble is achieved.
 - c. There is a delicate balance between pushing too much air and rupturing the bubble. Additionally, it is easy to push an inadequate volume of air and fail to achieve membrane separation.
 - d. Take care not to touch the membrane while measuring the size of the bubble.
 - e. This will allow for easier placement of the tissue in media. In other words, it won't float to the top of a vial or chamber.
 - f. Aids visualization of any damage induced by the procedure.

14. Peeling dissection (DMEK)

- a. Remove tissue from container and place on field epithelial side down, operator may use a sterile concave surface.
 - b. Score the DM at the limbus.
 - c. Place a few drops of trypan blue on the endothelium to stain the tissue .
 - d. Rinse the trypan blue with BSS and fill the endothelial side with a few drops of corneal storage solution.
 - e. Optional step: seat the cornea in a suction block to aid handling of the tissue.
 - f. Stain the DM with trypan blue and rinse with BSS.
 - g. Begin peeling the membrane from the scored edge using tying forceps.
 - h. Continue peeling until the membrane is freed as much as required to provide a large donor area for the surgeon.
- a. Use non-particulating surfaces and sponges when possible.
 - b. Care must be taken to minimize tears and minimize the depth of scoring to just beyond DM.
 - c. This aids visualization of the exposed membrane at the limbus.
 - d. The membrane edges should be visible at the limbus. A few drops on the endothelium may aid in peeling and protect the delicate cells
 - e. This will allow for easier manipulation of the membrane.
 - f. Aids visualization of any damage induced by the procedure.
 - g. If the membrane begins to tear, stop the peeling from that location and begin at another location.
 - h. It may be helpful to move the membrane back to its normal anatomic position to aid post-preparatory evaluation.

15. Place cornea into sterile media solution and container.

16. Label container.

17. Perform above procedure for mate tissue, if desired.

18. Perform a post-processing slit lamp and specular microscopy evaluation of the tissue.

18. It is necessary to inspect the tissue for suitability after processing.

19. Prepare Tissue Report Form.

- a. Diameter of cut or graft bed size.
- b. Pre and post-cut slit lamp and specular microscopy reports.

E1.230 Scleral Preservation

Purpose:

To provide uniform procedures for the aseptic preservation of scleral tissue for surgical use using either 70% or greater concentration of ethyl alcohol, sterile glycerin, a broad spectrum antibiotic solution, or other validated method of storing sclera tissue.

Regulatory:

21 CFR 1271.145 Prevention of the introduction, transmission, or spread of communicable diseases
21 CFR 1271.210 Supplies and Reagents

Reference:

Dailey, J. R., & Rosenwasser, G. O. (1994). Viability of bacteria in glycerin and ethanol preserved sclera. *Journal of Refractive and Corneal Surgery*, 10(1), 38-40.

Enzenauer, R. W., Sieck, E. A., Vavra, D. E., & Jacobs, E. P. (1999). Residual ethanol content of donor sclera after storage in 95% ethanol and saline rinse of various durations. *American Journal of Ophthalmology*, 128(4), 522-524.

Lucci, L. M., Yu, M. C., & Hofling-Lima, A. L. (1999). Decontamination of human sclera: An in vitro study. *Cornea*, 18(5), 595-598.

Romanchuk, K. G., Nair, P., & Grahn, B. (2003). How long can donor sclera be safely stored? *Cornea*, 22(6), 569-572.

Materials needed:

1. Sterile Supplies
 - 2 Tissue forceps
 - 2 small scissors, e.g., corneal tissue or iris scissors
 - Sterile scalpels or handles
 - Sterile #10 or #11 blades
 - Sterile gauze
 - Sterile jars
 - Sterile towel
 - Sterile gown or sterile sleeves
 - Sterile gloves
 - Sterile vials of preservation media, e.g., alcohol, glycerin
 - Broad-spectrum antibiotic solution
 - Eye tissue

2. Non-sterile Supplies
 - Moisture impermeable protective clothing
 - Hair cap Mask
 - Protective eyewear (goggles or face shield)
 - Sterile scrub brush for hands
 - Sterile towel
 - ISO Class 5 Hood or Biosafety Cabinet
 - Sealing material, e.g., shrink-wrap

Procedure	Rationale
<p>1. Assemble sterile instruments and supplies under the hood, biosafety cabinet, or on the work surface of an open container processing room. Preserve sclera at time of corneal preservation or refrigerate remaining ocular tissue following removal of corneas and preserve sclera later within time frame determined by the eye bank medical director. If sclera is stored for later preservation, wipe down the work surface of the hood, cabinet, or open container processing room with a disinfectant solution immediately after use and allow it to air dry. Document cleaning.</p>	<p>1. Sclera must be preserved using aseptic technique, the same as when preserving corneal tissue for transplantation.</p>
<p>2. Maintain the sterile field following preservation of the corneal tissue, or set-up new sterile field. Don protective clothing, cap, mask and eyewear. Perform surgical hand antisepsis and don sterile gloves and sterile gown or sleeves.</p>	<p>2. See procedures E1.200.</p>
<p>3. Grasp the remainder of the eye using sterile forceps and place onto the center of the sterile field. Perform a careful inspection of the remaining ocular tissue. It is important that aseptic technique be used and the sterile field is not compromised at any time.</p>	<p>3. Note any abnormalities of the globe such as discoloration, tumors, or thinning. Any information regarding ocular history noted on the screening form or patient's chart should be reviewed and thorough follow-up completed to rule out any problems that might be present with the eye tissue.</p>
<p>4. Inspect sclera for any muscle attachments, fascia, or connective tissue that remains adhered to the whole globe. Carefully excise any attachments using iris scissors and tissue forceps.</p>	<p>4. Since conjunctival tissue is an excellent medium for bacterial growth, it is important to rid the sclera of as much excess conjunctiva as possible. A thoroughly clean piece of scleral tissue is required for surgical use.</p>
<p>5. Gently remove intraocular material by running iris scissors between the sclera and choroid layer of the globe. Using forceps, iris scissors, sterile gauze or cotton tipped applicators, remove intraocular material.</p>	<p>5. Running scissors between the sclera and choroid layers helps to gently separate the choroid layer from the scleral wall and facilitates a clean dissection of the intraocular material.</p>
<p>6. Using sterile cotton-tipped applicators and gauze, clean the inside of the globe to remove all choroid and tissue fragments. Gauze, applicator, or entire globe may be soaked in antibiotic solution if needed to aid in the cleaning process.</p>	<p>6. Facilitates complete removal of all tissue or particulate material. Antibiotic soak loosens any remaining tissue fragments and reduces the microbial flora.</p>

7. Reshape sclera to its original spherical form, if necessary, after cleaning. Scleral tissue should be as smooth and round as possible prior to submersion in selected storage medium.
8. If sclera is to be segmented, section the sclera into desired sizes prior to placing in storage medium.
9. Using sterile cotton-tipped applicator or forceps gently place clean sclera into prepared sterile jars containing selected storage medium.
10. Place lids on containers and secure tightly. Seal lids with shrink-wrap, or other sealing material.
11. Label all storage containers with appropriate identification as follows:
 - A. Source eye bank, name, and location
 - B. ISBT 128 Tissue identifier, which includes the DIN, Product Code, and FIN(P).
 - C. Type of ocular tissue (Sclera)
 - D. Preservation method: Glycerin, concentration of alcohol used, or frozen tissue
 - E. Expiration date
 - F. Unique donor identification number for each piece
 - G. Date/Time of death
 - H. Date/Time of preservation
 - I. Statement that ocular tissue is for single patient use and not considered sterile.
12. Record preservation information on the form used by your eye bank.
13. Sclera should be distributed in the same manner as corneal tissue for surgical use. Recipient records must be kept and a package insert form must accompany each piece of sclera with information to include recommended storage temperature and re-hydration instructions.
7. Due to the dehydration of the scleral tissue, reshaping becomes difficult, even after soaking in sterile normal saline prior to surgery.
10. Prevents contamination of ocular tissue by leakage or evaporation (for alcohol preservations). Break in seal indicates tampering and potential contamination.
11. All ocular tissue must be labeled with a unique eye bank identification record number for proper quality control assurance. Proper labeling is required according to EBAA Medical Standards. See procedure J1.000.
13. Refer to EBAA Medical Standards section J1.000, Labeling, K1.000, Distribution of Tissue, L1.000, Documentation to accompany donor tissue and M1.000, Eye Bank Records.

Accepted Sclera Preservation Media

1. Alcohol Preservation: 70% or greater concentration of ethyl alcohol
 - A. Using forceps or sterile cotton-tipped applicator, clean sclera is placed in either prefilled sterile containers or 70% or greater concentration of ethyl alcohol is carefully added to the sterile containers so that the sclera is completely submerged in the alcohol solution.
 - A. Accomplishes complete dehydration of the scleral tissue.
 - B. **Sclera *must* remain in alcohol solution for at least 5 days prior to distribution.**
 - B. To provide adequate time for complete dehydration of ocular tissue.
 - C. Length of storage and storage temperature should be determined by your eye bank's medical director and recorded in the eye bank's procedure manual.
2. Sterile Glycerin
 - A. Glass eye jars should be prepared with molecular sieves, fill to a level deemed appropriate by your medical director, and sterilized with the lid loosened.
 - A. Maintains a softer sclera.
 - B. The jars containing the sterile molecular sieves should be filled with sterile glycerin to a level deemed appropriate by your medical director. Transfer sclera using sterile forceps and immerse in the sterile glycerin.
3. Cryopreservation (Freezing)
 - A. Sterile eye jars should be filled with an ophthalmic broad-spectrum antibiotic solution.
 - A. Retards microbial growth and is bacteriocidal.
 - B. Transfer the sclera to the solution.
 - C. Leave the sclera at room temperature in the antibiotic solution for 1 to 2 hours.
 - C. Activates bactericidal properties of antibiotic.
 - D. Aseptically remove the sclera from the antibiotic solution and place in sterile container that will withstand ultra low freezing temperatures.
 - E. Freeze the sclera at -80°C or lower in liquid nitrogen or freezer.

Length of storage and handling instructions

Per EBAA Medical Standards, a preservation date for use of ocular tissue shall be indicated.

Instructions in the form of a package insert for reconstituting or re-hydrating the sclera and preoperative handling must be provided with the tissue to the receiving surgeon.

E1.300 Use of Short and Intermediate Term Preservation Media

Purpose:

To describe the use and storage of short and intermediate term corneal preservation media.

Definition of terms:

Short or intermediate term corneal storage media: liquid preservation media used to maintain the viability of donor corneas prior to corneal transplantation.

Regulatory:

21 CFR 1271.145 Prevention of the introduction, transmission, or spread of communicable diseases
21 CFR 1271.210 Supplies and Reagents
21 CFR 1271.220 Process Controls

Reference:

Bourne, W. M., Nelson, L. R., Maguire, L. J., Baratz, K. H., & Hodge, D. O. (2001). Comparison of Chen medium and Optisol-GS for human corneal preservation at 4°C. Results of transplantation. *Cornea*, 20(7), 683-686.

Doughman, D. J. (1997). Ch. 39 tissue storage. In J. H. Krachmer, M. J. Mannis & E. J. Holland (Eds.), *Cornea, fundamentals of cornea and external disease* (pp. 509-517). St. Louis: Mosby.

Kaufman, H. E. (1999). Ch. 105 tissue storage systems: Short and intermediate term. In F. S. Brightbill (Ed.), *Corneal surgery: Theory, technique & tissue* (3rd ed.) (pp. 892-897). St. Louis: Mosby.

Kaufman, H. E., Beuerman, R. W., Steinemann, T. L., Thompson, H. W., & Varnell, E. D. (1991). Optisol corneal storage medium. *Archives of Ophthalmology*, 109 (), 864-868.

Lindstrom, R. L., Kaufman, H. E., Skelnik, D. L., Laing, R. A., Lass, J. H., & Musch, D. C. et al. (1992). Optisol corneal storage medium. *American Journal of Ophthalmology*, 114(3), 345-356.

Rosenwasser, G. O. D., & Nicholson, W. J. (2003). Media. *Introduction to eye banking: a handbook and atlas*. (1st ed.) (pp. 79-81).

Rosenwasser, G. O. D., & Nicholson, W. J. (2003). Commercially available storage media. *Introduction to eye banking: a handbook and atlas*. (1st ed.) (pp. 173-182).

Materials needed:

ISO Class 5 Hood or Biosafety Cabinet
Sterile instruments
Moisture impermeable protective clothing
Mask
Cap
Sterile Gloves

Procedure	Rationale
1. Store corneal preservation media at a temperature in accordance with the manufacturer's recommendation. Once refrigerated, media must be stored within the temperature range dictated by the media package insert (2–8° C for Optisol GS) in a monitored refrigerator with a temperature recording device. This device should be visible without opening the refrigerator.	1. A monitored refrigerator assures that media is stored within the prescribed temperature range. A portable recorder can be used for off-site storage (away from the eye bank laboratory) or media can be stored in a hospital pharmacy by contractual agreement.
2. If an eye bank manufactures its own media, the procedures used must be in accordance with FDA's Good Manufacturing Practices, and must be documented in the eye bank's procedure manual.	2. See EBAA Medical Standards section E1.300.
3. Visually inspect each vial or container of preservation medium prior to use for turbidity, color change indicating a pH shift (if phenol red has been added as an indicator), precipitates, or foreign bodies, which may indicate possible microbial contamination. Also check expiration dates. Inspect containers for cracks or leakage.	3. To prevent the use of preservation media suspected of being contaminated, which could result in an adverse reaction in a recipient, such as endophthalmitis.
4. If contamination of preservation medium vials/containers is suspected, do not use the medium for corneal tissue storage. The lot number shall be reported immediately and returned to the manufacturer.	
5. Record the lot numbers and expiration date of each vial of preservation medium used for each cornea on the corneal information form that accompanies the ocular tissue.	5. To facilitate recall of media or notification to receiving surgeons of medium being recalled by the manufacturer.

E1.400 Long Term Preservation

Purpose:

To describe the long term storage of donor corneas for surgical use.

Regulatory:

21 CFR 1271.145 Prevention of the introduction, transmission, or spread of communicable diseases
21 CFR 1271.210 Supplies and Reagents

Procedure	Rationale
<p>1. Organ Culture</p> <p>A. Donor corneas for penetrating keratoplasty may be preserved for longer periods, i.e., 1 month or more using organ culture techniques.</p> <p>B. If an eye bank uses organ culture techniques, the policies and procedures must be recorded and available for review at the time of EBAA site visit inspection.</p> <p>C. Organ culture techniques must provide for the aseptic preservation and storage of corneal tissue.</p>	<p>1. These preservation methods are more complicated than preservation in short or medium-term corneal storage medium and are not in common use in the U.S. at present. Organ culture is reported to be the preservation of choice in the United Kingdom and some western European countries.</p>
<p>2. Cryopreservation</p> <p>Donor corneas can be cryopreserved and stored in liquid nitrogen for several years. This method uses a cryoprotective agent, such as dimethyl sulfoxide (DMSO), to prevent the formation of damaging intracellular ice crystals. Donor corneas are frozen in a controlled-rate freezer down to liquid nitrogen temperature.</p>	<p>2. If an eye bank elects to use cryopreservation methods, a detailed policy and procedure shall be included in the eye bank's written policies and procedures manual.</p>

F1.000 Tissue Evaluation

Reference:

Sugar, A., Gal, R. L., Beck, W., Ruedy, K. J., Blanton, C. L., & Feder, R. S. et al. (2005). Baseline donor characteristics in the cornea donor study. *Cornea*, 24(4), 389-396.

F1.100 Gross Examination

Purpose:

To describe the technique of gross examination of ocular tissue prior to removal from the donor.

Materials needed:

Sterile ophthalmic irrigating solution such as normal saline
Non-sterile gloves
Personal protective equipment
Pen
Pen light
Portable slit lamp (optional)
Donor information form

Procedure	Rationale
1. Don Personal Protective Equipment.	1. Adhere to Standard Precautions and protect tissue from contamination.
2. Irrigate each eye with sterile ophthalmic solution.	2. Irrigation will wash away any particulate matter on epithelial surface.
3. Illuminate each eye obliquely with a pen light or portable slit lamp prior to prepping donor.	3. Many corneal defects can be observed upon gross examination with proper lighting at the right angle.
4. Examine the face, eyelids, cornea, sclera and conjunctiva.	
5. Note any abrasions, infiltrates, foreign bodies, opacities, scars, epithelial defects, presence of intra ocular lens, evidence of prior surgeries or other defects. Note any sclera discoloration, i.e. jaundice (icterus), or defects; eyelid or conjunctival abnormalities such as edema, trauma or foreign bodies; abnormal pupil or iris shape or color. Examine eye for symmetry, shape, curvature or other abnormalities.	5. Presence of extensive defects may determine whether the corneal tissue should be removed, particularly if it is not suitable for surgical or other use.
6. Record information on the appropriate form.	

F1.200 Slit Lamp Examination

Purpose:

To delineate the procedure for slit lamp biomicroscopy of ocular tissue in the laboratory.

Reference:

- Davis, R. M. (1997). Ch. 38 tissue evaluation. In J. H. Krachmer, M. J. Mannis & E. J. Holland (Eds.), *Cornea, fundamentals of cornea and external disease* (pp. 501-508). St. Louis: Mosby.
- Hirst, L. W., Lees, G. P., & Requard, J. (1981). *Slit lamp training atlas for eye bank technicians*. Baltimore: The Medical Eye Bank, Inc.
- Martonyi, C. L., Bahn, C. F., & Meyer, R. F. (Unknown). *Clinical slit lamp biomicroscopy and photo slit lamp biomicrography*. Ann Arbor: Kellogg Eye Center, University of Michigan.
- Reinhart, W. J. (1999). Ch. 104 gross and slit-lamp examination of the donor eye. In F. S. Brightbill (Ed.), *Corneal surgery: Theory, technique & tissue* (3rd ed.) (pp. 887-891). St. Louis: Mosby.
- Rosenwasser, G. O. D., & Nicholson, W. J. (2003). Introduction to slit lamp technique. *Introduction to eye banking: a handbook and atlas*. (1st ed.) (pp. 65-77).
- Rosenwasser, G. O. D., & Nicholson, W. J. (2003). Appendix 1 corneal folds grading atlas. *Introduction to eye banking: a handbook and atlas*. (1st ed.) (pp. 97-103).
- Rosenwasser, G. O. D., & Nicholson, W. J. (2003). Appendix 3 eye donor slit lamp pathology. *Introduction to eye banking: a handbook and atlas*. (1st ed.) (pp. 113-127).

Definition of terms:

- Arcus senilis: An opaque, grayish ring at the periphery of the cornea caused by deposits of lipids
- Bowman's membrane: The anterior elastic or limiting membrane of the cornea
- Condition of anterior chamber: Formed, shallow, flat, or evidence of blood
- Cornea: Clear transparent anterior portion of the outer coat of eyeball forming front of aqueous chamber
- Corneal edema: Haziness caused by excessive hydration of the cornea
- Keratic Precipitates: Inflammatory cells found on the endothelium
- Descemet's membrane: An elastic basement membrane produced by the delicate layer of endothelial cells that line the inner cornea
- Endothelium: A flat, monolayer of cells lining the inner surface of the cornea
- Epithelium: The outermost anterior multi-cell layer of the cornea
- Epithelial defects: Breaks or disruption of the epithelial surface caused by drying, erosion, sloughing, tears or abrasion
- Folds: Striations due to wrinkling of Descemet's membrane from excessive hydration, an extended period from time of death to time of procurement, or traumatic stretching of the cornea during removal
- Guttata: Dark, drop-shaped changes appearing on the corneal endothelium
- Polymegathism: Variations in endothelial cell size with some cells appearing larger than normal
- Pleomorphism (or polymorphic): Having multiple (two or more) forms or shapes of endothelial cells
- Slit lamp biomicroscope: A binocular microscope with varying magnification settings attached to a light source with varying intensity settings
- Stretch striae: Evidence of corneal endothelial stretching that appears as a streak or a line in a linear fashion (e.g., snail tracks)

Stromal infiltrates: Abnormal accumulation of cells and fluid in the corneal stroma

Specular microscope: A monocular microscope with an illumination of light directed through a series of prisms or mirrors through the optical lens onto the corneal endothelium

Materials needed:

- Slit lamp biomicroscope
- Utility clamp or other appropriate device to hold the ocular tissue
- Sterile Cotton-tipped applicators
- Sterile ophthalmic irrigating solution
- Sterile gloves
- Alcohol prep pads
- Mask and cap
- Rating scale
- Forms for documentation
- Tissue in containers

Procedure	Rationale
1. Allow the eye or cornea to reach normal room temperature. Avoid multiple repeated warming/cooling cycles.	1. In order to obtain an accurate evaluation of the corneal endothelium.
2. Don mask, cap, sterile gloves, protective clothing and protective eye wear when examining the whole eye. Note that performing a slit lamp examination on the whole globe prior to excision is optional.	
3. Remove eye jar lid and place it so that the inside of the cap is facing up in a clean area such as the hood or biosafety cabinet.	3. Prevents contamination of ocular tissue when lid is returned to eye jar.
4. Remove any excess liquid from eye jar.	4. Minimizes leakage on slit lamp biomicroscope and work area while evaluating.
5. Insert eye jar, vial, or corneal storage viewing chamber into utility clamp or other appropriate device.	5. This secures the ocular tissue while performing the evaluation.
6. Using sterile cotton-tipped applicators, gently manipulate eye cage, if one is used, to bring cornea within viewing range of slit lamp. Sterile forceps or hemostats can also be used instead of cotton-tipped applicators.	6. The contents of the eye jar are assumed to be sterile. Using sterile instruments during examination will ensure sterility is maintained.
7. For whole globe evaluation, moisten the eye with sterile ophthalmic irrigating solution as necessary.	7. This prevents excessive drying and possible contamination of corneal epithelium.
For a preserved corneal evaluation DO NOT OPEN the storage container.	Prevents contamination of cornea in media.
8. Perform a low power examination when evaluating an eye/cornea for the first time.	8. This gives orientation and location and entire view of cornea and eye simultaneously.

9. Diffuse illumination of the cornea is done with a wide slit of light directed on the cornea at approximately a 15° to 20° angle of incidence and then moved to scan the entire cornea.
10. Next perform direct focal illumination using high power examination to perform an in-depth evaluation of the cornea. Adjust the width of the beam; a narrower slit beam will allow more in-depth examination and detail. With specular reflection you can observe the endothelium, cell morphology, dark areas, and areas where the cells are absent.
11. Make notations on the donor information form regarding the evaluation and what was observed during initial evaluation.
12. Record and diagram any abnormalities present regarding epithelium, stroma, and endothelium. Bowman's layer and Descemet's membrane are not necessarily visible with slit lamp examination.
13. Evaluate and record the minimum information below:
 - A. Corneal clarity, noting any scars, edema, or significant arcus that would reduce the optical clear zone needed by the transplanting surgeon
 - B. Folds or striae, noting severity.
 - C. Presence or absence of epithelial defects, and amount
 - D. Presence or absence of guttata change and amount
 - E. Presence or absence of stretch striae
 - F. Presence or absence of polymegathism or pleomorphism and amount
 - G. Evidence of any technical problems in removal
 - H. Presence of any infiltrates or foreign bodies
14. Assign a rating to the ocular tissue, such as excellent, very good, etc., according to your eye bank's policy and rating scale. The classification used in the rating scale should be defined in the eye bank's procedure manual.
9. To properly evaluate and see endothelium, the angles indicated must be observed.
10. Corneal endothelium is a good indicator of the quality of ocular tissue. Anything other than normal hexagonal shaped cells should be noted and documented.
11. After preserving ocular tissue, the initial evaluation may differ from final evaluation.
12. It is important to record quality of ocular tissue when determining whether it is suitable for surgery.
14. Slit lamp evaluation of the cornea following removal from the eye and placement into tissue culture medium is mandatory and must be performed and recorded. See EBAA Medical Standards section F1.200.

15. If a slit lamp examination on the whole globe, repeat the evaluation of the cornea following the lab excision. One may also repeat slit lamp evaluation prior to tissue distribution.
15. Document each slit lamp examination of tissue intended for transplant. Note pre-excision slit lamp examination is optional.

F1.300 Endothelial Cell Density

Purpose:

To describe the examination of the donor cornea endothelium using specular microscopy.

Reference:

- Benetz, B. A., Gal, G.L., Rice, C., Karpinecz, L., Edwards, S., Ruedy, K.J., Beck, R.W., & Lass, J.H, (2006). Dual grading methods by a central reading center for corneal endothelial image quality assessment and cell density determination in the specular microscopy ancillary study of the cornea donor study. *Current Eye Res*, 31, 1-9.
- Laing, R. A. (1999). Ch. 12 specular microscopy. In F. S. Brightbill (Ed.), *Corneal surgery: Theory, technique & tissue* (3rd ed.) (pp. 101-112). St. Louis: Mosby.
- Rosenwasser, G. O. D., & Nicholson, W. J. (2003). Specular microscopy. *Introduction to eye banking: a handbook and atlas*. (1st ed.) (pp. 83-94).
- Rosenwasser, G. O. D., & Nicholson, W. J. (2003). Appendix 2 specular microscope atlas. *Introduction to eye banking: a handbook and atlas*. (1st ed.) (pp. 105-111).

Definition of terms:

- Folds: Striations due to wrinkling of Descemet's membrane from excessive hydration or traumatic stretching of the cornea during removal
- Guttata: Dark, drop-shaped areas or excrescences on the surface of the corneal endothelium
- Keratic precipitates: Cells that appear in response to an inflammatory condition, and which appear as small particulate matter on endothelial surface
- Polymegathism: Variations in endothelial cell size with some cells appearing larger than normal
- Pleomorphism (or polymorphic): Having multiple (two or more) forms or shapes of endothelial cells
- Specular microscopy: A technique by which illumination of light is directed through a series of prisms or mirrors through the optical lens into the donor cornea. The light that is reflected from the endothelium is used to visualize the corneal endothelium
- Endothelial cell density: The average calculated number of endothelial cells per square millimeter
- Endothelial Striae: Evidence of endothelial stretching that appears as a streak or a line on the endothelium (e.g., snail tracks)

Materials needed:

- Specular microscope configured for eye banking with image display and capturing capability
- Labeled corneal tissue in storage viewing chamber containing medium with intact shrink seal
- Option: Computer-based image capture system with the ability to produce a hard copy and adequate backup.

Set up:

The labeled viewing chamber or medical vial containing the medium and cornea with intact shrink seal is placed in the holding well of the specular microscope. The light source is turned on. Ensure that the image recording system is ready for use. Follow the manufacturer's recommended procedures for set-up, maintenance, calibration and operation for the particular specular microscope system in use. Document initial setup of system and keep a log of calibrations, cleanings and repairs.

Procedure	Rationale
1. Allow cornea to reach normal room temperature. The most optimal evaluation and cell count may be obtained soon following excision of the cornea.	1. This will allow an accurate evaluation of the endothelium and a clear picture of cell membranes.
2. Position chamber in holding well of microscope. With the adjustment knob of the microscope, lower the magnifying lens until it almost touches viewing chamber. Caution: Do not allow lens to touch surface of viewing chamber; this may scratch the lens.	2. Basic laboratory technique should be observed at all times when using any type of microscope.
3. Begin slowly raising the magnifying lens or cornea until cells come into focus; scan areas of the cornea for the brightest reflection of light.	3. If cells are not visible at first, scanning for bright lights can put you in a better position for illumination of cells.
4. Once cells come into focus, a cell count is obtained and measured by cells/square mm. (It is up to the individual eye bank's medical director to determine acceptable cell densities.)	4. Cell density for transplantable corneas may be established by the individual eye bank's medical director.
5. To obtain the most accurate endothelial cell analysis, a large field of cells (e.g. >150) or multiple fields (3 or more, central/peri-central) should be captured, counted, and/or averaged. 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.	5. The more cells or fields analyzed, the more representative it will be of the whole corneal endothelium. The best specular images are found in the central/peri-central area.
6. In the case of corneal tissue that is prepared for PK or EK on the microkeratome or femtosecond laser, a post-cut specular analysis must be taken.	6. This will ensure that there was not endothelial compromise due to the eye bank corneal processing. Poor specular images may occur post-cut and/or multiple days after date of donor death. However, this may not be indicative of poor endothelium. More warming time or Medical Director evaluation may be needed.
7. Include pertinent donor data on the specular image captured to identify it as per your eye bank's SOP.	7. A specular photograph can help assure the surgeon of the ocular tissue's quality. Labeling the image identifies it as the correct donor tissue for the evaluation form.
8. After obtaining specular micrographs, the ocular tissue should immediately be returned to the refrigerator. Try to minimize the duration that the cornea is at room temperature.	8. Ocular tissue preserved in corneal storage medium and maintained at optimal temperature will enhance cell viability.
9. Record the specular microscopic evaluation according to your eye bank's policy on the ocular tissue information form.	

G1.000 Quality Assurance

Purpose:

To outline the steps for an eye bank's quality assurance plan and required EBAA quality control measures in order to provide uniformly safe, high quality eye tissue for surgical use.

Definition of terms:

Review: An indicator may measure a result or outcome that is desirable or undesirable.

Indicators: A flag that identifies or directs attention to specific performance issues that need more intense review.

Quality Assurance: A continual process for monitoring and evaluating activities, the identification of problems, development and implementation of corrective actions, and specific procedures or practices which prevent recurrence of errors or accidents.

Regulatory:

- 21 CFR 1271.145 Prevention of the introduction, transmission, or spread of communicable diseases
- 21 CFR 1271.160 (a), (b) 2, 3, 5, 6, (c) Establishment and maintenance of a quality program
- 21 CFR 1271.195 (a) thru (d) Environmental control and monitoring
- 21 CFR 1271.200 Equipment
- 21 CFR 1271.260 Storage
- 21 CFR 1271.265 Receipt and Distribution
- 21 CFR 1271.320 Complaint file

Materials needed:

- Your eye bank's policy and procedure on quality assurance
- Quality control forms for monitoring and record keeping

Procedure	Rationale
1. Assign responsibility for your eye bank's quality assurance program to a responsible individual within your organization. Medical directors and/or executive directors are responsible overall, while another technical staff member(s) will be assigned specific monitoring and follow-up activities.	1. Eye bank medical directors and executive directors are ultimately responsible for all delegated quality assurance activities.
2. Define the scope of service for your eye bank. This will depend on the mission of your organization and other factors such as whether you procure bone and other tissue, provide professional education programs, etc. Scope of service for an eye bank may include the following: A. Suitable eye donors will be identified and ocular tissue recovered according to established criteria and protocol. B. Ocular tissue will be distributed to surgeons, dentists, and institutions requesting tissue according to EBAA Medical Standards.	2. These are meant to serve as examples and are not all-inclusive.

- C. Eye bank technical staff will routinely offer the opportunity for eye donation to next-of-kin, according to eye bank policy and procedure.
- D. The eye bank will provide public and professional education according to its written policy.

3. The executive director, medical director, and other designated individual responsible for quality assurance must identify those aspects of the eye bank's operation or service that are particularly critical to the overall functioning of the bank, that are important to avoid a potential adverse outcome, or are high-volume activities. For example, laboratory maintenance and cleaning procedures and refrigerator temperature monitoring are important for functioning of the laboratory and EBAA certification. Contaminated ocular tissue that results in a serious postoperative infection is a serious adverse outcome. Completion of donor and recipient records is another critical high volume activity.
4. Next, identify appropriate indicators that will flag or direct attention to specific areas requiring more intense review and follow-up.

A rate-based indicator measures the frequency of an event that may require further review if the rate exceeds predetermined thresholds. Indicators may measure outcome (what happens as a result of an action taken), or the process involved in arriving at an outcome, and may be a desirable or undesirable endpoint. An adverse reaction would be an undesirable outcome indicator.

5. Rates or thresholds must be determined for each identified indicator. These are based on EBAA Medical Standards and findings reported in the medical and eye banking literature. For example, EBAA Medical Standards requires that all donor tissue for surgical use be tested and found non-reactive for HIV 1/2-antibody prior to distribution. Using completion of eye bank records as another example, you may determine that records should be fully completed 100% of the time. A retrospective review of all records for one month would provide data on how frequently records are found incomplete. .

The rate of occurrence may be determined by the following formula:

3. Regulatory standards, such as the EBAA Medical Standards establish minimum expectations.

4. For example, a sentinel indicator, such as a reported adverse reaction that is an EBAA Medical Standards requirement, measures a serious, undesirable, often unavoidable outcome. Adverse reaction events are infrequent, but are of a sufficiently serious nature that a thorough investigation must be conducted for each and every occurrence.

5. EBAA Medical Standards require a 100% compliance rate or threshold.

The rate of occurrence is compared against the predetermined threshold. If the rate of record completion is found to be 80%, and it was determined that the threshold for compliance should actually be 100% then this would signal a problem requiring corrective action.

Number of records that were incomplete divided by" total number of records reviewed x 100 = the percent or occurrence of incomplete records.

5. The executive director and technical supervisor or other designated individuals must decide how to collect and organize the data from quality assurance activities, e.g. a checklist of information required in a donor's packet. This checklist should be the coversheet of the packet.
6. The collected data must be periodically reviewed and evaluated by the executive director, medical director, technical director, or other appropriate individual.
7. This information serves as the basis for identifying the need for corrective action.
8. Any corrective action taken based on data analysis and evaluation must be documented, per EBAA Medical Standards. Actions taken may include:
 - A. Revision of an eye bank's policy and procedure in the identified problem area.
 - B. Provision of education programs to staff, when deficiencies are identified.
 - C. Personnel action regarding the staff members involved.
8. These are only a few examples of corrective action.
9. Assess corrective action taken and document whether or not it was effective in correcting a problem or deficiency, and preventing its recurrence.

Documentation of this action should be retained as an occurrence in an incident log.

10. The information gathered and any corrective action taken should be communicated to all staff and medical director(s).
11. The entire quality assurance program for your eye bank must be documented in your eye bank procedures manual. This documentation should be specific as to indicators, thresholds, and procedures for corrective action.
12. EBAA required quality control procedures are detailed below.

Quality Control Procedures required according to EBAA Medical Standards include but are not limited to the following:

- | | |
|---|----------------------------------|
| A. Facilities | C3.000, C3.100 |
| B. Environmental control | C3.000, E1.000 |
| C. Equipment | C3.200 |
| D. Supplies and reagents | C3.300 |
| E. Recovery | E1.000, E1.100 |
| F. Processing and processing controls | E1.200 through E1.230 |
| G. Labeling controls | J1.000 |
| H. Storage | I1.000 |
| I. Receipt, pre-distribution shipment, and distribution | K1.000 |
| J. Donor eligibility determination, donor screening, and donor testing. | D1.000 through D1.230,
G1.200 |
13. Documentation of the eye bank's quality assurance program must be maintained for a minimum of 10 years. This includes any corrective or remedial action taken for detected deficiencies. This includes deficiencies discovered by accrediting or regulatory agencies.
14. The above documentation must be made available for review at the time of an accreditation inspection.

G1.050 Corrective & Preventive Action (CAPA)

Purpose:

To define the procedure by which the eye bank will investigate and resolve issues using a standardized process of investigation, action, effectiveness monitoring, and documentation.

Definition of Terms:

Containment Action: The immediate action taken to stop the incident or to stop the expansion of the scope of the incident. This is performed in order to minimize the impact of the incident or from preventing the initial occurrence of the incident. An immediate correction is considered part of the containment action.

Corrective Action: The action taken to eliminate the root cause of an existing incident and to prevent recurrence

Preventive Action: The action taken to eliminate the root cause of a potential incident and to prevent recurrence

Root Cause Analysis: An investigation technique that is used to identify the fundamental and underlying reason for the potential or actual occurrence of an incident and the potential actions to be taken to reduce or eliminate the likelihood of the occurrence or recurrence

Regulatory

FDA: 21 CFR Part 1271.160(b)(3)

Health Canada: *Safety of Human Cells, Tissues and Organs for Transplantation Regulations*. SOR/2007-118, Sections 43-54.

Materials Needed

Your eye bank's form (CAPA Form) used to document steps described in this procedure.

Procedure – Inputs

1. Using your eye bank's relevant procedure, determine if a CAPA is to be issued
2. Obtain your eye bank's CAPA form
3. Assign a tracking number to the CAPA
4. Describe the "trigger source" of the CAPA – i.e. what was the input that initiated the creation of the CAPA (such as customer complaint, audit finding, etc.)
5. Define timelines for Containment Action, Root Cause Analysis, Actions Implemented, and Verification of Effectiveness

Rationale – Inputs

1. There should be a mechanism within your quality system to initiate a CAPA
2. Use an approved and controlled form to document steps taken in this procedure
3. Used for traceability and reference
4. This will ensure the input is clearly documented
5. This will ensure the CAPA process is completed within a reasonable timeframe – *Note:* These timeframes may be pre-established in a policy or on a case-by-case basis depending on your eye bank's quality assurance program

6. Document the CAPA number and established timelines on the CAPA form

Procedure – Define, Assess, & Contain

1. Record the date that the CAPA was initiated on the CAPA Form
2. Using all available information, clearly describe the incident using as much detail as possible – include violated SOP, Standard, and Regulatory references as applicable – record on the CAPA Form
3. Document, on the CAPA Form, any actions that were immediately taken (prior to documentation on the CAPA form), if applicable
4. Perform a *containment action* and document such actions on the CAPA form

Procedure – Root Cause Analysis

1. Investigate the incident to determine the root cause of the incident
2. Enlist other employees and the Medical Director as necessary to assist with the root cause analysis
3. Document the root cause analysis on the CAPA form
4. Once the root cause analysis is determined, examine Containment Action to see if changes need to be made; document on the CAPA Form if changes were made

6. The CAPA form will be the central documentation of the incident and associated corrective/preventive actions

Rationale – Define, Assess, & Contain

1. Established timeframes will be based on this date
2. Clearly document the reason for the CAPA
3. Clearly document the immediate response if applicable
4. Stop the incident or stop the expansion of the scope of the incident as necessary
Note: this may require placing certain operations on hold in order to facilitate an effective containment action, it may be necessary to enlist support of Management

Rationale – Root Cause Analysis

1. Identify the root cause. This may include the use of common root cause analysis methods (fault tree, 5-why, etc.) in addition to interviewing staff, examining records, etc.
2. Use subject matter experts within your organization to have an accurate root cause determined
3. The Root Cause Analysis will determine the next steps
4. Depending on the root cause that was determined, additional containment actions may be necessary to prevent the expansion of the scope of the incident

Procedure – Corrective & Preventive Action

1. Using the determined root cause, develop an action (or actions) to eliminate or reduce the root cause of the incident; document on the CAPA Form

Examples: changing a process, using different equipment or materials, changing a procedure, staffing additions/reductions, training, and the like

Note: more than one action may be necessary depending on the incident and steps necessary to correct

2. If necessary, validate or verify the action per your eye bank's validation and verification procedures

Procedure – Effectiveness Monitoring

1. Develop a method to verify that the corrective and preventive actions taken in the previous section were successful in eliminating or reducing the root cause and preventing future recurrences of the incident; document on the CAPA Form
2. Obtain objective evidence to sufficiently document the effectiveness of the actions; attach documentation to the CAPA Form
3. If the actions prove to be unsuccessful, restart the *Root Cause Analysis* and *Corrective & Preventive Action* sections of this procedure to determine if the root cause was accurately determined and/or other possible corrective actions
4. If effectiveness monitoring proves that the actions were successful, document the success on the CAPA form and close the CAPA

Rationale – Corrective & Preventive Action

1. Correct the underlying issue (root cause) of the incident. The ultimate goal is to prevent or significantly reduce the recurrence of the incident that triggered the CAPA.

2. Validation or Verification may be necessary

Rationale – Effectiveness Monitoring

1. The goal is to ensure, with sufficient supporting documentation, that the actions taken were effective in eliminating or reducing the root cause of the incident
2. The correction should be well-documented

Procedure – Review, Approval, and Close

1. Ensure the CAPA form is complete
2. Attach all objective evidence, notes, and other documentation gathered during the investigation, action, and monitoring steps
3. Present the CAPA to reviewers specified in your eye bank's procedures; have the reviewers sign & date if approval is given
4. Retain the completed CAPA per your eye bank's record retention procedures

Rationale – Review, Approval, and Close

1. The goal is to ensure, with sufficient supporting documentation, that the actions taken were effective in eliminating or reducing the root cause of the incident
2. All referenced documentation should be attached to the CAPA form for easy review
3. Typically this includes Management and the Medical Director
4. Keep the CAPA on-file for subsequent inspection by regulatory authorities

Sample CAPA Form

CAPA Information			
CAPA #:		Date Initiated:	
Trigger Source:			
Person who Initiated this CAPA:			
Timelines:	Initiation to Containment Action:		Days
	Containment Action to Root Cause Analysis:		Days
	Root Cause Analysis to Actions Implemented:		Days
	Total Time of Effectiveness Verification:		Days

Clearly Describe the Incident
<i>Use as much detail as possible. Attach documentation as applicable.</i>

Violated SOP, Standards, and/or Regulations

Containment Actions / Any Actions Immediately Taken Upon Discovery

Root Cause Analysis

--

Potential Solutions to the Root Cause that was Determined

--

Corrective / Preventive Actions to be Taken

--

Effectiveness Monitoring
<i>Describe the method by which effectiveness will be monitored.</i>

Effectiveness Monitoring Summary
<i>Document the effectiveness of the corrective/preventive actions. Attach all necessary documentation to support the effectiveness determination</i>

Summary, Review, Approval, Closure			
Were the Actions successful?	<input type="checkbox"/> Yes <input type="checkbox"/> No	Is all supporting documentation attached?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Root Cause Analysis Team Members:			
Review & Approval, Quality Assurance:		Date:	
Review & Approval, Management:		Date:	
Review & Approval, Medical Director:		Date:	

G1.070 Deviation Investigation and Reporting Procedure

Purpose:

To outline the steps for an eye bank's quality assurance program to investigate and resolve deviations or departures from either procedures, regulations, and/or standards. Also, to outline the reporting requirements to FDA and EBAA.

Definition of Terms:

Deviation is a departure(s) from your eye bank's approved procedure, policy, FDA regulation, EBAA standard, or any other related regulatory agency.

A. According to FDA 21 CFR 1271.3(dd), a deviation is defined as an event:

1. That represents a deviation from applicable regulations in 21 CFR Part 1271 or from applicable standards or established specifications that relate to the prevention of communicable disease transmission or HCT/P contamination; or
2. That is an unexpected or unforeseeable event that may relate to the transmission or potential transmission of a communicable disease or may lead to HCT/P contamination.

B. EBAA definition

An event that represents a deviation from applicable regulations, standards, or established specifications, or is unexpected or unforeseeable.

C. Health Canada definition

Error – means deviation from the standard operating procedures or applicable laws that could adversely affect the safety of a transplant recipient or the safety, efficacy or quality of cells, tissues or organs.

Materials Needed:

1. Deviation Investigation Form
2. Flow chart
3. Deviation Identifier Log
4. Supporting Documentation

Regulations

A. FDA:

1. 21 CFR 1271 Human Cells, Tissue, and Cellular and Tissue-Based Products.
2. Guidance - Deviation Reporting for Human Cells, Tissues, and Cellular and Tissue-Based Products Regulated Solely Under Section 361 of the Public Health Service Act and 21 CFR Part 1271 (September 2017).
3. 21 CFR 1271.150 (b) Core GTP requirements.

Standards

A. EBAA:

Current Medical Standards

B. Only for eye banks that export tissue to Canada - Safety of Human Cells, Tissues and Organs for Transplantation Regulations

Guidance

A. EBAA Procedures Manual

B. FDA Guidance Documents:

1. [Deviation Reporting for Human Cells, Tissues, and Cellular and Tissue-Based Products Regulated Solely Under Section 361 of the Public Health Service Act and 21 CFR Part 1271; Guidance for Industry \(PDF - 171KB\)](#)
2. [Biological Product Deviation Reporting and HCT/P Deviation Reporting - Deviation Codes Page 23-27](https://www.fda.gov/downloads/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/BiologicalProductDeviations/UCM578229.pdf) <https://www.fda.gov/downloads/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/BiologicalProductDeviations/UCM578229.pdf>
3. [Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products; Guidance for Industry \(PDF - 502KB\)](#) (August 2007).
4. [Guidance for Industry: Current Good Tissue Practice \(CGTP\) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products \(HCT/Ps\)](#) (PDF - 291KB) (December 2011).
5. [Investigating and Reporting Adverse Reactions Related to Human Cells, Tissues, and Cellular and Tissue-Based Products \(HCT/Ps\) Regulated Solely under Section 361 of the Public Health Service Act and 21 CFR Part 1271 - Guidance for Industry \(PDF - 392KB\)](#) (March 2016).
6. [Donor Screening Recommendations to Reduce the Risk of Transmission of Zika Virus by Human Cells, Tissues, and Cellular and Tissue-Based Products; Guidance for Industry \(PDF - 86KB\)](#) Updated May 2018. This document supersedes the guidance of the same title dated March 2016.
7. [Use of Nucleic Acid Tests to Reduce the Risk of Transmission of West Nile Virus from Living Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products \(HCT/Ps\) : Guidance for Industry \(PDF - 97KB\)](#) September 2016. Corrected May 2017. This document supersedes the draft guidance of the same title dated December 2015.
8. [Revised Recommendations for Determining Eligibility of Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products Who Have Received Human-Derived Clotting Factor Concentrates; Guidance for Industry \(PDF - 55KB\)](#) (November 2016).
9. [Use of Nucleic Acid Tests to Reduce the Risk of Transmission of Hepatitis B Virus from Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products; Guidance for Industry \(PDF - 67KB\)](#) (August 2016).
10. [Use of Donor Screening Tests to Test Donors of Human Cells, Tissues and Cellular and Tissue-Based Products for Infection with *Treponema pallidum* \(Syphilis\); Guidance for Industry \(PDF - 176KB\)](#) (September 2015).

C. If exporting eye tissue to Canada - Health Canada Regulations and Guidance

1. Safety of Human Cells, Tissues and Organs for Transplantation Regulations 02/11/2015.
2. Guidance Document for Cell, Tissue and Organ Establishments - Safety of Human Cells, Tissues and Organs for Transplantation 05/31/2018.

Procedure

Rationale

1. All departures from any established approved procedure, policy, federal regulation and EBAA standards or any other applicable regulatory requirements must be fully investigated and properly documented.
 2. Deviations that need to be submitted to FDA, as described within this procedure, must be performed within 45 days from the time of discovery. The EBAA must be notified of any deviation that is reported to FDA within 10 business days after submission to FDA.
 3. The eye bank must have a standard operating procedure that describes how to investigate, document and report a deviation to the respective federal and state regulatory and accreditation agencies. Documentation must capture all aspects of the investigation. Include ocular tissue ID, donor ID or any other unique identifier that describes the item(s) affected in the deviation.
 4. All deviations must be reviewed and approved by QA and the eye bank's top executive officers, such as Medical Director and Executive Director of the eye bank. Together they must determine an appropriate corrective and preventive action so that the deviation is properly evaluated and resolved.
 5. The eye bank's personnel involved in the deviation must report and document the deviation as soon as it is noticed. The deviation report must be documented in the respective form and must be
1. FDA Regulation 21 CFR 1271 Human Cells, Tissues, and Cellular and Tissue-Based Products
 - 21 CFR 1271.150 (b) Core CGTP Requirements
 - 21 CFR 1271.160 Establishment and maintenance of a quality program (b) functions (6)
 - 21 CFR 1271.350 Reporting (b) Reports of HCT/P deviations (1)EBAA Medical Standards
 - G1.000 – Quality Assurance 1st bullet
 2. CFR 1271.350 Reporting (b) Functions
 3. FDA Regulation 21 CFR 1271 Human Cells, Tissues, and Cellular and Tissue-Based Products
 - 21 CFR 1271.47 What procedures must I establish and maintain? (d) Departures from Procedures
 - 21 CFR 1271.160 Establishments and Maintenance of a Quality Program (b) Functions (1-2)
 - 21 CFR 1271.350 Reporting (b) Reports of HCT/P deviations (1-2)EBAA Medical Standards
 - C3.400 Procedures Manual
 - G1.000 Quality Assurance 1st and 3rd bullet
 4. EBAA MS C1.000 Personnel and Governance
 - C1.100 Director
 - C1.200 Medical Director 4th paragraph
 5. Based on Good Tissue Practices

submitted to the eye bank's QA Program. Follow flow chart.

6. QA should assign a unique identifier to the deviation for tracking purposes. This identifier should be cross-referenced in the specific section of the source document where the deviation occurred. Any corrective actions generated as a preventive measure must be cross referenced to the deviation's unique identifier.
7. QA must immediately start an investigation. The investigation must include the review of the donor's chart relevant to the non-compliance when applicable. Review any processing procedure performed after recovery, if relevant, and any other supporting documentation related to the non-conformance.

Example:

If the deviation is tissue-related, then a thorough review of the donor's chart should be performed. Include any relevant microbiological culture results and supportive documentation with the deviation report.

For an equipment failure, include the unit recalibration and repair report with the deviation documentation. Ensure that the documentation clearly describes the part of the unit that became defective, the date it stopped functioning, and when it was repaired. Obtain a copy of the repairs and recalibration (if unit is calibratable). Also include how this defect might compromise the tissue if used during processing.

8. Investigate the probable root cause for the deviation.
9. QA must determine if the deviation was against a core CGTP regulation 1271.150 and follow the attached flow chart.

6. Current Industry Good Tissue Practice

7. According to Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)
 - V (I.) When HCT/P Deviations Occur, What is the Role of the Quality Program?

8. 21 CFR 1271 Human Cells, Tissues, and Cellular and Tissue-Based Products

21 CFR 1271.160 Establishments and Maintenance of a Quality Program (b) Functions (6)

9. 21 CFR 1271 Human Cells, Tissues, and Cellular and Tissue-Based Products

1. CFR 1271.150 (b) (1-10) Core CGTP Requirements
 - Requirements relating to facilities in 1271.190(a) and (b);
 - Requirements relating to environmental control in 1271.195(a);
 - Requirements relating to equipment in

1271.200(a);

- Requirements relating to supplies and reagents in 1271.210(a) and (b);
- Requirements relating to recovery in 1271.215;
- Requirements relating to processing and process controls in 1271.220;
- Requirements relating to labeling controls in 1271.250(a) and (b);
- Requirements relating to storage in 1271.260 (a) through (d);
- Requirements relating to receipt, pre-distribution, shipment, and distribution of an HCT/P in 1271.265 (a) through (d); and
- Requirements relating to donor eligibility determinations, donor screening, and donor testing in 1271.50, 1271.75, 1271.80, and 1271.85.

10. After the investigation is completed, QA must notify the executive officers about the deviation and discuss an appropriate corrective and preventive action to prevent the deviation from re-occurring. See EBAA Corrective & Preventive Action (CAPA) procedure for details.

10. EBAA Medical Standards

C1.000 Personnel and Governance

- C1.100 Director
- C1.200 Medical Director

Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)

- V (F) How Can a Quality Program Ensure that Appropriate Corrective Actions Related to Core CGTP Requirements Are Taken, When Necessary?

EBAA Procedure Manual

- G1.050 Corrective & Preventive Action (CAPA)

11. If the deviation is not against a core CGTP and it was not related to tissue, QA together with the executive officers should assign appropriate corrective action and approve the deviation.
12. If deviation was not against a core CGTP but it was related to the tissue but not distributed, then the tissue should be placed in quarantine until the final disposition of the tissue is determined.
13. If the deviation was not against a core CGTP but related to a distributed tissue and /or transplanted, assign appropriate corrective action and approve

the deviation.

14. If the deviation was against a core CGTP as previously described, but the tissue was not distributed, the tissue can be used for research/Training only. Tissue is NOT suitable for transplantation, approve the deviation and assign appropriate corrective action.
15. If the deviation was against a core CGTP, and tissue was distributed but NOT transplanted, recall the tissue back from consignee. Tissue can be utilized for research/training purposes, if the non-conformance cannot be resolved. Submit deviation to FDA and assign appropriate CAPA. Notify EBAA. Approve deviation.
16. If the deviation was against a core CGTP, and tissue was transplanted, report deviation to FDA and EBAA or any other respective regulatory/accreditation agencies. Assign appropriate CAPA and approve deviation. Report deviation to FDA and notify EBAA.

Note: There are instances when a deviation is against a core CGTP, but it is not directly related to a tissue (equipment, facilities, labeling etc.). If the tissue aseptic integrity has not been compromised or there was no cross contamination or contamination was not introduced, then the deviation is not reportable to the FDA.

17. If the eye bank has processing facilities and/or distributing centers, the facility that makes the eligibility determination should be responsible for investigating and reporting the deviation to FDA and EBAA.
18. The submitted deviation to FDA and EBAA may also generate a voluntary recall; the eye bank's Medical Director and Executive Officer determines the appropriate type of notification to send to transplanting surgeon. See recall procedure for details.

14. FDA regulation 21 CFR 1271.265 Receipt, predistribution shipment, and distribution of an HCT/P (c) Availability for distribution (2)

15. CFR 1271.350 Reporting (b) Functions

16. Based on FDA rejection letters rationale.

17. FDA Guidance - Deviation Reporting for Human Cells, Tissues, and Cellular and Tissue-Based Products Regulated Solely Under Section 361 of the Public Health Service Act and 21 CFR Part 1271 – III HCT/P Deviation Reporting (B) second paragraph

EBAA Medical Standard G1.000 Quality Assurance section defines source eye bank's responsibility for adverse reaction reporting. Should be applied to deviation reporting as well.

18. FDA regulations 21 CFR 1271

- 1271.440 Orders of retention, recall, destruction, and cessation of manufacturing
- 1271.160(b) functions (2)(iii)

EBAA Medical Standards

- G1.300 Tissue Recall or Tissue Withdrawal

EBAA Procedure Manual

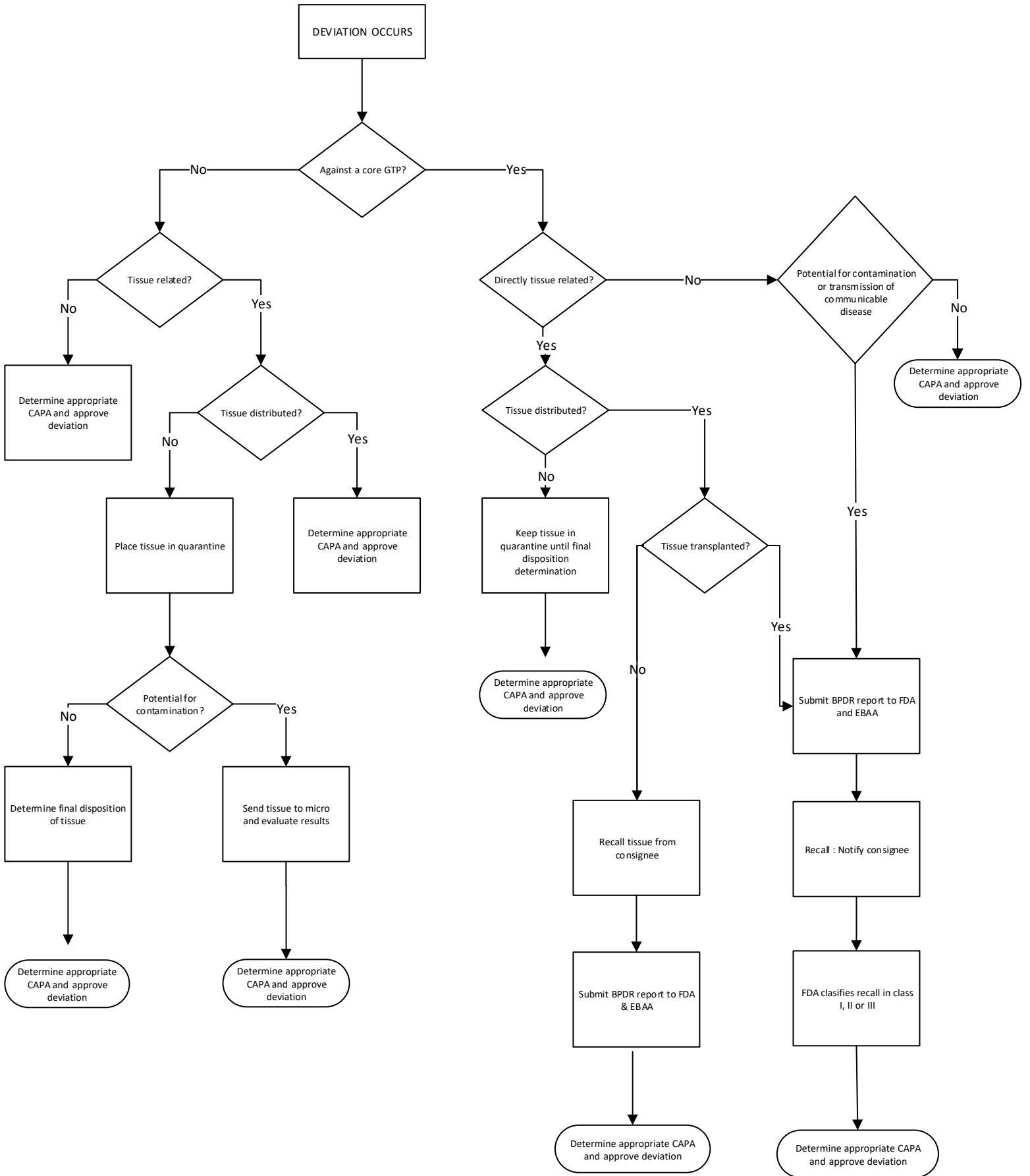
- G1.300 Tissue Recall
-

19. FDA submission:

- a. Go to the FDA online Biologics Product Deviation Reporting (BPDR) to submit the deviation.
- b. You must sign into the FDA's website using the organization and your personal credentials.
- c. Enter the required fields. Use the unique identifier as your tracking number.
- d. Enter the date when the deviation occurred.
- e. Enter the date when the deviation was discovered.
- f. Enter the current date when the deviation is being reported into their website.
- g. Select non-blood product.
- h. Select the corresponding BPD (biologic product deviation) code.
- i. Enter number of units and number of affected products.
- j. Enter a concise description of the deviation emphasizing the risk factor.
- k. Enter contributing factor/root cause.
- l. Enter what is your follow up action after submission.
- m. Enter tissue identification number including eye side designation.
- n. Enter expiration date (example: 14 days after recovery if using Optisol).
- o. Enter the 361 HCT/P s as the product type.
- p. Enter LH01 (human cornea) as the non-blood product code.
- q. Enter the corresponding disposition from the dropdown menu.
- r. Enter if a notification was sent to the surgeon who transplanted the tissue.
- s. Enter any additional information in the field provided.
- t. Select submit to FDA if submission is complete.
- u. You may save any information entered by selecting save.
- v. Once submitted, the FDA will contact you with any questions and for the deviation acceptance status.

19. <https://www.accessdata.fda.gov>

- w. Save the summary with the confirmation number.
 - x. Send a copy of the submission to the EBAA within 10 business days.
20. Deviation investigations must be made readily available to FDA inspectors for review upon request. Inspectors will not base their 483 observations on investigated and adequately resolved deviations. Their review is mainly to ensure that the deviation's resolution was adequate and that reportable deviations were actually reported.
21. If a deviation is generated during an inspection by a regulatory agency, such as FDA, the eye bank must inform the EBAA in writing within ten business days of receipt, including all future related correspondence.
22. Retain deviation reports for a minimum of 10 years.
- 19x. EBAA Medical Standard B1.200 Inspections by Other Official Agencies
20. EBAA Medical Standard B1.200 Inspections by Other Official Agencies
21. EBAA Medical Standards
G1.000 Quality Assurance



G1.100 Quality Control

Purpose:

To establish a policy and procedure for measuring, assaying, or monitoring properties of tissue.

Regulatory:

21 CFR 1271.145 Prevention of the introduction, transmission, or spread of communicable diseases
21 CFR 1271.160 (a), (b) 2, 5 Establishment and maintenance of a quality program
21 CFR 1271.260 Storage
21 CFR 1271.265 Receipt and Distribution

Procedure	Rationale
1. The director will be responsible for ensuring that tests and procedures are in place for measuring, assessing, or monitoring essential properties of tissues to ensure their safety for transplantation.	1. To ensure that the facility is following its policies and procedures.
2. These tests and procedures must be performed, documented and reviewed prior to release of tissue for transplant.	
3. Results of all such tests or procedures shall become part of the permanent record of all tissues processed.	

G1.200 Testing

Purpose:

To ensure that facilities that are performing their own microbiologic and/or serologic testing conform to state and federal regulations.

Regulatory:

21 CFR 1271.145 Prevention of the introduction, transmission, or spread of communicable diseases
21 CFR 1271.150 (a) Current Good Tissue Practice; General
21 CFR 1271.150 C ii and iii
21 CFR 1271.160 (b) 2, 5 Establishment and maintenance of a quality program
21 CFR 1271.160 (c) Audits

Reference:

Aiken-O'Neill, P. (1997). Ch. 41 governmental relations. In J. H. Krachmer, M. J. Mannis & E. J. Holland (Eds.), *Cornea, fundamentals of cornea and external disease* (pp. 525-529). St. Louis: Mosby.

Procedure

Rationale

Microbiologic

Microbiologic

1. The director will be responsible for ensuring that the eye bank meets all applicable accreditation requirements established under the Clinical Improvement Act (CLIA), as well as any state regulations.
2. Documentation of accreditation, verification of satisfactory compliance with a College of American Pathologists (CAP) Proficiency Testing Program, or other proficiency-testing program approved by CLIA, shall be available at time of site inspection.

1. To ensure compliance with CLIA.

Serologic

Serologic

1. The Director will be responsible for ensuring that the eye bank meets all applicable accreditation requirements established under the Clinical Laboratories Improvement Act (CLIA), as well as any state regulations.
2. Documentation of accreditation, verification of College of American Pathologists (CAP) Proficiency Testing Program, or other proficiency program approved by CLIA, shall be available at the time of site inspection.
3. Copies of the test kit manufacturer's guidelines must be kept on file.

1. To ensure compliance with CLIA.

G1.210 Microbiologic Culturing

Purpose:

To describe techniques for culturing donor ocular tissue prior to surgical use (optional).

Definition of terms:

Aerobes: Microorganisms that require the presence of oxygen for survival.

Anaerobes: Microorganisms that thrive or grow in the absence of oxygen.

Spores: Inactive forms of microorganisms. They are resistant to destructive methods, and may become active under favorable conditions.

Regulatory:

21 CFR 1271.145 Prevention of the introduction, transmission, or spread of communicable diseases

21 CFR 1271.220 Process Controls

Materials needed:

Your eye bank's policy and procedure on culturing ocular tissue
Culturette tubes

Sterile cotton-tipped applicators

Aerobic medium, e.g., blood agar plates

Anaerobic medium, e.g., thioglycolate broth tubes or trypticase soy broth
Incubator

Requisition forms

Procedure	Rationale
1. The eye bank's policy and procedure manual must include one of the following options regarding culturing of donor ocular tissue.	1. See EBAA Medical Standard G1.210. This applies to sclera as well as corneal tissue.

- A. No ocular tissue cultures are performed by the eye bank.
 - B. Corneoscleral rim cultures are performed using aerobic and anaerobic culturette tubes which are then submitted to a College of American Pathologists (CAP) approved laboratory for bacterial identification and antimicrobial susceptibility testing.
 - C. Corneoscleral rim cultures are performed using aerobic agar plates or broth and anaerobic broth tubes which are then incubated to permit growth.
2. Include a statement recommending culturing at the time of surgical use on the ocular tissue label, package insert form, or other form that accompanies the ocular tissue sent to the surgeon.
 3. If an eye bank elects to perform cultures of the donor ocular tissue, refer to your eye bank's protocol.
 4. Use culturette tubes or swabs to collect swab cultures.
 5. Complete necessary information on requisition form to be submitted with the specimen. Request both anaerobic and aerobic cultures according to your eye bank's policy.
 6. Set up sterile field and begin corneoscleral rim excision as usual.
 7. Take swab cultures before antibiotic drops are instilled.
 8. Take cultures at the time of corneal excision, whether in situ or laboratory. Cultures of the conjunctival sac are not recommended, since previously reported studies have shown that almost all donor eyes will be culture positive.
 9. Take cultures of the incision site prior to separation, or of the aqueous or sclera at the limbus. Or a piece of sclera may be removed and placed in trypticase soy broth.
- C. Eye banks which perform bacterial identification and antimicrobial susceptibility testing must participate in a CAP approved bacteriology proficiency testing program and be capable of reviewing gram stain slide preparations to assure the consistent reporting of accurate results.
2. See EBAA Medical Standards section G1.210. This statement is required regardless of whether the eye bank performs the cultures.
 8. See reference list.

10. Using aseptic technique, swab the incision site. If the culturette option is used, the swab should then be inserted into the culturette tube. If the cotton-tipped applicator option is used, one applicator may then be smeared on an agar plate followed by insertion into an aerobic broth tube and another inserted into an anaerobic broth tube. These steps should be performed on both eyes.
11. Label the specimen tubes with a unique donor identification number, date and time.
12. Submit specimen to a laboratory or incubate in the eye bank's incubator to observe for presence or absence of growth. If growth is observed, submit to a laboratory for identification of organism.
13. Record results in donor case record. Attach hard copy to the donor record.
14. If results are positive, notify the receiving surgeon immediately. Antibiotic susceptibility testing may be useful information to the surgeon. Record this notification.
15. Request that all surgeons who receive ocular tissue report any cases of postoperative infection with a positive corneoscleral rim culture.
12. See step 1-B above.
14. See EBAA Medical Standard G1.210.A.
15. See EBAA Medical Standard G1.210.B.

G1.220 Infectious Disease Testing and Screening

Purpose:

To outline the infectious disease testing to be performed as required by FDA, EBAA and other regulatory agencies as noted in this document before ocular tissue can be released for surgical use.

Regulatory

EBAA Medical Standards and Appendixes:

Medical Standards

D1.200 Donor Testing; D1.210 EBAA Testing Requirements; D1.220- FDA Testing Requirements; D1.230 Non-Required Testing Results

Appendixes

Appendix I: FDA Defined Relevant Communicable Disease Agents and Diseases.

Appendix II: FDA Defined Contraindications to Transplant

Appendix III: Donor Eligibility Determinations

Appendix IV: Testing

Appendix V: Accredited Eye Banks Not Located in the United States

FDA Regulations and Guidance:

Regulation

FDA 21 CFR 1271 Human Cells, Tissue, and Cellular and Tissue-Based Products

Guidance:

FDA 21 CFR 1271.145 Prevention of the introduction, transmission, or spread of communicable disease

FDA 21 CFR 1271.160 (b) 2, 5- Establishment and maintenance of a quality Program

Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps).

Use of Donor Screening Tests to Test Donors of Human Cells, Tissues and Cellular and Tissue-Based Products for Infection with *Treponema pallidum* (Syphilis)

References

List of Laboratories for CLIA verification:

<http://www.cms.hhs.gov/clia/>

HBV NAT:

<http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/UCM516650.pdf>

ZIKA Virus:

<https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/UCM488582.pdf>

Approved Licensed Donor Screening Test Kits List

<https://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/TissueSafety/ucm095440.htm#approved>

Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) 2007: <https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-bio-gen/documents/document/ucm091345.pdf>

Testing HCT/P Donors for Relevant Communicable Disease Agents and Diseases

<http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/TissueSafety/ucm095440.htm>

Canadian References

Canadian Standards Association Standards

CAN/CSA-Z900.1-17 National Standard of Canada. (2017) Cells, tissues and organs for transplantation: General requirements.

CAN/CSA- Z900.2.4-17 National Standard of Canada. (2017) Ocular tissues for transplantation.

Health Canada (2018) Guidance Document for Cell, Tissue and Organ Establishments. Safety of Human Cells, Tissues and Organs for Transplantation

See the following sections: Interpretation of Infectious Disease Test Results; Archived Samples; Tests that are Considered Appropriate and Effective: Mandatory Testing and Recommended Testing and Testing Facility Requirements.

Health Canada (2018) Guidance Document for Cell, Tissue and Organ Establishments. Safety of Human Cells, Tissues and Organs for Transplantation Appendixes

Appendix 2: Appropriate and effective tests for infectious disease test

Appendix 3: Revised Measures to address the potential risk of ZIKA virus transmission through human cells, tissues and organs

Materials

- Eye Bank procedure for Serology Testing Laboratory Qualification and Facility Audit
- Eye Bank SOP for Plasma Dilution Determination (including algorithm)
- Eye Bank for how to draw blood from donor and prepare sample for testing
- Eye Bank procedure for Discordant Test Results
- Eye Bank SOP for how to interpret serology results and determine donor eligibility
- Eye Bank procedure for Tissue in Quarantine
- Eye Bank procedure on Archiving Blood Samples
- Qualified Laboratory Test Requisition Form

<i>Procedure</i>	<i>Rationale</i>
1. Laboratories that perform serology donor screening tests must be certified either under the Clinical Laboratory Improvement Amendments (CLIA) or must meet equivalent requirements as determined by the Centers for Medicare and Medicaid Services. The Eye Bank should have a written policy and procedure on how to qualify such laboratory. The Eye bank must have these certifications readily available for inspections.	1a. Qualify testing laboratory certification must be performed as per CFR 1271.80(c) (FDA) 1b. EBAA Medical Standards Appendix IV I(a) 1c. Refer to Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) V. Donor Testing: General A. 2. 3 rd bullet 1d. These certificates can be verified at http://www.cms.hhs.gov/clia/
2. As part of the laboratory qualification, ensure that the approved serology testing laboratory uses FDA-licensed, approved, or cleared donor screening test kits to test the donor's blood sample(s). Indicate to the clinical laboratory that they must notify the eye bank of any changes to the FDA approved testing kits.	2. Refer to Licensed Donor Screening Test kit list in the reference section. Testing must be performed: CFR 1271.80(c) (FDA)
3. Tissue must be placed in quarantine and labeled as such until the donor eligibility is	

determined.

4. Donor tissue that is to be used for research, training and education purposes do not need donor screening or serology testing for infectious agents.
5. Blood sample must be drawn according to EBAA procedure manual.
 - 5a. Refer to EBAA Procedure Manual E1.140 to draw the blood specimen for testing.
 - 5b. Refer to EBAA Medical Standards Appendix IV: Testing
6. Eye Bank must evaluate the potential donor's plasma dilution according to EBAA standards and FDA guidance. Eye bank must have a written procedure as to how to determine if the donor's plasma at the time of blood draw was or not diluted and acceptable for testing.
 - 6a. See EBAA Medical Standards Appendix IV: Testing II. Assessment of Donor Specimens for Testing Suitability
 - 6b. FDA CFR 1271.80(d) Ineligible Donors (2)
7. Blood Sample requirements:
 - A. Specimen for testing must be drawn at the time of recovery or within 7 days before or after the recovery. Health Canada requires specimens within 7 days of death.
 - 7a. Refer to FDA Guidance: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps).
 - 7b. EBAA Medical Standards D1.200
 - 7c. FDA regulation 1271.80(b)
 - B. For infants:
 - If donor is a month old or less, a blood specimen from the mother must be collected for testing instead of a sample from the donor, you may use a pre-mortem specimen to test a cadaveric donor, as long as the specimen is collected within that timeframe.
 - The specimen for testing from the birth mother must be collected within seven days of donation by the infant. If a specimen from the birth mother of a donor one month of age or younger is unavailable, the donor is ineligible.
 - Specimens collected for any infant donor more than one month of age, including adopted infants, should be collected from the donor rather than the birth mother.
8. Verify that blood tube is not expired at the time of blood draw.
 8. See FDA CFR 1271.210 Supplies and Reagents (d)(1)
9. Follow the qualified laboratory's blood sample testing requirements so that blood sample does
 9. See FDA Guidance Eligibility Determination for Donors of Human Cells, Tissues, and

not become invalidated at the time of testing. (ex; specimen centrifuge and testing timelines).

Cellular and Tissue-Based Products (HCT/Ps)
V. Donor Testing General 1271.80 E.

10. Submit blood sample to the pre-qualified laboratory for testing using their laboratory's requisition form.

11. All serology test results for donors who are deemed eligible for surgical use must be non-reactive for the following infectious agents:

- A. HIV-1/2 antibody (with or without HIV-O)
- B. HIV-1 NAT
- C. Hepatitis B surface antigen
- D. Hepatitis B core total antibody (total Antibody to Hepatitis B core antigen (anti-HBc))
- E. Hepatitis C antibody
- F. Hepatitis C NAT
- G. Syphilis
- H. HBV NAT

11a. See EBAA Medical Standards Appendix IV: Testing V. Donor Testing: General E.

11b. See FDA CFR 1271.80(b) General Requirements for donor testing.

11c. HBV NAT:

See FDA HBV NAT Guidance Document

Note:

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 (Ref. Appendix V).

11d. See EBAA Medical Standards D1.200 Donor Testing

11e. EBAA Medical Standards Appendix V: Accredited Eye Banks Not Located in the United States

If the eye bank is not testing for HIV I/II using a test 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 Africa Republic, Chad Congo, Equatorial, Guinea, Gabon, Niger or Nigeria) after 1977 (risk factor for HIV group)).

11f. Appendix II: FDA Defined Contraindications to Transplant I. Risk Factors (x) and (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 who have received a blood transfusion or any medical treatment that involved blood in Cameroon, Central Africa Republic, Chad, Congo, Equatorial Guinea, Gabon, Niger or Nigeria after 1977 (risk factor for HIV group O)

12. If you have a potential donor who is negative or nonreactive for HBsAg and anti-HBc, but positive or reactive for anti-HBs. The presence of anti-

12. Refer to FDA guidance Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based

- HBs alone would not disqualify the donor, because it usually is an indication of vaccination against Hepatitis B. However, in this situation, if the anti-HBc were also positive or reactive, the donor is ineligible.
13. Even though screening for HTLV-I/II is not required by EBAA or FDA, if these are reported reactive to the eye bank, they should be acted upon by the medical director.
14. In some instances, procurement partners test for West Nile Virus. In the event that a shared donor is tested for the West Nile Virus and is reactive, the eye bank must defer the potential donor.
15. Screening for Syphilis:
- A. Eye banks must use appropriate FDA-licensed and approved screening kits to test for syphilis, go to FDA website listed on the reference section to verify approved test kits. Diagnostic screening testing kits for syphilis are no longer acceptable.
 - B. A non-treponemal FDA approved test kit such as ASiManager-AT can be used for screening. If the result is reactive then it must be confirmed with a specific FDA approved treponemal test to confirm result. If confirmatory testing for syphilis results are reactive then donor must be deferred. The specific treponemal test results will supersede the non-treponemal results.
16. If any of the above required tests are reactive, except for anti-HBs or non-treponemal test as previously described, donor must be deemed ineligible and therefore tissue cannot be used for transplant.
17. Place the reactive donor's tissue immediately in a separate designated section. The tissue must be physically separated from donor tissues that are found non-reactive. The Eye Bank must have a SOP on how to handle and manage the tissue in quarantine and released for transplantation.
18. Serology test results must be reviewed and documented prior to the release of tissue for transplantation. 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 and FDA within 10 days.
19. The eye bank must retain a copy of the
- Products (HCT/Ps) VI. Donor testing: specific requirements Hepatitis B surface antibody (anti-HBs) test
- 13a. See EBAA Medical Records D1.230
- 13b. European Centre for Disease Prevention and Control. Geographical distribution of areas with a high prevalence of HTLV-1 infection. Stockholm: ECDC; 2015.
14. EBAA Medical Standards Appendix 2: FDA contraindications to Transplant, (II) Clinical Evidence (e)
15. See FDA Guidance Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) VI. Donor Testing: Specific Requirements (1271.85) (A).
16. See CFR1271.80 (d)(1)
- 17a. Refer to EBAA Medical Standards C3.200 Equipment, Maintenance and Cleaning,
- 17b. Refer EBAA Medical Standards I1.000 Storage
- 18a. Refer to EBAA Medical Standards D1.200
- 18b. See FDA Guidance Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) III. The Donor-Eligibility Determination (1271.50) (I)
19. Good Eye Bank practices

laboratory's official serologic report. File the written or electronic hard copy results with the donor record.

- | | |
|---|---|
| <p>20. The Eye bank must maintain documentation of results and interpretation of all testing for at least 10 years.</p> <p>21. Rapid antigen and/or antibody testing for infectious disease can be performed in addition to the previously mentioned required tests to screen donors before recovery. Reactive test results can be used to defer a donor. Negative results MUST be confirmed with FDA approved screening kits.</p> <p>22. If procurement partners performed the same serological tests and results are discordant from the results the eye bank already has received, then eye bank should defer the potential donor. A standard procedure should be in place which describes how to handle these discordant results. Eye bank must share any reactive result with all procurement partners.</p> <p>23. If Eye Bank stores blood samples for future testing, they must have a SOP regarding the archiving of blood samples.</p> | <p>20a. Refer to EBAA Medical Standards M1.100 Length of Storage.</p> <p>20b. Refer to FDA 1271.55(d)(4)</p> <p>21. This test is currently used for a rapid determination to proceed with a recovery or not. This test kit DOES NOT substitute FDA approved test kits.</p> <p>22. Eye Bank Best Practices</p> <p>23. This is performed for retrospective testing of donors that are still in inventory when new tests are adopted for screening donors for existing or emerging pathogens</p> |
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G1.280 Non-Required Laboratory Results

Purpose:

To establish requirements on non-required laboratory results.

Regulatory:

21 CFR 1271.145 Prevention of the introduction, transmission, or spread of communicable diseases

Procedure	Rationale
1. The eye bank's Medical Director will be responsible for taking into account and/or acting upon non-required test results on tissue for transplantation.	1. Other tissue donation and/or state regulation may require serologic testing that is not required by the EBAA.

G1.290 Conflicting Serology Tests

Policy:

Conflicting serologic and positive non-required test results that may be indicative of risk for HIV or viral hepatitis will be reported to the EBAA, Medical Director, FDA and to any recipient surgeons for further follow up. Report must be made to EBAA within sixty days of receipt of discordant or positive test results. Additionally, positive serological results would be reported back to other associated agencies.

Regulatory:

21 CFR 1271.145 Prevention of the introduction, transmission, or spread of communicable diseases
21 CFR 1271.160(b) 2, 5 Establishment and maintenance of a quality program
21 CFR 1271.3(dd) Deviation reports for distributed HCT/PS

Procedure	Rationale
1. Positive serologic and/ or NAT results on any eye donors will be copied and sent to affiliated organizations such as OPOs or tissue bank if involved with the same donor.	3. Refer to EBAA Medical Standard G1.290.
2. Eye banks sharing donors with affiliated organizations should establish a protocol to receive positive serology results from those affiliated organizations.	

3. Any tissue that has been transplanted from donors with conflicting and/or positive serology [HIV 1/2 or Hepatitis] and/or NAT results will necessitate notifying the transplanting surgeon of the conflicting and/or positive serology results, as well as any findings from the quality assurance review process, which may help to identify confounding factors or data associated with sample collection, handling, storage, and testing.
4. Follow up with specific recipients will be at the discretion of the transplanting surgeon.
5. If possible, confirmatory tests will be run if any tissue has been transplanted.
6. Any tissue in stock from donors with conflicting serology results will be quarantined and discarded.
7. Discordant serology and/ or NAT test results will be reported to the EBAA within sixty days of the receipt of the results and to the FDA using form 3486 (Biological Product Deviation Reports).

G1.300 Tissue Recall

Purpose:

To outline a procedure for issuing a tissue recall

Materials Needed:

Eye bank distribution Record
Eye bank donor record
Eye bank recall form

Procedure	Rationale
1. When a tissue has been released for transplant and new information disqualifying the donor under the FDA Final Rule Human Tissue Intended for Transplantation 21 CFR Parts 16, 1270 and 1271, EBAA Medical Standards section D1.120, or the eye bank's policy and procedures becomes available, that tissue is considered unsuitable and some action must be taken for proper disposition	1. Medical Standards section G1.300 states "Eye banks must have a policy and procedure for potential recall of tissue." FDA Recall Policies and Procedures 21 CFR Part 7 describes the guidelines for initiating a voluntary recall.
2. Review recall procedures established by your eye bank, as needed.	
3. Assemble needed materials and information as listed above.	
4. Further distribution of any remaining tissue from the disqualified donor should cease immediately. Destroy any remaining tissue or place in quarantine until such time as the recall can be lifted through correction.	
5. Review the eye bank records for the disposition of each tissue from the disqualified donor.	
6. Notify all parties who received tissue from the disqualified donor immediately. If the transplant has not occurred, cancel the surgery and make arrangements to have the tissue returned to the eye bank for destruction or quarantine.	
7. If the tissue has been used for transplant consult your Medical Director to develop a recall strategy.	
8. Notify the receiver or transplanting surgeon of the new information, within 45 days, documenting the conversation in the eye bank donor records.	
9. Send written notification of the recall to the receiver of ocular tissue. Written notification should be brief and to the point, clearly identify the tissue in question, as well as explain the	

reason for the recall and any potential hazards involved. Make a copy of the notification letter for the eye bank donor record.

10. The transplanting surgeon is responsible for determining patient therapy and course but may request consultation with the eye bank's Medical Director.
11. FDA requests eye banks notify their district office of any voluntary recall.

H1.000 Non-Surgical Donor Tissue

Purpose:

To outline the procedure for handling donor eye tissue distributed for non-surgical purposes.

Definition of terms:

Screening or Screening Tests: Laboratory tests, licensed by the FDA, which rule out the presence of infectious disease such as HIV and hepatitis B and C.

Procedure	Rationale
1. Label the ocular tissue in the usual manner with source eye bank, ISBT 128 Tissue identifiers, plus a label "For Non-Clinical Use Only."	1. See procedure J1.000 and H1.000.
2. HIV 1/2, hepatitis B and C screening are not required by EBAA for non-surgical donor eye tissue.	2. See EBAA Medical Standards section H1.000.
3. If HIV 1/2, hepatitis B and C screening are not performed, the donor tissue must be labeled with a red or orange biohazardous symbol and statements indicating the tissue has not been tested and the tissue is potentially hazardous biological material, or some other designation acceptable by CDC guidelines	3. The label will alert the person receiving the ocular tissue to exercise infectious disease precautions.
4. Attach the label to the container, i.e., jar, vial, or viewing chamber in a prominent place. The label should be bright orange or red.	4. The label will alert the person receiving the ocular tissue to exercise infectious disease precautions.
5. The ocular tissue should be appropriately stored according to its method of preservation.	5. Consult your eye bank's policy for storage of non-surgical tissue.
6. Distribute the ocular tissue according to your eye bank's policy and procedure.	
7. Distribution records should be kept and a donor ocular tissue information form should accompany the tissue.	

I1.000 Storage

Purpose:

To delineate the conditions under which donor eye tissue is to be maintained and stored.

Definition of terms:

Asepsis: To keep free from bacterial contamination.

Potentially hazardous biological material: Any donor tissue that has not been screened for infectious disease.

Quarantine: To isolate tissue until infectious disease screening is completed.

Screening or Screening Tests: Laboratory tests, approved by the FDA, which rule out disease such as HIV, Hepatitis B and Hepatitis C.

Materials needed:

Sterile container, e.g., vial or jar

Preservation or storage solutions for the particular type of tissue

Refrigerator with temperature recording device, backup power supply or alarm system.

Procedure	Rationale
1. Surgical eye tissue (whole eye, corneas or sclera) is preserved in a manner appropriate for use of the ocular tissue. Research tissue should be maintained according to your eye bank's protocol.	1. To maximize the potential for a successful surgical procedure by preserving the integrity of the ocular tissue.
2. Maintain the temperature of the eye tissue according to EBAA requirements. The ocular tissue must be stored in a refrigerator with a continuous temperature-recording device and visible without opening the refrigerator. Refer to section C3.200 of this manual.	2. The temperature must be maintained within stipulated limits in order to ensure optimal viability of the ocular tissue.
3. Store all ocular tissue aseptically in separate vials or jars. Asepsis is to be maintained throughout the storage of the donor eye tissue.	3. Asepsis must be maintained to prevent contamination of the ocular tissue.
4. Quarantine all ocular tissue until the results of HIV 1/2, HBsAg, and HCV testing have been reported as non-reactive and a hard copy of the results have been received and recorded. If any other screening tests are performed, they must also be considered before any ocular tissue can be released from quarantine.	4. Quarantine assures that "potentially hazardous material" is not released for surgical use.
5. Ocular tissue is to be quarantined by designating an area within the refrigerator that is labeled "Quarantine".	5. A designated "quarantine area" ensures that ocular tissue is not distributed until all testing is completed and suitable determination has been made.

6. A second area is to be designated for ocular tissue for which all serologic testing is non-reactive and where all donor screening has been completed (for example Medical/Social History screening, obtaining gross autopsy results). This area may be termed "Transplant Tissue" or "Non-Reactive Serology". Tissue in this area must have documentation completed in the donor record to indicate that the Medical Director or designee has released the tissue for transplant.
7. Move surgical ocular tissue for which the blood screening had been completed and the results are non-reactive to the transplant area only after a hard copy or results of serology have been received and all other required screening procedures have also been completed. The donor record must be reviewed and tissue "released" for transplant must be noted prior to placing tissue in the "Transplantable" area. Only ocular tissue that has been removed from quarantine can be distributed for surgical use.
8. Ocular tissue for which the serologic testing has been completed and has been reported as "reactive" or positive is to remain in quarantine until repeat testing is completed according to the individual eye bank's policy.
9. Ocular tissue that is repeatedly positive or reactive for any one of the serologic tests performed is to be removed from the refrigerator and discarded according to section C3.700 of this manual and the policy of the individual eye bank.
10. Research ocular tissue, whether tested or untested, should be stored in your eye bank's refrigerator in an area labeled "Research Tissue". Untested research tissue must have an additional biohazardous legend label affixed.
6. This designated "transplant tissue" area further ensures complete separation of transplantable and quarantine tissue to minimize the likelihood of accidental distribution of quarantine tissue that has not been released for surgical use.
7. Assures that the ocular tissue is safe to release for surgery. Preliminary hard copy results may be faxed to the eye bank by the laboratory.
8. To prevent the release of "potentially hazardous" ocular tissue for surgery.
9. Biohazardous material must be disposed of quickly and safely.
10. See procedure H1.

J1.000 Labeling

Purpose:

To delineate the EBAA procedure for labeling of ocular tissue from time of procurement through time of distribution for surgical use, research, and teaching.

Definition of terms:

Intermediate or temporary label: A temporary label applied at time of procurement to identify the ocular tissue until a permanent label can be affixed.

Permanent label: The final label for all ocular tissue distributed by an eye bank.

Materials needed:

Temporary or intermediate label: Masking tape, sterilization indicator tape or other tape on which you can write.

Pen

Permanent label: Your eye bank's label with preprinted information

Pen, typewriter, or word processor

Procedure	Rationale
1. Each ocular tissue must be in a labeled container with a unique identification at all times.	
2. Write the donor's identification number, name, or other unique identifier with the date and time of procurement and whether right or left eye on a piece of masking tape or other adhesive backed plain paper. Also include the name of the technician or enucleator.	2. Intermediate or temporary labeling provides identification of the ocular tissue prior to final processing and application of a permanent label.
3. Once the ocular tissue has been transported back to the laboratory for final processing and disposition, determine the type of final or permanent label that the ocular tissue will require. This will depend on whether the ocular tissue will be used for corneal transplantation, sclera for surgical use, whole globes for lamellar keratoplasty, research or teaching, or disposal.	
4. All ocular tissue for surgical use, including corneas, sclera, and whole eyes, shall have a permanent label that conforms to EBAA Medical Standards. Preprinted labels are recommended, but not required. These labels shall include the following:	4. See EBAA Medical Standards section J1.000
A. Name of source eye bank	A. The Source Eye Bank is defined as "the entity that releases tissue following donor eligibility determination and is responsible for maintaining donor records and evaluating adverse reaction

reports."

- B. ISBT 128 tissue identifier. The ISBT tissue identifier includes the Donation Identification Number (DIN), Product Code, and Processing Facility Information Code (if applicable).
 - C. Type of ocular tissue.
 - D. Date and time of donor's death, in the international format (YYYY-MM-DD).
 - E. Date and time of ocular tissue preservation, e.g., cornea, sclera, or other, in the international format (YYYY-MM-DD).
 - F. If the cornea has additional processing, clearly indicate this on the label.
 - G. The statement that the ocular tissue is intended for single application only. Also a statement that the ocular tissue is not considered sterile.
 - H. Expiration date of the tissue, in the international format (YYYY-MM-DD).
 - I. Type of storage solution.
 - J. Label ocular tissue products distributed internationally with ISBT 128 data structures within two-dimensional (2-D) data matrix symbols. (effective 1/1/2017)
5. If ocular tissue is provided for research and serologic screening is not performed, then a biohazardous legend label must be applied and a statement that tissue is for "non-clinical use only".
5. See EBAA Medical Standards section H1.000, which requires a statement alerting the receiver of this ocular tissue that this tissue is potentially hazardous biological material.

K1.000 Distribution of Tissue

Reference:

- Farge, E. J. (1997). Ch. 42 ethics and eye banking. In J. H. Krachmer, M. J. Mannis & E. J. Holland (Eds.), *Cornea, fundamentals of cornea and external disease* (pp. 531-535). St. Louis: Mosby.
- Lindenauer, M. R., & Johnston, F. M. (1997). Ch. 40 tissue distribution. In J. H. Krachmer, M. J. Mannis & E. J. Holland (Eds.), *Cornea, fundamentals of cornea and external disease* (pp. 519-524). St. Louis: Mosby.
- Requard, J. J. (1997). Ch. 34 the evolution, structure, and function of eye bank networks. In J. H. Krachmer, M. J. Mannis & E. J. Holland (Eds.), *Cornea, fundamentals of cornea and external disease* (pp. 475-480). St. Louis: Mosby.

Purpose:

To provide consistent criteria for the distribution of ocular tissue as a foundation for an individual eye bank's defined system of distribution and to ensure compliance with EBAA Medical Standards and with applicable state and federal regulations.

Definition of terms:

- Distribution of ocular tissue:** 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.
- Eye Bank:** Individual FDA-registered eye bank carrying out distribution of eye tissue.
- Tissue distribution system:** The policies and procedures followed by an individual eye bank in distributing/allocating human donor eye tissue.

Materials needed:

Completed donor record that includes:

- Donor screening form
- Medical history, reviewed by medical director or designee
- Ocular tissue evaluation/rating
- Serology results
- Autopsy results (if performed)
- Culture results (if available)
- Any other relevant information
- Computer terminal or PC

Procedure for distribution as defined by each eye bank
List of professionals/institutions approved by the eye bank to receive ocular tissue
Eye bank forms to record distribution

Procedure	Rationale
1. Review distribution procedures established by your eye bank, as needed.	1. EBAA Medical Standards section K1.300 states that "Eye banks must establish and document a system of distribution". Ensures consistency in distribution practice.

2. Assemble needed materials and information as listed above.
3. Verify that the Medical Director or designee has reviewed the medical history and ocular evaluation. Document that the medical and laboratory information is in accordance with EBAA Medical Standards and state and federal regulations for each ocular tissue to be distributed.
4. Identify potential receivers of ocular tissue according to eye bank procedures.
5. Distribute ocular tissue, using the procedure established by the eye bank, which may be patient-based or surgeon-based.
6. The recommended order of priority is a) emergency request, b) eye bank service area, c) EBAA accredited, FDA registered eye banks within region according to tissue sharing protocol, d) other FDA registered eye banks, and e) eye banks in other countries.
7. Offer ocular tissue to potential receiver, providing information to assist him/her to determine acceptability of the ocular tissue being offered, according to EBAA Medical Standards and individual eye bank procedures.

Record each offer of ocular tissue and outcome of offer.
8. Continue to offer ocular tissue for surgical use, according to eye bank procedure, until tissue has been placed or until time limits established by the eye bank for surgical use have expired.
2. Availability of materials facilitates efficient communication of needed information and minimizes potential errors.
3. EBAA Medical Standards section K1.100 states that "Medical director or his/her designee must review and document that the medical and laboratory information is in accordance with medical standards prior to the distribution of ocular tissue for transplantation". Standard D1.120 identifies contraindications for surgical use of ocular tissue. EBAA Medical Standards section F1.000 identifies methods for ocular tissue evaluation.
4. Eye bank should maintain a list of persons and/or institutions eligible to receive ocular tissue from the individual eye bank. The consignee is responsible for tracking, traceability, and adverse reaction reporting per K1.200.
5. EBAA Medical Standards section K1.300 states that "eye banks shall establish and document a system of distribution which is just, equitable and fair to all patients served by the eye bank. Access to tissue shall be provided without regard to recipient sex, age, religion, race, creed, color or national origin."
6. Bona fide emergency cases take precedence over scheduled elective or waiting list cases. Emergencies include corneal perforations or lacerations, acute corneal infections, and corneal/scleral "melts".
7. Sufficient information on donor medical history (e.g., age, time, cause of death, ventilator time, relevant health conditions, lab results), tissue characteristics (e.g., tissue evaluation, cultures done and results, if available) and procurement information (e.g., procedure, death to preservation time, tissue culture medium) to enable the receiving surgeon to make an informed decision about accepting the tissue.

EBAA Medical Standards section F1.000 states that "the ultimate responsibility for determining the suitability of the tissue for transplantation rests with the transplanting surgeon".
8. Consideration should be given to how long it takes the ocular tissue to reach its destination and whether it would still be suitable for its original intended use. Long distances or

prolonged travel times may increase the time interval beyond acceptance limits between death of the donor and preservation of the ocular tissue, to the time of grafting.

9. If ocular tissue cannot be distributed for its original intended use, e.g., surgical use, follow eye bank procedure for distribution for alternative utilization, e.g., research or disposal.

9. Each eye bank should establish and document a system for distribution of ocular tissue for research and training needs that meets EBAA Medical Standards for fairness, equity, and safety. (EBAA Medical Standards sections K1.000, H1.000)

Research Tissue: Requests for research tissue are filled in relation to specific research needs and protocols within the eye bank service area. Eye banks may communicate with agencies such as the Foundation for Glaucoma Research, Retinitis Pigmentosa Foundation, and National Disease Research Interchange (NDRI) to fulfill requests for ocular tissue for researchers working in specialized areas.

Practice/Teaching Tissue: Requests are filled on an as needed basis from either fresh donor eye tissue or stored frozen specimens.

In some situations, research tissue may be released prior to obtaining a complete medical history due to the necessity of some biochemical studies being performed within 2 to 3 hours maximum of death. This ocular tissue should be distributed with a label indicating that is a potential biohazard, in accordance with section H1.000 of the EBAA Medical Standards.

10. Record distribution according to eye bank procedure.

10. EBAA Medical Standards section K1.300 specifies that documentation shall include requests for, offers of, and delivery of eye tissue.

Documentation of distribution shall be available for inspection by the EBAA Accreditation Board.

K1.400 Returned Tissue

Purpose:

To outline the minimum information necessary to document the return of a cornea distributed for transplant.

Materials Needed:

Eye bank form to record storage and return information

Procedure	Rationale
1. Assemble the eye bank forms needed to document a return when a receiver of tissue notifies the eye bank of the need to return a cornea.	1. Documentation at the time of notification is an efficient method for obtaining the necessary information from a source that is familiar with the circumstances.
2. Record the method of transportation used to return the cornea to the eye bank including the method and condition of storage while the cornea was outside the eye bank.	2. EBAA Medical Standards section K1.400 states that "For corneas returned and redistributed, tissue transportation and storage information must be documented and made available to the eye bank and transplanting surgeon." Provides the eye bank with storage information critical to determining if the cornea is suitable for re-distribution.
3. Examine tissue storage container's tamper evident seal and the condition of the tissue.	3. Check seal integrity to determine if tissue was opened prior to being returned. Additionally, evaluating the condition of the tissue after transportation is advised to determine tissue suitability.
4. Provide storage and transportation information to the potential receiver of ocular tissue if the cornea is offered for transplant again. The storage and transportation information must be retained in the eye bank records also.	4. Allows transplanting surgeon to have all the information to determine the suitability of the cornea for the intended patient.

L1.000 Documentation to Accompany Donor Tissue

Purpose:

To describe the minimum information and forms which must accompany each piece of ocular tissue at the time of distribution.

Materials needed:

Ocular Tissue Report Form
Package Insert Form

Procedure	Rationale
1. The Eye Bank must have and maintain a policy that describes the required documentation to accompany each tissue at the time of distribution. This policy should address the method used to enclose these forms with the tissue. This may be in an envelope placed within the transport container or in a plastic sleeve taped to the outside of the transport container. The method used should maintain confidentiality for the donor information.	
2. The EBAA requires, at minimum, the ocular tissue report form and the package insert form. Additional forms may include a packing list, recipient information form, blank adverse reaction form, purchase order, Bill of Lading or invoice. <u>A re-hydration procedure must be included as a package insert for all sclera preserved in alcohol.</u>	2. See EBAA Medical Standards section L1.000 for information that must be included on the ocular tissue report and package insert forms.
3. Complete all forms fully and accurately prior to enclosure with the tissue.	
4. Retain a copy of the ocular tissue report form for your eye banks records.	4. See EBAA Medical Standards section M1.400 for information that must be retained by the eye bank.

L2.000 Packaging, Sealing and Packing for Transport

Purpose:

To outline the minimum requirements and procedures for packaging, sealing, and packing ocular tissue for transport to a hospital, surgeon, or eye bank.

Reference:

Halberstadt, M., Athmann, S., Winter, R., & Hagenah, M. (2000). Impact of transportation on short-term preserved corneas preserved in Optisol-GS, Ikorol, Ikorol-dx, and MK-medium. *Cornea*, 19(6), 788-791.

Miller, T, Maxwell, A, Lindquist, T, & Requard, J. Validation of cooling effect of insulated containers for the shipment of corneal tissue and recommendations for transport. *Cornea*, 2013; 32:63-69.

Materials needed:

- Ocular tissue for shipment in a labeled container
- Tamper-evident shrink wrap or seal
- Sealing device
- Shipping container
- Frozen water beginning to melt sealed in plastic bag
- Packing material, e.g., cardboard or foam insert to cradle ocular tissue vials inside shipping canister
- Forms to accompany ocular tissue
- Tape
- Labels for outside of shipping container

Procedure	Rationale
1. Each eye bank shall have a written procedure for packaging ocular tissue.	
2. Seal each ocular tissue (cornea, whole eye, sclera) in a container with a tamper-evident shrink seal. The seal shall not interfere with visual inspection of the ocular tissue for integrity and suitability for use.	2... To alert the receiver if any tampering of donor tissue occurred prior to receipt. See EBAA Medical Standards section L2.000.
3. Wrap each ocular tissue in a waterproof bag or sealable pouch prior to local distribution or shipment to another eye bank.	3. To prevent melted water from ice or coolant from wetting labels on ocular tissue container.
4. Absorbent material must surround each tissue so that if the storage container is broken, potentially biohazardous liquid/material will not leak from the shipping container.	4. To comply with federal standards for shipping known or potentially biohazardous materials.
5. Place cornea, whole eye, or research tissue in an appropriate transport case with coolant and secured for local distribution/delivery.	5. To maintain ocular tissue at proper temperature, cushion it to prevent breakage of ocular tissue container, and maintain container in an upright orientation.
6. For export to another eye bank or corneal	6. To maximize the vapor barrier function of the

surgeon via airline, bus, etc., place the ocular tissue in a waterproof bag/pouch in an appropriately insulated shipping container and secure. The secured ocular tissue shall be placed in an inner plastic bag with an appropriate coolant (wet ice is best). The plastic bag is sealed and placed in an eye bank shipping container. The shipping container is then closed and taped shut.

7. Use a shipping container that will maintain donor tissue at a temperature between 2-8 C for a minimum of 24 hours for domestic shipment, and a minimum of 48 hours for international shipment.
8. Attach appropriate labels to the shipping container identifying the contents as "**Human Eye Tissue**", and listing the addressee/destination and source eye bank, including telephone numbers to be contacted if there is a delay or problem in transit. Affix IATA DGR "Exempt Human Specimen" label as per Current regulations.
9. Attach on the outside or include on the inside package insert information. If placed inside, it must be sealed in a waterproof bag or pouch.
10. Donor tissue for research with a known infectious agent, such as HIV, shall be packaged and labeled in accordance with Federal regulations for the shipment of biohazardous materials (see Appendix).
11. Ocular tissue preserved in ethanol or glycerin, or fixed in formalin for histopathological study does not have to be refrigerated during shipment. (Glutaraldehyde fixatives do require refrigeration.)

entire container assembly in order to maintain proper temperature and prevent leakage of melt water during shipment.

The use of "wet" or water ice should be distinguished from dry ice that can decrease the temperature in the transport container to 0° C or lower, resulting in frozen ocular tissue.

9. See EBAA Medical Standards section L1.200.
10. See EBAA Medical Standards section H1.000.

M1.050 Eye Bank Record Entry and Entry Correction

Purpose:

To describe recommended practice in recording eye donor information and a legally correct method of altering or changing an eye bank medical record entry.

Materials needed:

Black or blue pen
Record to be altered

Note: **White out must never be used**

Procedure	Rationale
<p>1. Use standard good practice when recording eye donor information.</p> <ul style="list-style-type: none">A. Write neatly and legiblyB. Use proper spelling and grammarC. Use black or blue indelible ink penD. Use military time (24 hour clock)E. Use authorized abbreviations onlyF. Record information promptlyG. Do not leave blanks on forms	<p>1. To avoid inaccurate or erroneous assumptions based on illegible record entries; to avoid confusion and misunderstanding. Black and blue indelible ink shows up best when a record is photocopied.</p>
<p>2. Use the following procedure to correct a mistaken entry:</p> <ul style="list-style-type: none">A. Draw a single line through the incorrect entry using black or blue indelible ink. Be sure the original entry is readable.B. Write in the appropriate information.C. Place the date and the eye bank technician's initials next to the revised entry. Complete mistaken entry corrections as soon as possible after they are detected.D. Document in clear, concise, unambiguous terms.E. Records revised electronically must have an audit trail that includes the altered information, date of revision, and the individual who made the revision.	<p>2. Never attempt to cover up an error with white out or correction tape. This serves as a red flag in medical-legal situations should eye bank records be reviewed by an attorney.</p>
<p>3. Do not tamper with any existing eye bank record. Tampering includes:</p> <ul style="list-style-type: none">A. Adding to an existing record by filling in the blanks.	<ul style="list-style-type: none">A. Trying to recall details long after the fact is prone to inaccuracy due to memory lapses.

- B. Rewriting a paper record. Never discard original notes and rewrite an entire record. Always retain the original page if you must rewrite notes. Indicate this on the rewritten pages.
 - C. Adding to another person's notes.
 - D. Revising electronic records without an audit trail.
4. Source paper records that are scanned to an electronic image may only be destroyed if:
- a) the scanned document is compared visually with the source paper record to ensure it is complete accurate and legible;
 - b) scanned electronic image is stored in an electronic system that is secure, retrievable, and able to be printed as a hard copy.
5. Eliminate bias from recorded entries. Avoid descriptive terms such as bad, good, etc. Chart objectively by describing specific observations, e.g., instead of saying tissue was rated as bad for transplantation, describe appearance in terms used in your corneal rating system.
6. Record all information you report to the medical director and his or her decision. Date and time this information.
- B. Rewriting notes because of coffee stains for example may be interpreted to mean information was destroyed because it was damaging.

M1.550 Adverse Reaction Reporting

Purpose:

To outline the process for investigating and reporting an adverse reaction.

A reportable adverse reaction is any communicable or other disease transmissible by, and attributable to, transplantation of donor eye tissue, including infection (as manifested by endophthalmitis, keratitis, or systemic viral disease) and biologic dysfunction (such as immediate donor endothelial failure or donor corneal dystrophy).

Regulatory:

FDA: 21 CFR Part 1271.350(a) Adverse reaction reports

Health Canada: *Safety of Human Cells, Tissues and Organs for Transplantation Regulations*, SOR/2007-118, Sections 47-54, 59(h), 62(2))

Florida Agency for Health Care Administration (AHCA), Section 59A-1.011 Adverse Reactions.
https://www.flrules.org/gateway/notice_Files.asp?ID=1805284

Reference:

Guidance Document for Investigating and Reporting Adverse Reactions to the EBAA, V2
OARRS Website: https://restoresight.org/wp-content/uploads/2017/08/OARRS-Guidance_07_2017.pdf

FDA's HCT/P Adverse Reaction Reporting
<http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/ucm152576.htm>

[Investigating and Reporting Adverse Reactions Related to Human Cells, Tissues, and Cellular and Tissue-Based Products \(HCT/Ps\) Regulated Solely under Section 361 of the Public Health Service Act and 21 CFR Part 1271 - Guidance for Industry 3/2016](#)

<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/ucm434760.htm>

Form FDA 3500A - Mandatory Reporting (2/2013)
<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048334.pdf>

Safety of Human Cells, Tissues and Organs for Transplantation Regulations, SOR/2007-118, September 10, 2015. Sections 47-54, 59(h), 62(2))
http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/pubs/medeff/guide/2010_guidance-directrice_indust_cto/2010_guidance-directrice_indust_cto-eng.pdf

Florida Agency for Health Care Administration (AHCA), Section 59A-1.011 Adverse Reactions.
https://www.flrules.org/gateway/notice_Files.asp?ID=1805284

Forms:

http://ahca.myflorida.com/MCHQ/Health_Facility_Regulation/Laboratory_Licensure/docs/organ_tissue/AdverseReactionFormPartI.pdf

Materials Needed:

Eye bank's Adverse Reaction Form
 Computer with internet access
 OARRS Login information

Procedure	Rationale
<p>1. Eye banks must have a mechanism in place for surgeons to report an adverse reaction following transplantation of ocular tissue. Postoperative adverse reactions must be reported immediately. Distributing eye banks must seek recipient follow-up information concerning possible adverse reactions on all tissues distributed between three and six months postoperatively. A mailing to the transplanting surgeon requesting outcome data for a tissue referenced by its unique identifiers is an appropriate mechanism. Diligent pursuit of information may be required.</p>	<p>1. Early referral of post-surgical complications allows remaining tissue from the donor to be scrutinized or recalled. Patients may develop an adverse reaction at some time other than the immediate postoperative period. These occurrences are thought to be under reported. A follow-up interaction requesting outcome data helps ensure industry trends are being tracked. See Medical Standard M1.500.</p>
<p>2. The distributing eye bank will forward the adverse reaction information to the source eye bank, which made the donor eligibility determination. The source eye bank initiates and coordinates the investigation, and is responsible for notifying all entities involved in the recovery, processing, storage, distribution, tissue evaluation, and donor eligibility determination of the results of the investigation. The transplanting surgeon is asked to provide information about the recipient, intraoperative complications, type of adverse reaction, and microbiology cultures if performed. The source eye bank should contact the mate cornea surgeon to inquire the recipient's status in regards the donor tissue transplant, if applicable. The source eye bank must provide information concerning the donor tissue and mate status. The eye bank Medical Director is asked to make an assessment whether the adverse reaction was possibly due to donor tissue. Diligent pursuit of information may be necessary in order to collect data from multiple sources.</p>	<p>2. Some information requested may be difficult to collect. Surgeons should be assured patient identification information would be treated anonymously.</p>
<p>3. The source eye bank will report any Possible, Likely/Probable, or Definite/Certain graft-transmitted adverse reactions to the EBAA within 30 days of the first report to the eye bank. The Eye Bank Association of America has created an Online Adverse Reaction Reporting System (OARRS) to collect and analyze this information.</p>	<p>3. The OARRS reporting system summarizes information allowing the EBAA to look for trends that may impact eye banking practice.</p>

4. If the adverse reaction involved a communicable disease and there is a reasonable possibility that the tissue caused the response, the bank which made the tissue available for distribution must report to the FDA within 15 days of the initial receipt of the information. The FDA MedWatch mandatory reporting form (Form FDA-3500A) should be used to report adverse reactions involving a communicable disease if it: a) is fatal; b) is life-threatening; c) results in permanent impairment of a body function or permanent damage to body structure; or d) necessitates medical or surgical intervention, including hospitalization.
4. Adverse reaction reporting is required per 21 CFR 1271.350 Reporting.
5. The completed Adverse Reaction Report will be copied and distributed to:
 - A. The processing eye bank, if different than the source eye bank.
 - B. The distributing eye bank, if different than the source eye bank
 - C. Other parties affected, e.g., infectious disease offices, state health departments, regulatory agencies or the surgeon reporting the adverse reaction.
5. Distribution of the Adverse Reaction Report to the affected parties allows for information to be gathered in the interest of patient safety, quality assurance, and infection control. Eye banks operating within universities, hospitals or other institutions may need to report these reports to an infectious disease office. Some states may require their health departments be informed of certain adverse reactions.
6. Adverse reaction records shall be kept for at least ten years. Adverse reaction records shall be available for EBAA site inspections.
6. Maintaining an adverse reaction file for inspection helps ensure eye banks are seeking outcome data on distributed donor eye tissue.

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This Procedures Manual was originally written under the auspices of the EBAA Medical Standards Committee, during Dr. William Reinhart's tenure as chairman from 1987 through 1991. We thank the following members of the ad hoc committee, and its Chair, Mary Beth Danneffel-Mandelkorn, RN, who contributed valuable time and effort in writing the various chapters:

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Implementation Guidance Document

Uniform Donor Risk Assessment Interview Forms

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May 20, 2015*

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Dedication

The project to create this *Implementation Guidance Document, Donor Risk Assessment Interview Forms*, and support documents is dedicated to all organ, tissue and eye donation professionals involved in communicating directly with donor family members and others to obtain information used to assess a donor's eligibility. These documents have been created to assist with performing this challenging and important part of the donation assessment that requires not only a thorough understanding of technical screening requirements but also compassion, patience, and empathy when interacting with acutely bereaved individuals. Providing this service is personally demanding in a number of ways, and you are recognized for your dedication and sacrifices. The important role you fulfill results in successful transplantation for many.

Respectfully,
Your colleagues

AATB, EBAA, and AOPO recognize the efforts of the following individuals who generously donated their time and expertise to creating and/or advising on the content of this document.

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A special thank you to Peter Mecnas for creating a Visio version of the “Child Donor - Form Selection/Decision Flowchart” (see Appendix A).

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IMPLEMENTATION GUIDANCE DOCUMENT

UNIFORM DONOR RISK ASSESSMENT INTERVIEW FORMS

I. INTRODUCTION

Organ, tissue, and eye (OTE) donation and transplantation professionals have long understood the value of collecting relevant medical, behavioral risk, and travel history information about potential donors to assess infectious disease risk as well as determine factors that can affect the quality of an organ or utility of the tissue. Testing today is greatly improved and valuable, both for detecting infectious diseases and understanding expected organ function, however, gaps remain (i.e., testing ‘window periods,’ health history that assists with predicting long term organ functionality) that can be filled by collecting accurate information from a proxy (or proxies) providing information on behalf of the OTE donor. In the past, OTE donor medical and behavioral risk questionnaires have not been studied to assess interviewee comprehension or interviewer perspectives on the functionality of formats, and these are known to be a root cause of mistakes. After reports of the successful development of a qualified blood donor questionnaire, the OTE donation community started a project to develop similar tools for screening donors for transplantation. To develop these tools, lessons learned from the blood donation community’s experiences were used as well as knowledge and experience from our own professionals involved with interviewing recently grieving donor family members or others in close relationship to the donor.

This *Implementation Guidance Document* outlines expectations and contains useful descriptions and references for the person administering any of the *Uniform Donor Risk Assessment Interview* (DRAI) forms (i.e., Donor >12 years old, Child Donor ≤12 years old, and Birth Mother). Following these instructions and utilization of support documents (see Support Tools) should promote uniformity in donor screening activities and optimize donation outcomes.

To access components and considerations for developing and implementing an effective quality assurance program for personnel performing the DRAI process, refer to the current version of the AATB-EBAA-AOPO Guidance Document titled “*Effective Quality Assurance of the Donor Risk Assessment Interview.*”

A. History and Purpose

The UDHQ-OTE Project was an acronym used for the development of a **Uniform Donor History Questionnaire for Organ, Tissue, and Eye** donors. This project was conceptualized in late 2006 and became a major effort involving experienced professionals from organ, tissue, and eye donation organizations and related associations, as well as government agencies. Its purpose was to create qualified, uniform donor history questionnaires, one for a child donor and one for an adult donor, with supporting documents for use by OTE donation professionals when screening for risks and applying policies used to determine donor eligibility. Supporting documents include this *Implementation Guidance Document*, references, and a flowchart for each interview question.

Historically, questionnaires used to screen OTE donors in the United States (US) and Canada have had problems similar to those identified at the turn of the century by blood donation professionals in North America. These include:

- content and formats that have never been formally evaluated for effectiveness;
- inclusion of questions that are not necessary and can act as distractors;
- incorporation of many long, often compound, questions;
- use of terminology and word phrases that the general public may not comprehend; and
- lack of standardization among organizations, which affects tissue and eye bank quality program review processes and interpretation of answers by organ transplant professionals.

During 2007, a multi-organizational UDHQ-OTE Task Force was formed to begin work on a consensus questionnaire based on screening requirements of regulations and professional standards, best practices from the vast amount of experiences of members, and new concepts learned from the development in the US of a universal blood donor questionnaire, as well as one for donors of cellular therapy products. This new Task Force met periodically by conference call over the next three years. On December 1, 2010 the Task Force released a draft version of a questionnaire to be used for an OTE donor >12 years old, as well as one for a child donor, and requested constructive comments from professionals and the public. Incorporation of these questionnaires can prove to streamline this critical donor risk assessment process and increase satisfaction of all stakeholders involved in providing donor information (the interviewees), those administering the interviews, and those who review the answers to the donor risk assessment questions. These tools are expected to:

- optimize identification of eligible donors;
- minimize errors due to inaccurate rule out;
- accurately identify an organ donor risk designation; and
- reduce complexity to facilitate comprehension by a bereaved interviewee.

The questions were designed to meet requirements and expectations of state, national and international regulations, laws, policies and/or standards. The concept surrounding how the interview can be done has been optimized by use of broad-based *filter questions*, a process that assists with a respondent's understanding of the questions. Further questioning to identify specific risk is only performed when indicated. Sub-questions were developed to gather appropriate, supportive information about the risk being evaluated.

In April 2011, a steering committee, the "UDHQ Stakeholder Review Group," was formed to review more than 500 comments received during the comment period and to finalize the forms. This group included representatives from appropriate government agencies such as FDA/CBER, HRSA, CDC and NCHS, as well as two OPTN/UNOS committees (DTAC, and the OPO Committee), and professional societies, namely, AATB, AOPO, EBAA, NATCO, AST, and ASTS. A few members of the UDHQ Task Force completed the membership of this review

group. They finalized a new draft version of the Uniform DRAI for a donor >12 years old after careful consideration of comments received. Officials from FDA/CBER offered a few final comments for improvement that were incorporated so the form was sure to meet federal expectations when screening human donors of cells and/or tissues. This next version was made available for use on May 7, 2012 by the professional donation and transplantation societies above. Updates to questions occurred in early 2013 to ensure the Uniform DRAI for a donor >12 years old meets expectations of the “*PHS Guideline for Reducing Human Immunodeficiency Virus, Hepatitis B Virus, and Hepatitis C Virus Transmission Through Organ Transplantation.*”

The Uniform DRAI for a donor >12 years old was further scrutinized throughout 2013 by the foremost authority regarding development of effective public health and behavioral history surveys in the US. Professionals from the CDC’s National Center for Health Statistics (NCHS) performed a series of cognitive interviewing studies using a final draft version of the ‘adult’ donor questionnaire. This science-based, qualitative evaluation of the questions was funded by the Office of Blood, Organ and Other Tissue Safety at CDC, via an Interagency Agreement. Authored by Stephanie Willson PhD, a report is available from NCHS: *Cognitive Evaluation of the Donor Risk Assessment Interview (DRAI): Results of Interviews Conducted April – December, 2013.*

The UDHQ Stakeholder Review Group was reformed and, using the report from NCHS, they finalized versions of three DRAI forms released on September 10, 2014:

- *Uniform DRAI - Donor greater than 12 yrs old;*
- *Uniform DRAI - Child Donor less than or equal to 12 yrs old; and*
- *Uniform DRAI - Birth Mother.*

A few support documents/tools have also been issued:

- *Implementation Guidance Document, Uniform Donor Risk Assessment Interview Forms;*
- *Effective Quality Assurance of the Donor Risk Assessment Interview;*
- *Uniform DRAI - Requirements Crosswalk Documents; and*
- Question flowcharts.

An online portal hosted by AATB (at www.aatb.org) is planned to collect constructive suggestions from users. This information will be reviewed regularly by a Stakeholder Review Group and changes made where appropriate. Periodic updates may also occur when any change is announced to requirements (e.g., to policies, regulations, guidance, or standards). If using the Uniform DRAI forms, adherence to published updates is expected.

B. Abbreviations

The following abbreviations are used in this Guidance Document:

AOPO – Association of Organ Procurement Organizations
AATB – American Association of Tissue Banks
AST – American Society of Transplantation
ASTS – American Society of Transplant Surgeons
CBER – Center for Biologics Evaluation and Research

CAN/CSA – Canada/Canadian Standards Association
CDC – Centers for Disease Control and Prevention
CTO – cell, tissue, and organ
DRAI – Donor Risk Assessment Interview
DTAC – Disease Transmission Advisory Committee
EBAA - Eye Bank Association of America
FDA – US Food and Drug Administration
HHS – Health and Human Services
HRSA – Health Resources and Services Administration
LEP – Limited English Proficiency
NATCO – “The organization for transplant professionals”
NCHS - National Center for Health Statistics (a division within CDC)
OPO – organ procurement organization
OPTN – Organ Procurement and Transplantation Network
OTE – organ, tissue, and eye
PHS – Public Health Service
UDHQ – Uniform Donor History Questionnaire
UNOS – United Network for Organ Sharing
US – United States
yrs - years

C. Definitions

As used in this Guidance Document, the following definitions apply:

Donor Risk Assessment Interview (DRAI) – (aka Medical History Interview - FDA) 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 (i.e., a *knowledgeable person*). Alternatively, a living donor may complete a written questionnaire. The relevant social history is elicited by questions regarding certain activities or behaviors that are considered to place such an individual at increased risk for a relevant communicable disease agent or disease (RCDAD).

Filter question – A question asked in order to determine if further questioning is necessary to assess risk.

Knowledgeable person – the person interviewed which can 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, who would be familiar with the donor’s relevant medical history and social behavior.

II. ORGANIZATIONAL CONSIDERATIONS

A. Compliance Expectations

1. Acceptable Alterations to the Form

Users of the Uniform DRAI forms are strongly discouraged from changing the content or order of any questions, preambles to questions, or the format designed to enhance flow and mental time travel. Alteration of the form removes the ability to apply qualitative analysis findings by NCHS because the interview tool is different from the tested version. Versions with revisions outside the scope listed below may not be presented as a “Uniform DRAI.” Only the following changes are considered acceptable for an organization to title/refer to their DRAI form as a “Uniform DRAI”:

- The name/title of the form can be changed, however, the establishment’s policies and/or procedures should contain a reference that describes the new title’s link to the respective Uniform DRAI form.
- There is space provided in the header on page one to insert the logo of the program using the form as well as their address. Alternative styles can be used to document this information, but provision of the identity of the program is required. Adding information to the area before the first preamble is allowed.
- Information on page one that provides the name of a second person interviewed and their contact information can be adjusted to meet local needs.
- The sequence of questions must remain unaltered, however, individual questions can be removed if not required for that donation. For example;
 - if eye tissue only can be donated and no organs or other tissues, questions not required for eye donation can be selectively removed; and
 - if a test kit being used for HIV-1 **Ab** testing is labeled to include HIV-1 Group O, the questioning associated with HIV-1 Group O risk can be removed.
- If any new questions are added, they can only be inserted before the first numbered question or after the last numbered question.
- Follow-up questioning for a “yes” response to a filter question can include more directions (i.e., in *italics*) for the interviewer to follow. For example, “*If this occurred within the past 12 months ask:*” could be added if it applies, however, eligibility requirements must be met.
- On the Uniform DRAI – Child donor ≤12 years old, a different format or process can be used for instructions at question number 1, however, the actual questions at “1a.” and “1a(i).” cannot be changed. For more information, see Section III. The Interview Form, part C. Special Consideration for a Donor ≤12 years old.
- The Uniform DRAI - Child donor ≤12 years old and the Uniform DRAI - Birth Mother can be combined into a single document, if local policy describes it.

2. Unique Circumstances
Although this guidance document addresses many scenarios, it's not possible to represent all of them. When unique circumstances arise, local policy should provide guidance that meets relevant requirements and there may be a need to consult with, for example, the institution's medical director or the appropriate manager on call.
3. Form Updates
Compliance with published updates of the Uniform DRAI forms is expected within the deadline announced.

B. Local Policies/Procedures

1. Living Donation
The category of "living donor" may include (but is not limited to) a living organ donor or organ donation from an individual in the context of imminent death (e.g., mechanical ventilation willingly discontinued by the patient being treated), reproductive tissue donors, and other tissue donation (e.g., placenta for amnion, skin from abdominoplasty, surgical bone donation, etc.). For these donations, the donor would provide directly their medical, behavioral and travel history. Local policy should dictate how current the living donor's DRAI must be, relative to the donation event, but it is recommended that this donor screening step occurs close to the donation date. Procedural considerations should include how the interview with a living donor must be conducted. If a prospective donor is allowed to self-administer the DRAI questionnaire, consultation with professional staff (such as a donation coordinator) must occur to ensure a dialogue so questions are understood and answers are interpreted correctly.
2. When to Stop the Interview Process
Policy should be established with consideration of written agreements/contracts of local organizations involved in the donation and procurement/recovery process. Direction needs to be clear for organs versus tissue/eye and/or research scenarios. If individual local policy allows, the interview may be stopped for a tissue or eye donor if a definitive risk is identified that indicates the donor is not eligible.
3. Alternative Languages
In order to collect accurate relevant medical, behavioral risk and travel history information about the potential donor, the knowledgeable person must be able to understand and respond to the questions being asked. If it is determined during the conversation with the knowledgeable person that they have a Limited English Proficiency (LEP), every reasonable effort should be made to ensure that the opportunity for donation is provided such as utilization of:
 - a professional interpreter service;
 - staff fluent in the language; and/or

- a family member or friend of the family to translate.

Regarding use of an alternative language form, see section III., part B. Format and Use.

C. Electronic Use of the Form

The Uniform DRAI forms can be formatted as electronic files, however, the software program used must be capable of providing an audit trail to account for any revisions to the original, concurrent documentation. Note: A fillable PDF (Adobe® Systems Incorporated) version does not meet this expectation. As with all electronic records, the DRAI tool should be programmed to the same security and verification standards. Version identification should be visible on the electronic system (or printed, if applicable) on the screen (or paper). Programming of questions and response choices (e.g., “yes”, “no”, “N/A”) should include audit capabilities for verification of the documenter. If built within an existing electronic documentation system, the DRAI will carry the same expectation for validation of any modifications or enhancements. Policies must be in place if the electronic system is not used and a backup plan must be in place if the electronic system is not working.

D. Approval of Changes

To promote compliance to regulations, laws, standards and policies, any changes to the Uniform DRAI forms must be approved prior to use. Local policy should include notification and/or approval steps (e.g., with a tissue processor making the determination of final donor eligibility/suitability).

E. Document Control

Organizations should implement a plan consistent with their management of internal forms and documents. This may include, but not be limited to:

- naming the document;
- identifying an implementation date;
- assigning a version number;
- approving each version with signatures;
- requiring regular review and training of the form; and
- archiving former versions.

Organizations must have a method to ensure that staff has access to the current version of the form, whether electronic or paper.

III. THE INTERVIEW FORMS

A. Important Concepts and Expectations

- The Uniform DRAI forms are tools designed to optimize the process used to gather relevant information from the knowledgeable person(s) identified to provide medical, behavioral, and travel history for a deceased donor. This tool can also be adapted for use with a living donor of an organ or tissue.
- These interview tools are not intended to assist with policy decisions in all scenarios. For example, actions to take after answers and information have been provided in the Final Questions are at the discretion of users.
- Uniform DRAI forms must be completed concurrently while performing the interview in the question order provided and according to local policies and procedures.
- The questions are designed to meet requirements and expectations of state, national and international regulations, laws, policies and/or standards. If donor criteria between users differ, this can promote confusion, and jeopardize the process uniformity to which donation and transplantation stakeholders have agreed is best.
- Each question is constructed to be as short as possible but with the ability to gather necessary information to cover requirements. Although kept to a minimum, there are a few questions where screening redundancy occurs. Entirely restricting screening for risk to one possibility does not always occur and this is deliberate (i.e., risks related to travel). This allows for interviewees to remember diseases, surgeries, procedures etc. that they may not have thought of with the initial question.
- Use of “she/he*” in questions is intentional to consistently remind the interviewer to mix the appropriate pronoun with other terms with which the interviewee can relate: the donor’s given name; their nickname; or by inserting “your” father, mother, husband, wife, sister, brother, daughter, son, or child (as indicated). By using this approach, the interviewer is afforded real-time instructions throughout administration of the questionnaire, versus simply using “the donor” or “the deceased” to lead off questions.
- The Uniform DRAI forms use the *filter question* approach, which covers a broad topic initially, and when an affirmative answer is given, provides follow-up sub-questions that must also be asked to elicit additional, necessary information/details. Since specific donor eligibility criteria may vary from one facility to another, an affirmative response to some questions may require consultation with the facility’s policies.
- A few questions and preambles include examples to educate the interviewee regarding risk being assessed. For instance, after communicating with officials at FDA, a *filter question* can be used to initially assess sexual risk but only when “sexual activity,” “sex,” or “sexual act” has been defined first for the interviewee. Considering the sensitive nature of this topic, an acceptable preamble and question were developed for each of the

Uniform DRAIs. Additionally, providing examples of these terms aids in reducing the number of questions considered intrusive.

- Our nation's foremost authority on health history and behavioral risk surveys, the National Center for Health Statistics (NCHS), a division of the CDC, analyzed the original DRAI form for a Donor >12 years old. Their qualitative evaluation used cognitive interviewing techniques that included bereaved persons. Users are strongly discouraged from changing any questions, preambles to questions, or question order used on the Uniform DRAI forms because doing so removes the ability to apply findings by NCHS to an adulterated form. If any questions are added, they can only be inserted before the first question or after the last question. The name of the forms can be changed and users are encouraged to identify the form with their name, address, and logo. Refer to section II., part A. Compliance Expectations above.
- Questioning begins with current and recent history, and sequentially proceeds through the past 12 months, past 5 years, then EVER. This mental time travel order is known to enhance the interviewee's ability to recall.

B. Format and Use

A format was selected for the Uniform DRAI forms from a variety of styles. The following points are considered to enhance use, and concepts described in the *Effective QA of the DRAI Guidance Document* and garnered from the *Cognitive Evaluation of the Donor Risk Assessment Interview (DRAI): Results of Interviews Conducted April – December, 2013* apply:

- A quiet area for both the interviewer and interviewee(s) is desired so questions and responses can be clearly heard, and privacy is preferred to maintain confidentiality.
- All *filter questions* are designed to be asked first. In paper format, they appear in the left-hand column.
- Questions must not be skipped unless directed to do so by the questionnaire.
- To optimize interviewee recall, questions are designed to be read in numbered order.
- Questions should be read in their entirety and as written. Specific word choices were intentionally made and further developed after the original DRAI form was tested using cognitive interviewing techniques. Reading questions verbatim is not a requirement unless directed by your internal policy and procedures, but it is highly encouraged.
- Each Uniform DRAI form is intended to facilitate an interactive conversation (dialogue) designed to collect and document pertinent information, but a consistent intent of the questions regarding specific risk must be communicated to interviewees if not read verbatim. Rephrasing questions is discouraged and may miss the intent of a question's assessment of risk.
- In paper format, the No - Yes answer selections are arranged in the middle column vertically instead of horizontally to avoid confusion. If a Yes response is received, sub-questions that must be asked next appear directly across from the Yes selection to promote ease of flow.

- The format provides more space in the column to the right for documenting detailed information for the sub-questions.
- Lines can be added to facilitate documentation for sub-questions and spacing between questions can be adjusted to meet local needs.
- Documentation of answers to sub-questions can be provided in a horizontal fashion instead of vertically. Example: when documenting “What kind?, Where?, and When?” for travel or residency outside the US or Canada, documentation methods can align across the answer area. This may only be practicable for some questions.
- Questions periodically contain instructions to the interviewer that are not read to the interviewee. These appear as text in *italics*.
- The preambles appear in bold type to enhance visibility to the interviewer and are intended to be read to the interviewee to preface questioning. The preambles are part of each Uniform DRAI form and their style was studied when assessing comprehension.
- Time periods (i.e., past 12 months, past 5 years, and EVER) appear in bold type to stress relevance to the interviewer.
- When relevant risk history is known by the interviewee, it must be captured, but there can be instances when an “I don’t know” answer is initially given to a question. It’s important to remind the interviewee(s) to answer to the best of their knowledge. If the answer is again “I don’t know,” then ask “Do you have actual knowledge of....” (be sure to repeat the question in a format that fits the question). Local policies and training should describe how to handle this scenario.
- In cases where the interviewee repeatedly answers “I don’t know,” the interviewer needs to assess if someone else must be interviewed.
- If more than one person is interviewed, refer to local policy for documenting answers to questions.
- If it is determined that an additional person is needed to answer specific questions, document that determination in the “Additional Notes” section. Document which question(s) the second person answered.
- When interviewing one knowledgeable person for two or more donors, or for more than one history (i.e., interviewing a parent about her/his children, or interviewing a child about her/his parents), the interview can be conducted simultaneously, if consistent with organizational policy/procedure.
- Responses should be documented with sufficient detail. Local policies and procedures must define how responses to sub-questions will be documented on the Uniform DRAI.
- Use of a translated form (alternative language) is encouraged when indicated and Compliance Expectations must be met. Refer to section II., part B., listing 3. on page 12.
- Local policy and interviewer training/education should address documentation practices when responses to questions are provided using slang or other descriptions. This can occur for an affirmative (yes) response (e.g., yeah, yep, absolutely, I believe so, etc.) or

for a negative (no) response (e.g., never, nah, he wouldn't do that, I really don't think so, not to my knowledge, etc.).

- Follow good documentation practices as outlined in local policies. Elements may include handwritten or electronic entries (i.e., requirements for use/non-use of N/A boxes, documentation for use/non-use of multiple Uniform DRAI forms).

C. Special Considerations for a Donor ≤ 12 years old

- If a child donor's history includes being fed breast milk in the past 12 months and it was sourced from a person other than the birth mother, local policy should be established to assess risk. Consideration could include whether the breast milk originated from an establishment accredited by the Human Milk Banking Association of North America. Their standards include screening donors for high-risk behavior and testing donors for relevant communicable diseases. Donated milk is pasteurized using validated methods to remove potentially harmful bacteria and viruses. See <https://www.hmbana.org> for more information.
- The Uniform DRAI – Child donor ≤ 12 years old uses EVER in referencing a time period in filter questions. If a yes answer is given, further questioning often begins with “when,” however, “how long ago” could be substituted for “when.”
- Scenarios can occur when a child donor ≤ 12 years old has been continuously hospitalized since birth. In this scenario, the Uniform DRAI – Child donor ≤ 12 years old is not required to be completed, however, the donor's relevant medical records at the hospital shall be used to assess the medical and behavioral history risks required for donor screening per guidance, policies and standards. Note that when completing the Uniform DRAI – Birth Mother form under such circumstances, the otherwise optional interview question regarding family history of CJD must be asked. If the Uniform DRAI – Birth Mother form is not completed in this circumstance (i.e., child's age > 18 months but ≤ 12 yrs, and has not been fed breast milk in past 12 months), the otherwise optional interview question regarding family history of CJD must be asked and documented. The timing of this interview can be adjusted to meet local needs or for certain scenarios. For example, this interview can occur before, during, or after the process when the Document of Authorization is completed.
- Local policy could address a scenario where the child donor is older than 5 years and was fed breast milk within the past 12 months.

D. Special Considerations for the Birth Mother Assessment

Scenarios can arise where the birth mother of a deceased child donor was a surrogate mother or the birth mother received Assisted Reproductive Technology (ART) procedures such as embryo transfers or artificial insemination that resulted in the child donor's birth. Questions regarding risk for communicable disease should be directed toward the woman who had carried the child, independent from the manner in which she was impregnated.

IV. SUPPORT TOOLS

A. Flowcharts for Questions

Flowcharts are provided for questions on the Uniform DRAI forms to guide the interviewer through the interview process and they can also be used for quality assurance purposes. They are intended as a resource that, where indicated, may be revised by programs to reflect local policy as long as eligibility decisions are not made less strict than those indicated by relevant requirements. Users of the Uniform DRAI forms should have policies and procedures that describe acceptable methods for gathering necessary information when a response to a question indicates follow-up is needed. The flowchart for each question can be tailored to meet local policy, when applicable.

Each question is a separate flowchart, and each one contains the following information:

- Question: Question number and the question.
- Donor Eligibility: Provides additional information regarding eligibility considerations
- Note: an optional field related to the specific question.
- Flowchart: Uses standard flow-charting symbols.
 - Square/Rectangle = statement
 - Diamond = question/decision point (Uniform DRAI questions are within red diamonds)
 - Oval = action
 - Arrow = move to next question

Each question ends with an arrow that indicates to “move to the next question,” however, programs must follow their own policies and procedures concerning eligibility determinations based on information collected (which may indicate the donor is not eligible). A condition or history that is not an absolute rule-out can be directed to “Consult your policy.”

B. Uniform DRAI Requirements Crosswalk Documents

Uniform DRAI Requirements Crosswalk documents are available that provide the relationship between questions on each Uniform DRAI form with donor screening expectations from applicable federal regulations, guidance and policies, as well as state laws and professional standards. These documents are updated when any requirements change or when the forms are updated for other reasons.

C. Effective Quality Assurance of the DRAI (AOPO-EBAA-AATB Guidance Document)

This multi-agency guidance document provides expectations and describes best practice for managing an effective Quality Assurance Program that provides a high level of assurance the DRAI process is being performed consistently as intended. It contains direction regarding

components of the program such as: standard operating procedures; staff qualifications, training and competency; sampling plans for quality control measures; auditing examples; and corrective and preventive action including timely notification. The current version can be accessed on the websites of AOPO, EBAA, and AATB.

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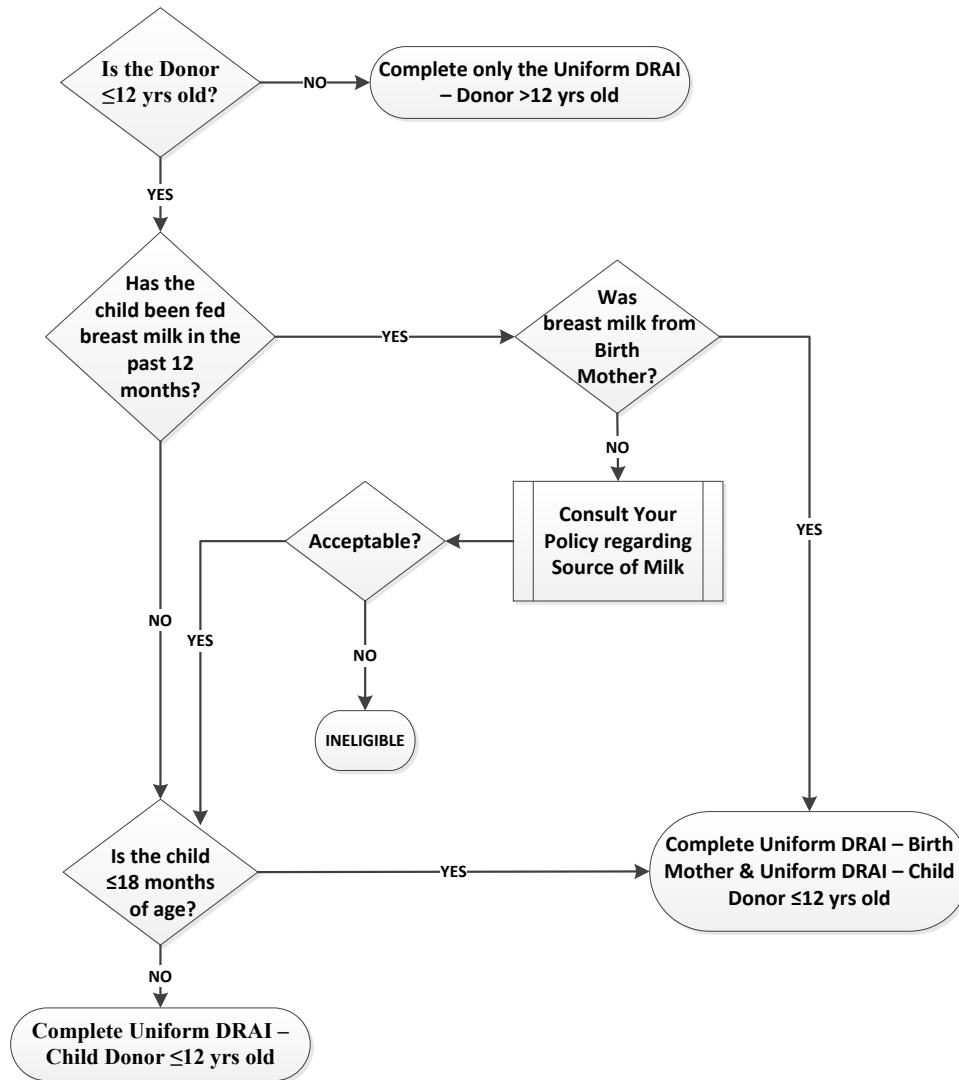
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VI. APPENDIX

A. Child Donor – Form Selection/Decision Flowchart



Note: If the child had been continuously hospitalized since birth, a *Uniform DRAI - Child Donor <=12 yrs old* form does not need to be completed, however, Question #27 must be answered when completing the *Uniform DRAI - Birth Mother* form. If this latter form is also not completed (i.e., child's age >18 months but <=12 yrs, and has not been fed breast milk in past 12 months), the otherwise optional interview question regarding family history of CJD must be asked and documented.



Guidance Document

Effective Quality Assurance of the Donor Risk Assessment Interview

*Version 2
September 16, 2013*

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The Associations recognize the efforts of the following individuals who generously donated their time and expertise to creating this updated document.

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AATB/AOPO/EBAA GUIDANCE DOCUMENT EFFECTIVE QUALITY ASSURANCE OF THE DRAI

I. INTRODUCTION

An essential safety element of *tissue* donor screening and ultimately the determination of a deceased *donor's eligibility* is the administration and completion of the *donor risk assessment interview* (DRAI). This guidance document describes components and considerations for developing and implementing an effective *quality assurance program (QA Program)* process for the DRAI.

The DRAI *record* is considered a *relevant medical record* used to determine initial and final *donor eligibility*. Two methods exist to obtain information required to complete the DRAI and each generates a concurrent *record* of the information gathered. Interviews may be conducted face to face, often in a hospital setting for a potential organ/tissue donor, but, more often, the interview is conducted by telephone for a potential tissue donor. For each method, the expectation is that a knowledgeable person regarding the donor's relevant medical history and social behavior is identified and interviewed for the DRAI. In all cases, the interview is conducted according to *standard operating procedures (SOPs)* and concurrently documented using a standardized form to ensure all requirements of the SOP are addressed.

Note: For the purposes of this guidance, the term "*tissue bank*" includes an eye bank, an organ procurement organization, or a tissue bank (but not a tissue bank that handles reproductive tissue only). When used for the first time in the body of this document, a term is italicized if a definition for it appears in section "B. Definitions and Acronyms."

A. Executive Summary

This guidance document provides expectations and describes best practice for managing an effective QA Program that provides a high level of assurance the DRAI process is being performed consistently as intended.

The QA Program must include all of the following:

- comprehensive SOPs;
- staff qualification, training, and *competency assessment and verification*;
- *quality control* of the documented *record* of the interview;
- an internal *audit* program which includes the performance of periodic assessment of the effectiveness of the SOP and compliance with the SOP; and
- corrective and preventive action as warranted.

Recommendations included in this consensus document represent the collective expertise of many procurement professionals. The definitions, regulatory expectations, components of a QA Program, and reference documents are provided for use by all professionals performing these functions, or entities for which these functions are performed. An effective QA Program as described in this guidance document is expected to be in place.

B. Definitions and Acronyms

These definitions originate from current standards of the AATB and the EBAA, except where noted:

AUDIT – A documented review of procedures, records, personnel functions, equipment, materials, facilities, and/or suppliers to evaluate adherence to the written *SOPM*, standards, applicable laws and regulations.

COMPETENCY – The ability of an employee to acceptably perform tasks for which he/she has been trained.

COMPETENCY ASSESSMENT – The evaluation of the ability of an employee to acceptably perform tasks for which he/she has been trained.

DEVIATION – An event that is a departure from a procedure or normal practice.

DONOR ELIGIBILITY— Determination made based on donor screening and testing for relevant communicable disease agents and diseases (This definition is derived from § 1271.45(b).

DONOR RISK ASSESSMENT INTERVIEW (aka Medical History Interview, Medical/Social History Questionnaire, or Uniform Donor History Questionnaire/UDHQ) – 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. The relevant social history is elicited by questions regarding certain activities or behaviors that are considered to place such an individual at increased risk for a relevant communicable disease agent or disease (RCDAD).

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

QUALIFIED - Deemed competent by a recognized authority.

QUALITY – The conformance of tissue or a process with pre-established specifications or standards.

QUALITY ASSURANCE (QA) PROGRAM – The policies and environment required to meet standards of quality and safety, and provide confidence that the processes and tissue consistently

conform to quality requirements.

QUALITY CONTROL (QC) – Specific tests or activities defined by the *QA Program* to be performed to monitor authorization/informed consent, donor screening, recovery, 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 tissue bank’s equipment and operational procedures, as well as the monitoring of supplies, reagents, equipment, and facilities.

RECALL – An action taken by a tissue bank to locate and retrieve tissue from distribution and dispensary inventories. This includes withdrawals; see <http://www.fda.gov/Safety/Recalls/ucm165546.htm>

RECORD - Information that is inscribed on a tangible medium or that is stored in an electronic or other medium and is retrievable in perceivable form.

RECOVERY —Tissue surgically removed from a donor that is intended for use in human transplantation, therapy, research or education.

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 which 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.

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

STANDARD OPERATING PROCEDURES MANUAL (SOPM) – A group of standard operating procedures (SOPs) detailing the specific policies of a tissue bank and the procedures used by the staff/personnel. This includes, but is not limited to, procedures to: assess donor eligibility; recovery; processing; quarantine; release to inventory; labeling; storage; distribution; and recalling tissue.

TISSUE (aka human cell, tissue and cellular and tissue based products (HCT/Ps)) – A functional group of cells. The term is used collectively to indicate both cells and tissue, and includes ocular tissue.

TISSUE BANK (aka Tissue Establishment) – An entity that provides or engages in one or more services involving donated ocular and/or conventional tissue from living or deceased individuals for transplantation purposes. These services include assessing donor eligibility, recovery, processing, storage, labeling, and distribution of tissue.

VERIFICATION – The confirmation by examination and provision of objective evidence that

specified requirements have been fulfilled.

Acronyms:

AATB – American Association of Tissue Banks
aka – also known as
AOPO – Association of Organ Procurement Organizations
AST – American Society of Transplantation
ASTS - American Society of Transplant Surgeons
CDC – Centers for Disease Prevention and Control
CFR – Code of Federal Regulations
DRAI – donor risk assessment interview
EBAA – Eye Bank Association of America
FDA – United States Food and Drug Administration
HCT/Ps – human cell, tissue and cellular and tissue-based products
HBV – hepatitis B virus
HCV - hepatitis C virus
HIV - human immunodeficiency virus
HRSA – Health Resources and Services Administration
NATCO – The Organization for Transplant Professionals
NCHS – National Center for Health Statistics
QA – quality assurance
OPTN – Organ Procurement and Transplantation Network
QC – quality control
RCDAD - relevant communicable disease agent or disease
SOP - standard operating procedure
SOPM – standard operating procedures manual
TSEs - Transmissible Spongiform Encephalopathy(ies)
UDHQ - Uniform Donor History Questionnaire
UNOS – United Network for Organ Sharing
vCJD – variant Creutzfeldt-Jakob disease
WNV – West Nile virus

II. Regulatory Expectations

A. Federal

An evaluation of applicable FDA regulations at 21 CFR Part 1271 and related guidance for human cell, tissue, and cellular and tissue-based products (HCT/Ps) reveals relevant headings that can be applied to functions when performing the DRAI (aka FDA’s “donor medical history interview,” a donor screening function). A list of relevant requirements and a summary of expectations are provided in Appendix A.

1. Recommendations

- Develop your SOPM to reflect the following:

- the documented record of the interview is made concurrently by the interviewer performing the steps;
 - the documented *record* is the *relevant medical record* and is retained and/or shared; and
 - if made, the audio recording of the DRAI is used for *quality* review purposes only, and is not intended to be the documented record that's retained and/or shared.
- The interview must be conducted in accordance with the SOP.
 - Staff members who administer the DRAI must be *qualified*, be provided with appropriate training, and designated as “authorized” to perform the task.
 - Regularly scheduled assessments of all personnel shall be performed to verify compliance with the SOP.
 - The documented record is expected to accurately reflect the DRAI event.
 - A QA program must include sampling plans that verify the process used, whether the DRAI is recorded or not.
 - When an audio recording is made, an adequate QA sampling policy and *procedure* for reviewing and comparing the written or electronic record to the audio recording of the DRAI must be developed.
 - After sampling has occurred, changes made to any records already shared must be communicated in a timely manner.
 - The decision to retain the audio recording on file and the retention timeframe must be determined by each tissue establishment based on the tissue establishment's use of the recording in determining donor eligibility.

If the audio recording is not used for donor eligibility determination:

- Time periods selected should be reasonable for your operations and tied to quality control measures (e.g., see C. Quality Control, 1. Sampling Plan). The SOPM should include a description that when the record is produced concurrently with the voice recording, and a robust sampling plan is used after recordings are made, there is no need to retain the audio recording for an extended period of time.

If the audio recording is used for donor eligibility determination:

- The retention time period selected must be 10 years from the time of creation.

- The written agreement/contract between a tissue bank receiving donor tissue and the establishment that performs the DRAI on their behalf should ensure that responsibilities are clearly described and understood in regard to activities performed.

III. Components of a Quality Assurance Program

A. Standard Operating Procedures

Development of an effective, practical SOP is critical. The DRAI takes place when the interviewee may be distraught due to the recent death of the potential donor. This situation presents particular challenges to the interviewer if the SOP is written in a restrictive manner (e.g., requiring that the interview material be read verbatim).

While it is critical to gather all the relevant information required in the DRAI, a well-designed SOP and questionnaire can greatly assist both parties in the interview process. The DRAI is intended to be an interactive conversation (dialogue) designed to collect pertinent information. The use of ‘capture’ questions limits repetitious questioning and can quickly elicit required information. A capture question asks a broad question leading to more specific questioning only if needed.

Note: A group of donation and transplantation professionals representing AOPO, EBAA, NATCO, HRSA, OPTN/UNOS, AST, ASTS, NCHS, CDC, FDA and AATB have developed a uniform donor history questionnaire structured to address challenges when conducting the DRAI. The capture question approach described above is used and is preferred. It is recommended that all agencies performing DRAI activities evaluate this questionnaire for adoption into their processes and, as appropriate, adjust SOPs and staff training accordingly.

B. Staff Qualification, Training and Competency

The DRAI shall be performed by staff members who have sufficient qualifications, which equates to completion of a formal training program and documented *competency assessments*. To remain *qualified*, interviewer knowledge must be updated when new or revised policies and procedures are implemented.

Effective training of personnel performing DRAI activities is another area of opportunity for assuring the *quality* of the information gathered during the DRAI process. Interviewers are faced with many challenges during this process and should be trained to be sensitive to a number of factors. These include the:

- need to provide empathy to the donor family member(s) or other person interviewed;
- sensitive nature of many questions;
- criticality in obtaining the best information possible to facilitate donor eligibility determination;

- accuracy in completion of the documented record of the interview; and
- management of the interview process when an interviewee desires to limit the questions or the length of time spent on the DRAI.

A varied and challenging number of ‘priorities’ are present in the DRAI process; therefore, it is important to include in training programs for staff, not only the SOP content but also the perspective of the stakeholders in this process. Of particular importance is providing information related to the reason for, and intent of, each question as this may not be intuitive to the interviewer. In the absence of this understanding, interviewers might rephrase the question and miss the intent of a question’s assessment of risk. For example, this can include intent behind questions related to geography and travel during certain periods of time (i.e., related to risk associated with vCJD). As part of their training, personnel shall be made aware of the consequences of the improper performance of their specific jobs.

Discussion of ‘lessons learned’ is effective in maintaining the learning culture. Material for these discussions can be gathered from inside the organization, from reports of problems encountered by other agencies, as well as from audit findings where interviews may not have been completed as required or planned.

Competency assessments shall be conducted by organizations to ensure that the behavior, knowledge, skill, and ability of personnel performing the DRAI align with expectations including criteria of regulations, standards, and SOPs. Competency *verification* shall be done prior to personnel performing the DRAI role independently and should be performed on a recurring basis (such as annually). Recommendations include the use of tools and methods such as:

- observation and assessment of on-site or recorded performance of the DRAI personnel. These reviews can include mock DRAI scenarios and actual DRAIs (recorded or live);
- use of a competency assessment checklist to include all expectations required to complete a comprehensive DRAI. Such expectations should include that the interviewer:
 - provides proper instruction to the interviewee at the start;
 - asks all required questions;
 - executes the intent of the questions;
 - appropriately probes and follows up on responses during the DRAI, as needed; and
 - documents relevant responses accurately.
- clearly defined thresholds for competency. Data should be collected for error tracking and performance trends;
- improvement plans for personnel that have not achieved or retained an acceptable level of competence;
- competency exams to demonstrate knowledge and understanding for the questions and

their intended purpose; and

- inclusion of competency *verification* documentation in the individual's training record.

C. **Quality Control**

Quality Control activities shall be described in the SOPM and consist of a timely review of documented records soon after interviews are conducted. This may include direct observation of the administration of the DRAI, listening to audio recordings, and review of the documentation of the DRAI. The intent of quality control measures is to determine if the documented record:

- complies with the established SOP;
- accurately reflects information obtained from the interviewee; and
- is complete and legible.

Note: An audio recording of the dialogue that takes place for the DRAI is not mentioned in, or required by, FDA regulations or guidance, and is not required by standards of the AATB [1], AOPO [2] or EBAA [3]. Because some *tissue banks* record DRAIs in addition to concurrently completing a record, these practices need to be managed using appropriate quality assurance concepts.

Quality Control activities are usually structured and planned based on a confidence level for the process. Therefore, a number of variables should be considered in order to provide confidence in the documented record created concurrently during the course of the interview. Variables that should be taken into account include:

- experience with the current DRAI form and associated SOP;
- interviewer training;
- past results of quality control measures; and
- other quality assurance activities where *deviations* from *procedure* versus desired outcome have been identified.

In the event the DRAI is not completed in accordance with the SOP, the timely performance of corrective measures is essential. Any need to re-contact the interviewee to clarify responses or to obtain missing information should be done as soon as possible.

1. **Sampling Plan**

A sampling plan must be used to conduct the quality control program. An effective sampling plan takes into account certain variables (e.g., number of donors, assurance level) that determine an adequate sample size. Sampling plans should be applied to ensure that the sample includes multiple interviewers, that each interviewer is sampled periodically, and if there have been changes in the SOP or the DRAI, sampling may need to be increased. Routine reviews of this

activity should not be used as a substitute for competency assessment. All Quality Control activities must be documented including identification of which records were sampled, whether the activity was acceptable or, if deviations are noted, what immediate corrections were made. If applicable, a description of any long-term corrective actions should be included.

Considerations for **internal** process sampling include:

- select a short period of time, such as within 30 (thirty) days from date of performance, to prevent recurrence of any identified deviation;
- identify a satisfactory, representative number from all interviews done during this time period. See http://guidebook.dcma.mil/226/tools_links_file/stat-sample.htm where this type of sampling plan is provided:

Total # of Donor Records	# of Donor Records to Review
2 – 150	13
151 – 280	20
281 – 500	29

An additional reference for developing an acceptance sampling system is the American National Standards Sampling Procedures and Tables for Inspection by Attributes (ANSI/ASQ Z1.4-2008).

- the number of interviews each interviewer has completed during this established time and sample each person;
- frequency and sample size may need to be increased when there have been any changes in the SOP or DRAI form, or when a deviation has been identified; and
- interviewers that are newly authorized may require more frequent sampling at onset of performing these activities.

Determination of a sampling plan (schedule) must be documented and the rationale justified. The sampling plan should be robust and as data and experience is gathered, a step-wise adjustment in the sampling frequency may be justified.

Note: An audio recording of the DRAI is not required. . When an audio recording is used as a quality assurance tool, its retention status should be defined in policy and in your written agreement/contract. If an audio recording is utilized to make the donor eligibility determination, it is considered to be a relevant medical record and retained accordingly.

Considerations for **external** process sampling may include the components described above for an internal process. For example, the frequency of the audit and sample size may be modified to reflect the length of time since last audit, availability of recordings, as well as previous audit findings (this includes deviations).

D. Audit

A robust audit program should be designed to periodically assess the ongoing effectiveness of several areas of activity related to the DRAI process. Audit results will provide information on the adequacy of SOPs from the perspective of meeting external requirements (regulations or accrediting body standards). Audits also check internal processes such as compliance with SOPs, quality control, training activities, and competency assessments.

Audits are performed on a planned basis and their frequency is usually determined as part of an overall, internal audit program. Audits include all aspects of the DRAI process. They are typically performed at least once per year by someone not directly involved in the process. The results of past audits as well as the current state of compliance should be considered in determining the need to increase the frequency of audits to ensure the stability of the program.

Audits may include random observations of actual conducted interviews and/or the review of audio recordings of interviews in comparison with the concurrent record. See ‘III. C. 1. Sampling Plan’ above. Consideration should also be given to ensure that the audit program ensures that each interviewer is included. Findings from these audit activities, indicating evidence of compliance or the need for correction, must be documented to demonstrate adequate review and reflect the scope of the audit activity. The quality assurance audit process is not intended to replace quality control activities.

1. Examples

- Upon reviewing an audio recording of the DRAI, it is determined that the interviewer failed to ask the interviewee, “In the past 5 years has the donor had sex in exchange for money or drugs?” The interviewer documented a “no” response to this question on the written DRAI and the tissue was ultimately distributed for transplantation.
 - In this instance, in the absence of other information addressing such high risk behavior, the donor determination was incomplete. The tissue bank that released the tissue would submit an HCT/P Deviation Report to FDA, providing a synopsis of the occurrence, detailing the root cause, and delineating corrective actions to be performed. Corrective actions could include: contacting the interviewee again to ask the question, *recall* of the tissue, -re-training the interviewer, and an audit of other past interviews performed by the interviewer. Reporting to state agencies and accrediting bodies may also need to occur, as applicable.
- Upon reviewing an audio recording of the DRAI, it is determined that the interviewer inappropriately paraphrased a question. For example, the tissue bank’s DRAI includes the question, “Was the donor or any of his/her blood relatives diagnosed with or been told they were at risk for Creutzfeldt-Jakob Disease or variant Creutzfeldt-Jakob Disease?” The interviewer actually asked the interviewee, “Did the donor ever have mad cow disease?” The interviewer documented a “no” response to this question on the DRAI and the tissue was ultimately distributed for transplantation.
 - FDA guidance states that if the person interviewed “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." In this instance, the interviewer did not first ask about "Creutzfeldt-Jakob Disease" or "variant Creutzfeldt-Jakob Disease" and did not ask about the donor's blood relatives, so this risk was not assessed as required. The tissue bank that released the tissue would submit an HCT/P Deviation Report to FDA, providing a synopsis of the occurrence, detailing the root cause, and delineating corrective actions to be performed. Corrective actions could include: contacting the interviewee again to ask the question, *recall* of the tissue, re-training the interviewer, and an audit of other past interviews performed by the interviewer. Reporting to state agencies and accrediting bodies may also need to occur, as applicable.

- While observing the interview process in real time, it is determined that the interviewer omitted part of a question. For example, the tissue bank's DRAI includes the question, "Has the donor ever used a needle to inject drugs into his/her veins, muscles, or under the skin for non-medical use?" The interviewer actually asked the question, "Has the donor ever used a needle to inject drugs?" The interviewer documented a "no" response to this question on the DRAI and the tissue was ultimately distributed for transplantation.
 - In this instance, the essence of the question was actually asked. It can be argued that the question that was asked was actually more inclusive than the question on the DRAI. For example, if the donor ever injected drugs for a medical purpose, that would be captured in this question. Moreover, the question asked simply queries if the donor ever used a needle to inject drugs, so a negative response would rule out needing to determine the route. If the interviewee provided a "yes" response, then further clarification would be needed. The interviewer provided a "no" response" so no reporting to any regulatory agency or accrediting body would be necessary. For this example, documentation justifying this decision should be maintained in donor records and shared if applicable. Corrective action necessitates re-training the interviewer and possibly performing an audit of other past interviews performed by the interviewer.
- Upon reviewing an audio recording of the DRAI and comparing it to the DRAI record, it is determined that the interviewer failed to accurately document the interviewee's actual response. For example, the tissue bank's DRAI includes the question, "Did the donor drink alcohol?" The interviewee reported that the donor drank 4 beers each night, but the interviewer documented the response as "no." The tissue was ultimately distributed for transplantation.
 - In this instance, given that the additional medical information does not indicate an increased risk for a relevant communicable disease agent or disease, no HCT/P Deviation Report need be submitted. However, the tissue bank releasing the tissue should document justification why the error is not relevant to disease transmission. The tissue bank would still need to document its findings in their QA report and treat it as a deviation, along with any corrective action(s) it deems necessary, such as re-training the interviewer and possibly performing an audit of other past interviews performed by the interviewer.

Note: Corrected DRAI records need to be shared appropriately, and without delay, with all tissue banks involved with recovery of tissue, or receipt of tissue, from the donor.

E. Corrective and Preventive Action

Quality assurance should also include documented investigations, corrective actions and effectiveness checks when deviations from SOP, regulations, or standards related to the DRAI process are identified. Deviations can be identified:

- during quality control activities;
- as the result of audits or inspections; and
- via feedback from entities with whom the documented record has been shared.

An effective corrective action plan should address immediate action to be taken to rectify the deviation and consider process improvement to prevent recurrence. Effectiveness checks should be performed to confirm that corrective actions have been effective in eliminating the root cause of the deviation. In addition, if a deviation is seen during routine quality control sampling or audit, the sample size may be increased until the corrective action is deemed effective.

The scale and scope of a corrective action plan will depend on factors such as severity and extent of deviation. Severity is best considered from the perspective of the use of the DRAI information in determining final donor eligibility. Extent may be a factor of multiple interviewers and/or length of time the deviations have been identified as occurring.

If quality control activities are performed in a timely manner as described above, the length of time and extent of the deviation is likely to be limited. It may be necessary to prioritize aspects of the investigation based on the risk posed. Risks include inappropriate donor eligibility determination, potential for communicable disease transmission, and/or *recall* of tissue grafts. If the deviation is determined to be extensive, additional resources may be necessary to complete the plan in a timely manner.

Examples of corrective action activities (*resolutions*) may include:

- Notifying without delay all tissue banks that have received the DRAI and reaching agreement on any necessary follow-up actions (e.g., providing frequent updates as action plans are implemented, sharing additional or corrected information, etc.).
- Identifying the need to re-contact interviewees if the intent of the DRAI was not met, or if information provided by the interviewee appears to have been misunderstood or incorrectly recorded by the interviewer.
- Development of a plan to re-contact the interviewee(s) or obtain missing information. Plans should include actions to be taken if there is difficulty locating the person or if she/he is unable or unwilling to assist in clarifying or providing information. If initial attempts to correct or clarify information are unsuccessful, other viable options include:

an inquiry with the primary care physician of the donor; locating another knowledgeable person; or, the use of a private investigator to locate the original interviewee.

- Evaluating existing processes to identify the root cause of a deviation. Training and retraining is often identified as a root cause and/or corrective action and care should be taken to assure that if retraining is determined to be the appropriate corrective action, effectiveness checks are performed and confirm that this was root cause rather than the underlying SOP or process.
- While every effort should be made to obtain information required from the DRAI, in the event it is not possible, a risk assessment should be performed for each case. This risk assessment should be completed in collaboration with the tissue processor(s) that determines donor eligibility. A careful review of additional records may provide missing, or clarify questionable, information.
- When a deviation is discovered, an investigation must be performed to determine the scope of the problem. Depending on the circumstances/results of the investigation, a planned audit of other interviews performed by that interviewer may be indicated.

1. Timely Notification

Timely notification is critical. When tissue associated with a deviation related to the DRAI have been distributed for transplant, the tissue processor has a time frame of no more than 45 (forty-five) days to report the incident to FDA under HCT/P Biological Product Deviation reporting requirements. Actions required prior to submission of this report include obtaining additional information and performing a health hazard (risk) assessment. If it is not possible to resolve or address the deviation and the associated risks, further actions may be necessary (e.g., disposition of the tissue remaining in quarantine or inventory, a recall may be indicated for tissues that were already distributed for transplant).

IV. Appendix

A. Federal Expectations [4, 5, 6, 7] and Summary

Subpart C - Donor Eligibility Final Rule

§ 1271.3 How does FDA define important terms in this part?

(n) *Donor medical history interview*

(s) *Relevant medical records*

§ 1271.50 How do I determine whether a donor is eligible?

(a) *Determination based on screening and testing.*

(b) *Eligible donor.*

§ 1271.55 What records must accompany an HCT/P after the donor-eligibility determination is complete; and what records must I retain?

(a) *Accompanying records.*

(b) *Summary of records.*

- (d) *Record retention requirements*
- § 1271.75 How do I screen a donor?
 - (a) *All donors.*
 - (d) *Ineligible donors.*

HCT/P Donor Eligibility Final Guidance

IV. DONOR SCREENING (§ 1271.75)

- C. What sources of information do I review?
- E. What risk factors or conditions do I look for when screening a donor?

Subpart D – Current Good Tissue Practice Final Rule

§ 1271.150 Current good tissue practice requirements.

- (a) *General.*
- (b) *Core CGTP requirements.*
- (c) *Compliance with applicable requirements*
 - (1) *Manufacturing arrangements*

§ 1271.160 Establishment and maintenance of a quality program.

- (a) *General.*
- (b) *Audits.*

§ 1271.170 Personnel.

- (a) *General.*
- (b) *Competent performance of functions.*
- (c) *Training.*

§ 1271.180 Procedures.

- (a) *General.*
- (b) *Review and approval.*
- (c) *Availability.*
- (d) *Standard procedures.*

§ 1271.270 Records.

- (a) *General.*
- (b) *Records management system.*
- (c) *Methods of retention.*
- (d) *Length of retention.*
- (e) *Contracts and agreements.*

Current Good Tissue Practice Final Guidance

III. CGTP REQUIREMENTS (§ 1271.150)

- C. How Do I Ensure that Another Establishment with Which I Have a Contract, Agreement or Other Arrangement Complies with CGTP Requirements?
- D. What Steps Should I Take if I Become Aware and Then Determine that the Establishment Performing Any Step in Manufacture for Me is No Longer in Compliance with Part 1271?

V. ESTABLISHMENT AND MAINTENANCE OF A QUALITY PROGRAM (§ 1271.160)

- A. What is a Quality Program?
- B. Which Establishments Must Establish and Maintain a Quality Program?

- C. What is the Role of the Quality Program Regarding Procedures?
- D. What Must I Do When Information is Received From Sources Outside the Establishment, and What Must I Do with this Information?
- E. With Whom Must an Establishment Share Information Pertaining to the Possible Contamination of or Potential for Transmission of Communicable Disease by an HCT/P?
- F. How Can a Quality Program Ensure that Appropriate Corrective Actions Related to Core CGTP Requirements Are Taken, When Necessary?
- G. What Must the Quality Program Ensure Regarding Personnel?
- H. How Does the Quality Program Ensure that Appropriate Monitoring Systems Are in Place?
- I. When HCT/P Deviations Occur, What is the Role of the Quality Program?
- J. What Are the Requirements for Performing Quality Audits of Your Establishment?
- K. Will FDA Review the Quality Audit During Inspection of the Establishment?

VI. PERSONNEL (§ 1271.170)

- A. What Are the Specific Requirements for Personnel at HCT/P Establishments?
- B. How Would I Ensure that Personnel Have the Necessary Education, Experience and Training to Perform Their Job?

VII. PROCEDURES (§ 1271.180)

- C. May I Use Procedures From Established Industry Standards?

XII. RECOVERY (§ 1271.215)

- B. What Are Some Ways that a Recovery Establishment Could Ensure that HCT/Ps Are Recovered in a Way That Does Not Cause Contamination or Cross-Contamination During Recovery, or Otherwise Increase the Risk of the Introduction, Transmission, or Spread of Communicable Disease?
- D. What Are Ways in Which a Processor Receiving HCT/Ps From a Recovery Establishment Under Contract with the Processor Could Verify the Identity of the Donor and Could Ensure That the Donor Records Are From the Same Donor as the HCT/Ps?

XIX. RECORDS (§ 1271.270)

- A. What are the General Requirements for Records?
- B. What Kind of Records Management System Must I Have?
- C. What Are Acceptable Methods of Record Retention?
- D. For How Long Must I Retain my HCT/P Manufacturing Records?
- E. What Records of Contracts and Agreements Must I Maintain?

In summary, regulatory requirements include:

- Tissue donors must be screened for relevant communicable disease and disease agents (RCDADs) and a donor must be determined ineligible who is identified as having a risk factor for, or clinical evidence of, any RCDAD (HIV types 1 & 2, HBV, HCV, human TSEs, *T. pallidum* (syphilis), WNV, vaccinia, sepsis, and risk associated with xenotransplantation).
- Donor eligibility determinations, including donor screening, are considered “core CGTP” requirements and includes contracts, agreements or other arrangements with parties that

perform these functions on behalf of a tissue establishment.

- A quality program must be in place that addresses all core CGTP requirements. Expected functions that must be covered:
 - Establishing and maintaining appropriate procedures relating to core CGTP requirements, and ensuring compliance with respect to such procedures, including review, approval, and revision;
 - Ensuring that procedures exist for documenting information related to core CGTP requirements;
 - Ensuring that appropriate corrective actions relating to core CGTP requirements, including re-audits of activities where deviations have been identified, are taken and documented.
 - Verifying corrective actions to ensure actions taken have been effective and are in compliance with CGTP. Where appropriate, corrective actions must include both short-term action to address the immediate problem and long-term action to prevent the problem's recurrence.
 - Ensuring proper training and education of personnel involved in activities related to core CGTP requirements;
 - Establishing and maintaining appropriate monitoring systems as necessary to comply with requirements;
 - Investigating and documenting deviations (and trends) relating to core CGTP requirements. Each investigation must include a review and evaluation of the deviation, efforts made to determine the cause, and the implementation of corrective action(s) to prevent recurrence.

- A quality audit of activities related to core CGTP requirements must be periodically performed for review by management.

- An establishment that performs functions on your behalf must have a quality program that addresses these operations, and it's expected that periodic compliance audits of the establishment are performed. During the audit, you should consider reviewing a representative sample of the donor medical history interview records that were previously provided by the recovery establishment to confirm their accuracy by checking with the source of the information.

- A recommendation is that contracts, agreements or other arrangements describe the responsibilities of all parties. When donor eligibility is determined following a review of records obtained by another establishment, the contract, agreement or other arrangement should specifically identify what records will be obtained, in what format they will be provided, responsibilities for record retention and access, and if the reviewing firm will convey donor eligibility conclusions back to the firm that collected the information.

- Regarding personnel, a sufficient number to ensure compliance with requirements is expected; they must have the necessary education, experience, and training to ensure competent performance of their assigned functions; they can perform only those activities for which they are *qualified* and authorized; and all personnel must be trained, and

retrained as necessary, so they perform their assigned responsibilities adequately.

- Procedures must be established and maintained to meet core CGTP requirements for related steps that the tissue establishment personnel perform. You must design these procedures to prevent circumstances that increase the risk of the introduction, transmission, or spread of communicable disease.
- Before implementation of procedures, a responsible person must review and approve them, and procedures must be readily accessible to personnel in the area where the operations to which they relate are performed.
- A “donor medical history interview” must be obtained and it is considered a “relevant medical record.”
- A review of “relevant medical records” must occur. When review of the donor medical history interview is performed you should make inquiries when circumstances indicate that follow-up information might be relevant.
- SOPs must be established and maintained to assure review of relevant medical records is properly conducted.
- SOPs must ensure records, such as the donor medical history interview, are current, complete and reliable as well as accurate, indelible, and legible.
- Records must be maintained concurrently with the performance of each required step and must be as detailed as necessary to provide a complete history of the work performed. Any requirement where an action can be documented involves the creation of a record, which is subject to the requirements for records.
- If other records are “available” and they can include information pertaining to risk factors for relevant communicable disease (e.g., social behavior, treatments), you should make inquiries to obtain all relevant information.
- “Available” means that a record or information exists, or is pending, and can be obtained through due diligence, within a reasonable amount of time. A “reasonable” amount of time is a period of time that would allow for the collection of important information without compromising the utility of the tissue.
- The initial tissue establishment that performed the donor medical history interview should document the findings. The establishment that makes the HCT/P available for distribution should review the records of the findings to make sure that all release criteria (including donor eligibility) were met, and would retain the documented findings.
- You must establish and maintain a records management system. Records must be maintained in such a way as to facilitate review of the HCT/Ps history before making tissue allografts available for distribution. The regulations do not specify the details of a

records management system, but you should organize your records in a useful manner in accordance with the requirements in this section. The recovery establishment must maintain copies of all transferred records and organize them in its records management system.

- You may retain required records as original paper records, or as true copies such as photocopies, microfiche, or microfilm. Equipment that is necessary to make the records available and legible, such as computer and reader equipment, must be readily available. Records stored in electronic systems must be backed up.
- Records must be retained for 10 years after their creation, or at least 10 years after the date of administration of an HCT/P, or if the date of administration is not known, then at least 10 years after the date of the HCT/P's distribution, disposition, or expiration, whichever is latest.
- A list of the responsibilities of any establishment that performs a manufacturing step for you should be maintained and this should ensure that responsibilities are understood. For-cause and random comparisons of documentation should be performed.
- If non-compliance by a contractor is discovered, you must take reasonable steps to ensure the establishment develops a corrective action plan and you should review the plan and verify that corrective actions have been taken under the establishment's quality program.

V. References

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Minimizing the Risk of Disease Transmission During Corneal Tissue Processing

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Abstract: Corneal transplantation is undergoing significant change because the dysfunctional portion of the cornea may now be selectively transplanted. After recovery of corneoscleral tissue, further processing of such tissue as in microkeratome preparation of endothelial keratoplasty lenticules is defined as “open-container processing” by the Eye Bank Association of America. Airborne bacterial contamination during preparation of corneal tissue is a potential source of postoperative infection. This review addresses ways to minimize the risk of disease transmission as corneal tissue is processed for lamellar keratoplasty, endothelial keratoplasty, or femtosecond laser–assisted penetrating keratoplasty and to minimize risk to eye bank personnel or physicians preparing the tissue. Secondly, quality assurance measures are described that qualify the environment in which corneal tissue is being processed. We propose that the environment in which corneal tissue is being processed must be able to demonstrate acceptable levels of airborne microbial contamination annually as measured by settle plates to estimate airborne bacterial sedimentation. It is recommended that any environment where corneal tissue is prepared should meet the minimum standard of a conventional operating room which is <25 colony-forming unit per 90-mm settle plate per 1-hour exposure.

Key Words: cornea transplant, endothelial keratoplasty, airborne bacterial contamination, settle plates

(*Cornea* 2009;28:481–484)

Corneal transplantation is undergoing remarkable change because the dysfunctional portion of the cornea may now be selectively transplanted. Deep anterior lamellar keratoplasty replaces dysfunctional stroma in patients with stromal

dystrophies, thinning, or scarring.¹ Endothelial keratoplasty selectively transplants the dysfunctional posterior cornea while maintaining the structural integrity of the eye, resulting in rapid visual recovery with minimal refractive changes.² The femtosecond laser is also being used to prepare donor and recipient corneas for penetrating keratoplasty using incisional patterns previously unavailable to the surgeon, that may allow for more rapid and improved wound healing, less astigmatism, and better initial incision integrity.^{3–5}

Initially, human donor corneas intended for endothelial keratoplasty were stored in the eye bank as a corneoscleral rim until prepared for endothelial keratoplasty by the surgeon in the operating room. However, endothelial keratoplasty lenticules may now be prepared by eye bank personnel using a manual microkeratome that has made this procedure available to many more corneal surgeons.⁶

Endothelial keratoplasty lenticules may also be prepared by the femtosecond laser. Tissue so treated has been investigated and found to be just as effective as manual microkeratome pre-cut tissue in preserving endothelial cell density.⁷ The femtosecond laser may also be used to prepare stromal lenticules for use in lamellar keratoplasty.

The Eye Bank Association of America (EBAA) through its Medical Advisory Board has established standards “to assure consistently acceptable levels of quality, proficiency, and ethics in dealing with eye tissue for transplantation and to define the minimum standards of practice in the recovery, preservation, storage, and distribution of eye tissue for transplantation and research.”⁸ After recovery of corneoscleral tissue and placement into an appropriate preservation medium, further processing of such tissue as in microkeratome preparation of endothelial keratoplasty lenticules is defined as “open-container processing” by the EBAA.⁸ This review addresses ways to minimize the risk of disease transmission as corneal tissue is processed for lamellar keratoplasty, endothelial keratoplasty, or femtosecond laser–assisted penetrating keratoplasty and to minimize risk to eye bank personnel or physicians preparing the tissue. Secondly, quality assurance measures are described that qualify the environment in which corneal tissue is being processed.

One important consideration is the facility in which corneal tissue is being processed. In the United States of America, many states require adherence to the American Institute of Architects document “Guidelines for Design and Construction of Health Care Facilities” during facility construction, expansion, or renovation.⁹ Ventilation requirements

Received for publication August 7, 2008; revision received March 11, 2009; accepted October 6, 2008.

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The members of the Policy and Position Research Subcommittee of the Medical Advisory Board of the Eye Bank Association of America are listed in Appendix 1.

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for areas affecting patient care including operating rooms, laser eye rooms, or procedure rooms require a minimum of 15 air changes per hour, of which 3 air changes must be outside air. Two filter banks are required: the first being a MERV (Minimal Efficiency Rating Value) 8 filter and the second a MERV 14 filter. Humidity is to be maintained between 30% and 60%, and temperature should be maintained between 70 and 75°F (21–24°C). Airflow supply and exhaust shall be controlled to ensure general movement of air from “clean” to “less clean” areas. Surface requirements, such as for countertops, include ease of maintenance, nonporous, unable to support microbial growth, nonflammable, durable, and nontoxic.⁹

Operating rooms are considered cleanrooms in which the concentration of airborne particles is controlled and which are constructed and used to minimize the introduction, generation, and retention of particles inside the room. Cleanrooms with more strict requirements than operating rooms are used for nanofabrication and compound semiconductor device preparation. Airborne particulate cleanliness is designated by a classification number established by the International Organization for Standardization (ISO) Standard 14644-1 (Table 1). This ISO Classification replaces Federal Standard 209E that was canceled by the US General Services Administration on November 29, 2001. The main differences between Federal Standard 209E and ISO 14644-1 are that ISO establishes 0.1 μm as the “standard” diameter and creates 3 new cleanliness classes. For example, Class 100 (Federal Standard 209E) has been replaced by ISO Class 5 (Table 2).

Surgical site infection is a major complication after surgery. Microbial contamination of the surgical site is a necessary precursor for infection. For most surgical site infections, the source of pathogens is the endogenous flora of the patient’s skin, mucous membranes, or hollow viscera. Using DNA probes, Speaker et al¹⁰ demonstrated that the patient’s own eyelid flora was causative in cases of endophthalmitis after cataract surgery. In contrast, in an operating room where prosthetic replacement arthroplasties are performed, it has been well established that the level of

airborne bacterial contamination correlates with the incidence of postoperative wound infection.^{11–14}

Most conventional operating rooms are ventilated with 20–25 changes per hour of high efficiency filtered air delivered in a vertical flow.¹⁵ High efficiency particulate air systems remove bacteria and particles measuring 0.5–5 μm to obtain downstream bacteria-free air. The operating room is under positive pressure in relation to the surrounding corridors to minimize inflow of air into the room.¹⁶

In total joint replacement surgery, ultraclean (laminar flow) operating room air has been shown to reduce the rate of infection.^{11–13} Laminar flow systems deliver high efficiency particulate air–filtered unidirectional airflow at a uniform velocity (0.3–0.5 $\mu\text{m}/\text{s}$) to prevent retrograde air movements and obtain a dilution effect.¹⁶ Although the air may be relatively free of particulates when blown into the operating room, the number of biologic particles circulating around the room is nearly in direct proportion to the movement of people in the room.^{11,17,18} The level of airborne bacterial contamination in the operating room is predominantly caused by contaminated skin scales from the surgical team^{11–13,17,19} and can be reduced by limiting the traffic and controlling the activity and the number of operating room personnel.^{18,19} When airborne bacterial contamination was assessed in laminar airflow operating rooms, Friberg et al¹¹ demonstrated that normal skin flora only was cultured on settle plates. Flora was dominated by coagulase-negative *Staphylococci* in addition to *Micrococcus* and *Corynebacterium* species.¹¹

In corneal transplantation procedures, the potential sources of a postoperative infection could be the donor cornea, the recipient’s endogenous flora, or could be introduced by airborne bacterial contamination during preparation of corneal tissue. The EBAA Medical Standards⁸ require aseptic technique during recovery of corneal tissue and contact of povidone–iodine solution with the surface of any ocular tissue intended for transplantation. An appropriate corneal storage medium that has been manufactured in accordance with Food and Drug Administration Good Manufacturing Practices is also required. Corneal storage media currently available contain antibiotics in the media. The use of 5%

TABLE 1. Airborne Particulate Cleanliness Classes

Class	No. Particles Per Cubic Meter by Micrometer Size					
	0.1 μm	0.2 μm	0.3 μm	0.5 μm	1 μm	5 μm
ISO 1	10	2	—	—	—	—
ISO 2	100	24	10	4	—	—
ISO 3	1000	237	102	35	8	—
ISO 4	10,000	2370	1020	352	83	—
ISO 5	100,000	23,700	10,200	3520	832	29
ISO 6	1,000,000	237,000	102,000	35,200	8320	293
ISO 7	—	—	—	352,000	83,200	2930
ISO 8	—	—	—	3,520,000	832,000	29,300
ISO 9	—	—	—	35,200,000	8,320,000	293,000

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TABLE 2. Comparing Federal Standard 209E With the ISO 14644-1

Airborne Particulate Cleanliness Class Comparison		
ISO 14644-1 ISO Class	FED STD 209E	
	English Metrics	
1	—	—
2	—	—
3	1	M1.5
4	10	M2.5
5	100	M3.5
6	1000	M4.5
7	10,000	M5.5
8	100,000	M6.5
9	—	—

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povidone-iodine solution in preparation of the recipient eye for corneal surgery is universally recommended.^{20,21}

According to the UK National Health Service, in conventional operating rooms during surgical procedures, the number of airborne bacterial colony-forming units (CFU) should not exceed 180 per cubic meter.²² The most realistic indicator of airborne bacterial contamination in areas critical for surgery is the use of sedimentation plates (passive sampling) that represent a technically easier method than air sampling (active sampling).^{14,23} Referring to the European Commission Good Manufacturing Practice correlation between active and passive sampling, the 180 CFU/m³ value roughly corresponds to 25 CFU after 1-hour exposure on settle plates 90 mm in diameter.²⁴

However, the National Health Service²² recommends that ultraclean (laminar flow) operating room air sampled close to the wound during orthopedic implant surgery should contain <10 CFU/m³ (196 CFU/m²/hr) that corresponds to 1.25 CFU on settle plates 90 mm in diameter after 1-hour exposure. For ultraclean operating room air, Friberg et al¹⁴ have suggested a maximum value of 350 CFU/m²/hr, which corresponds to approximately 2.5 CFU on settle plates 90 mm in diameter per 1-hour exposure. Pasquarella et al¹³ have suggested a maximum value of 786 CFU/m²/hr, which corresponds to 5 CFU on settle plates 90 mm in diameter per 1-hour exposure. Published recommended levels of airborne bacterial contamination for ultraclean air measured passively range from 1.25 to 5 CFU on settle plates 90 mm in diameter exposed for 1 hour.^{12,13,14} Recommended levels of airborne bacterial contamination for conventional operating rooms measured passively are 25 CFU on settle plates 90 mm in diameter exposed for 1 hour.²²

Friberg et al¹⁴ have proposed that the “use of sedimentation plates to assess operating room standard is both a convenient and relevant method that can be recommended

for more extensive application, for example, in quality control programs.” We propose that the environment in which corneal tissue is being processed (an operating room, an eye bank procedure room, a laser suite, or a femtosecond laser laboratory) must be able to demonstrate acceptable levels of airborne microbial contamination annually as measured by settle plates to estimate airborne bacterial sedimentation. It is recommended that any environment where corneal tissue is prepared should meet the minimum standard of a conventional operating room, which is <25 CFU per 90 mm settle plate per 1-hour exposure.²² The judicious use of periocular antibiotics that can achieve high concentrations after corneal surgery²⁵ makes the standard for ultraclean air during corneal tissue preparation unwarranted. A quality assurance program to monitor compliance shall be instituted by each eye bank preparing corneal tissue.

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APPENDIX 1.

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IMPLEMENTATION GUIDE

Use of ISBT 128 in North American Eye Banks

Version 1.4.0

November 2016

Tracking Number ICCBBA IG-040



Published by:
ICCBBA

PO Box 11309, San Bernardino, CA 92423-1309 USA

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1 Introduction

1.1 Purpose

The purpose of this document is to provide guidance to North American and other eye banks accredited by the Eye Bank Association of America (EBAA) in the implementation of ISBT 128. It is a joint document of the EBAA and ICCBBA.

1.2 Scope

This document is a supplement to the *ISBT 128 Standard Technical Specification* (ST-001), the *ISBT 128 Standard Labeling of Ocular Tissue* (ST-009), and the *Implementation Guide: Use of Product Code [Data Structure 003] for Ocular Tissue* (IG-032). It provides specific guidance for North American eye banks as they implement ISBT 128 and takes the requirements of the Eye Bank Association of America (EBAA) into consideration. This document also addresses concerns for software developers.

This document will discuss implementation of ISBT 128 following both the EBAA Medical Standards and the ISBT 128 Standard.

1.3 Intended Audience

The intended audience of this document is staff (management, information technology, quality, validation, procurement, laboratory, and processing) at North American eye banks, as well as eye banks accredited by the EBAA in other regions; transplant centers; software developers and label/software vendors that provide products to eye banks and transplant centers.

1.4 Normative References

Eye Bank Association of America Medical Standards (October 2014)

ISO/IEC 16022:2006(E): Information technology—International symbology specification—Data Matrix (and correction ISO/IEC 16022:2006/Cor 1:2008)

ISBT 128 Standard Technical Specification (ST-001)

ISBT 128 Standard Terminology for Medical Products of Human Origin (ST-002)

ISBT 128 Standard Labeling of Ocular Tissue (ST-009)

1.5 Other Reference

ICCBBA Website (www.iccbba.org)

Implementation Guide: Use of Product Code [Data Structure 003] for Ocular Tissue (IG-032)

Implementation Guide: Use of Data Matrix Symbols with ISBT 128 (IG-014)

Implementation Guide: Use of the Donation Identification Number [Data Structure 001] (IG-033)

1.6 Background

There is wide recognition of the need to standardize the terminology, coding, and labeling of medical products of human origin (MPHO) in order to improve traceability and transparency. The 2010 World Health Assembly Resolution WHA63.22 called on member states to “encourage the implementation of globally consistent coding systems for human cells, tissues and organs as such in order to facilitate national and international traceability of materials of human origin for transplantation.” ICCBBA is working with WHO in order to achieve this objective using the ISBT 128 Information Standard. On its website (http://www.who.int/transplantation/tra_isbt/en/), WHO describes ISBT 128 as the sole global standard for the identification and coding of MPHO.

Many countries around the world use ISBT 128 for blood and there is a steady global movement toward implementation of ISBT 128 for cells, tissues, and other MPHO. The use of ISBT 128 for tissues began in the United Kingdom more than a decade ago and has since expanded to a number of other countries in Europe and North America. The Eye Bank for Sight Restoration in New York City was among the first eye banks to implement ISBT 128 in 2014. Since then, many eye banks have implemented ISBT 128, or are in the process of implementing it.

The Eye Bank Association of America has requirements in their standards for the use of ISBT 128. These include:

- Eye banks were required to use ISBT 128 DINs and standardized product codes by January 1, 2016.
- Internationally shipped products must be bar coded using ISBT 128 data structures by January 1, 2017.

1.7 Changes in this Version

The following table indicates the major changes between Version 1.3.0 and Version 1.4.0. Actual changes or additions to requirements of the ISBT 128 Standard are in bold print; changes to formatting or organization, or additional guidance, are in regular print. When changes were a result of a formal proposal, the number of the proposal is listed in the Rationale column.

Use of ISBT 128 in North American Eye Banks, Version Control: Version 1.3.0 versus Version 1.4.0

	Version 1.3.0	Version 1.4.0	Change	Rationale
	Chapter, Section, Table, or Figure	Chapter, Section, Table, or Figure		
1.	1.6	1.6	Updated the information in this section.	This information included dates, some of which have passed.
2.	New Information	3.2	Added Data Structure 002	This was added to support encoding of special messages such as Quarantine/hold for further testing or processing
3.	New Information	3.6.2	Added two new types of time encoded within Flexible Date and Time [Data Structure 031]	Time of Preservation and Time of Donor Death were added at the request of eye banks.
4.	New Information	4.3.2, Table 3	Added the Attribute group Ocular Tissue, Non-Clinical	This is a new Attribute group.
5.	4.3.4	4.3.4	Changed the phrase "Additional Text" to "Text not associated with electronically-readable information."	This expression better describes the text.
6.	New Information	5.3	Added an example of an in-process label using Data Structure 002	This was added to provide clarity.
7.	New information	7.2	Added information about the order in which text should appear for Ocular Tissue, Non-Clinical	This is a new Class and Attribute group.

2 Getting Started: Registration with ICCBBA

2.1 Registration

Facilities wishing to use ISBT 128 must register with ICCBBA. Information about this process and a registration form may be found on the ICCBBA Website (<http://www.iccbba.org/registration-licensing>).

Once a facility is registered, it will be assigned a Facility Identification Number (FIN) that may be used with Donation Identification Numbers (DINs) and in the Processing Facility Information Code used to uniquely identify products.

There is flexibility in how eye banks with multiple sites may use FINs. Eye banks with multiple locations may opt to have a single FIN and manage the sequence number allocation across all of their locations centrally, or they may request multiple FINs with each facility controlling its own sequence number allocation.

- It is recommended that an organization with a single processing center, but multiple recovery locations, have a single Facility Identification Number (FIN).
- It is recommended that an organization with multiple processing centers request a different FIN for each location. While each location can have a different FIN, registration can be as a single organization or each location can register separately.

2.2 Use of Electronically-Readable Information

The EBAA standards will require that products shipped internationally have electronically-readable information (bar codes). While electronically-readable information is always desirable, it is not required for products that are only distributed within a country. Facilities that do not distribute products internationally may choose to follow only the sections of this guidance document that deal with text.

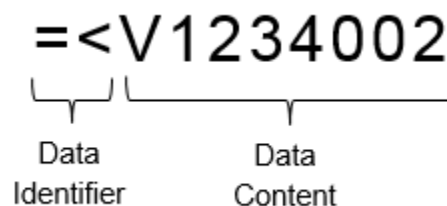
3 Data Structures Used to Label Ocular Tissue

Data structures are the means by which information about ocular tissues is put into computer-friendly codes. Data structures define the technical characteristics necessary for the interpretation of the information. They specify the context and structure and provide the links to the appropriate reference tables for conversion of codes into meaningful information.

Data structures comprise two elements:

- Data identifier: a two- or three-character code that identifies the data structure [described in more detail in the *ISBT 128 Standard Technical Specification (ST-001)*].
- Data content: the data characters that provide the information to be conveyed (e.g., coded information that conveys the product is a cornea).

Figure 1 Data Structure



ISBT 128 data structures are used in bar codes on labels of MPHO for electronic communication.

There are many ISBT 128 data structures and not all will be used in the labeling of ocular tissue. Data structures that are required for **traceability** include:

- Donation Identification Number [Data Structure 001]
- Product Code [Data Structure 003]

If the facility that assigns the Product Code is not the same as the facility that assigned the DIN, then an additional data structure is required for traceability:

- Processing Facility Information Code [Data Structure 033]

Because EBAA requires 2-D symbols (Data Matrix), eye bank computer systems must also be able to support:

- Compound Message [Data Structure 023]

Other data structures that may be useful to eye banks, but that are not essential to traceability, include:

- Blood Groups [ABO and RhD] [Data Structure 002] (for special messages that can be encoded in this data structure)
- Expiration Date and Time [Data Structure 005]

- Collection/Recovery Date and Time [Data Structure 007]
- Production Date and Time [Data Structure 009] (This data structure may be used to record the date and time of preservation.)
- Dimensions [Data Structure 029]
- Flexible Date and Time [Data Structure 031] (This data structure may be used to encode the date and time of preservation and/or the date and time of death.)

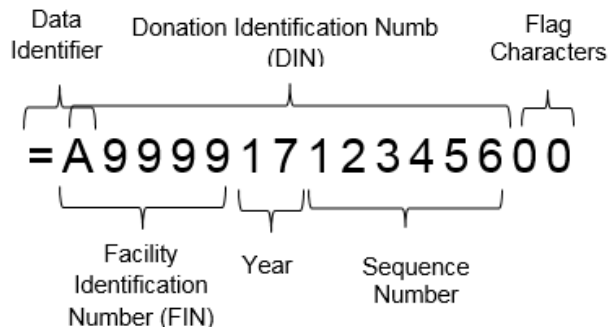
This chapter will include a high level description of the required data structures as well as other data structures that users may find useful in the labeling of ocular tissue. Specific details of coding are found in the *ISBT 128 Standard Technical Specification (ST-001)* Guidance on how and when to use these data structures appears later in this document and/or in one of the documents referenced in Section 1.5.

3.1 Donation Identification Number [Data Structure 001]

Data Structure 001 specifies a Donation Identification Number (DIN) that is a unique identification of a donation/recovery event from anywhere in the world over a one hundred year period.

This data structure is unique in that the second character of the data identifier also serves as the first character of the data content.

Figure 2 Donation Identification Number Data Structure



3.1.1 DIN

The DIN contains three elements.

- The first element, the Facility Identification Number (FIN), is assigned to a facility by ICCBBA and supports global uniqueness. In order to obtain a FIN, eye banks will need to register with ICCBBA. ICCBBA maintains a database of code assignments and this table is available to licensed users of the ISBT 128 system. It is called “Registered Facilities” and is found in a password-protected area of the ICCBBA Website (www.iccbba.org). The FIN within the DIN identifies the organization that assigned the DIN.
- The second element is a two-digit year and supports uniqueness for a 100-year period. This is a nominal year identifier and should not be used as an alternative to other date structures (such as collection date, expiration date, etc.). Its purpose is solely to support the requirement for 100 year uniqueness. The year code reflects the date of recovery. *Note: In practice, this is the “nominal” year. To cut down on wastage, DIN labels may be used for up to one month in the year before, and one month in the year after, the year shown on the label.*
- The third element is a sequence number assigned by the facility. The facility is responsible for ensuring the sequence number is unique to each recovery event for a given year and FIN.

Together, the three elements create global uniqueness for the DIN.

3.1.2 Flag Characters

Flag characters, used for process control, are also a part of this data structure although not a part of the DIN itself. These characters allow a facility to indicate where a bar coded DIN appeared (e.g., on the product, a sample test tube, or a donor record) and can be used to facilitate automated process control. These flag characters are optional and, if not needed, the flag value of "00" should be used. Systems receiving ISBT 128 labeled products should accept any valid final product flag characters. In the text presentation, flag characters are rotated clockwise by 90 degrees (see Figure 8 on page 25).

3.1.3 Check Character

Although not a part of the data structure (or the bar coded information), a check character is added to the end of the DIN to support verification of correct keyboard entry. This check character is calculated following MOD 37-2 within ISO/IEC 7064:2003(E). Whenever ISBT 128 DINs are printed in eye-readable format on a product label, the manual entry check character should appear to the right of the DIN and flag characters and enclosed in a box (see Figure, page 25). The check character may be any one of the thirty seven characters in the set (0-9, A-Z, asterisk). Care should therefore be taken to use a font which clearly distinguishes between similar characters (0 and O, I and 1 etc.). Where computer systems accept manual entry of a DIN, the check character should always be a required part of the entry and software should verify the character is correct.

See Implementation Guide: Use of the Donation Identification Number [Data Structure 001] (IG-033) for further information.

3.1.4 Options for Eye Banks

The DIN is assigned for each recovery event. Therefore, if cornea from both the right and left eyes are recovered, they will have the same DIN. Product Codes will be used to differentiate multiple products from the same recovery event.

3.1.4.1 When to Assign a DIN

As this guidance is focused on the use of ISBT 128 on final products, it does not directly address the point at which the ISBT 128 donation numbering is introduced. Two possible situations are identified for informational purposes, but no recommendation is made, as the most suitable option will vary according to the needs of the eye bank.

Assignment at Time of Recovery

Some eye banks may wish to assign the ISBT 128 DIN at the point of recovery. This could be done either by the eye bank allocating a DIN from their own range or by a recovery organization having its own FIN and DINs.

In all cases the assigned DIN should remain with the ocular tissue and appear on all final labeled products from that donation. If the facility that assigned the Product Code is different from the one that assigned the DIN, the identification of the processing facility [called the FIN(P) in 3.4)] shall be on the label.

It is a long term goal that DINs would be assigned at the time of recovery and be used from recovery to processing and transplant.

Assignment at Time of Processing

If existing numbering systems are used for the earlier part of the donation pathway, then the eye bank will assign the ISBT 128 DIN some time during processing before final labeling of the product. The eye bank is responsible for ensuring traceability between the ISBT 128 DIN and other identifiers.

3.1.4.2 Use of Existing Identifiers within a DIN

If a facility has an identifier that is numeric and has six or fewer characters, that identifier may be incorporated into the sequence number portion of the DIN for easier mapping between the two identifiers. Leading zeroes may be used for numbers with fewer than 6 characters. For example,

The FIN is A9999 and the existing identifier is 0238, then the DIN could be W9999 17 000238

or

if the FIN is A9999 and the existing identifier is 123456, then the DIN could be A9999 17 123456.

If the existing identifier includes other information such as year and a product code, it is not necessary to carry this information into the DIN since this information is present elsewhere in ISBT 128. For example, an existing identifier is 17-0003-200 where the 17 is the year of recovery, the 0003 is the sequence number assigned to the donor, and 200 is the code for a cornea, anterior and posterior layers, right. The year (17) is already captured in the DIN and the code for the product is captured in an ISBT 128 Product Description Code.

3.2 Blood Groups [ABO and RhD] [Data Structure 002]

While ocular tissue is not labeled with ABO and RhD, this data structure provides a means of encoding special messages such as quarantine status. For ocular tissue, Data Structure 002 shall convey special messages such as the status of a collection, restrictions on use, or processing instructions.

- gg** shall, for ocular tissue, specify a range of special messages as shown in Table 1
- r** shall be set to 0 (zero) indicating the data structure does not contain information about these red cell phenotypes
- e** shall be reserved for future use. The value of e shall always be set to 0 (zero)

Figure 3 Data Structure 002

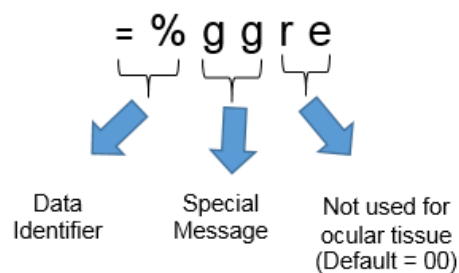


Table 1 Special Messages for Data Structure 002 (Excerpt of RT06)

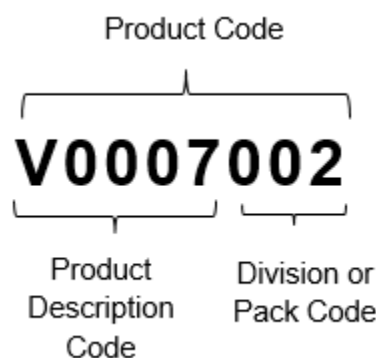
gg	Interpretation
Mb	Biohazardous
Md	Discard (to be destroyed)
Mq	Quarantine/hold for further testing or processing
Mr	For research use only

3.3 Product Code [Data Structure 003]

Data Structure 003 uniquely identifies a product intended for human use. The Product Code contains two elements:

- A 5-character Product Description Code (PDC) is assigned by ICCBBA to each product description. Products are described using terminology created by expert advisory groups such as EBTAG. These groups utilize a scheme of Classes (broad descriptions of product such as Cornea or Sclera) and Attributes (more detailed information such as storage solutions or pathogen reduction methods) to describe products. Each product is described minimally with a Class and may also have one or more Attributes. Detailed information on creating PDCs may be found in *Implementation Guide: Use of Product Code [Data Structure 003] – Ocular Tissues* (IG-032). A database, called the ISBT 128 Product Description Codes Database, lists all assigned codes and the corresponding product descriptions. The database is found in a password-protected area of the ICCBBA Website (www.iccbba.org) and is accessible by licensed users.
- For ocular tissues (PDCs beginning with the letter “V”), a 3-character Division (or Pack) Code allows each product with the same DIN and PDC to be uniquely identified. For example, if there are two products from the Sclera, both described as Right, Hypothermic storage, Part, not specified with the code V0007, from the same donor (A9999 15 123456), each will be uniquely identified using the Division (Pack) code (001 and 002). If there are not multiple packs with the same DIN and PDC, this code is set to 000. See Figure 4.

Figure 4 Product Code Data Structure for Ocular Tissue



A-D National or Local Codes

The block of PDCs A0000-D9999 has been reserved for use as nationally- or facility-defined PDCs. There shall be no international interpretation associated with these values.

These codes should ONLY be used where there is not an appropriate international code and there is good reason why an international code should not be allocated. For example, local codes should be used when a product is only produced in one or a very small number of facilities. If there is any uncertainty whether the code assigned to a product should be international or local/regional/national, the user should contact the ICCBBA office.

National agencies may reserve a range of these values for national assignment. **In the US, B7000 through B9999 have been reserved for national use. There are no nationally reserved codes for Canada at this time.**

Individual facilities may also assign codes for their own use provided that these do not conflict with codes assigned at the national level. Where such codes are used, the facility shall ensure that definitions are provided for use within their service region, and that products bearing such codes are not transferred outside their normal distribution network. Care shall be taken in interpreting the product description from a local code as this will be specific to the supplier.

In all cases, the product definition for nationally- or facility-assigned codes shall be retained permanently for traceability purposes. Once assigned, codes shall not be reassigned.

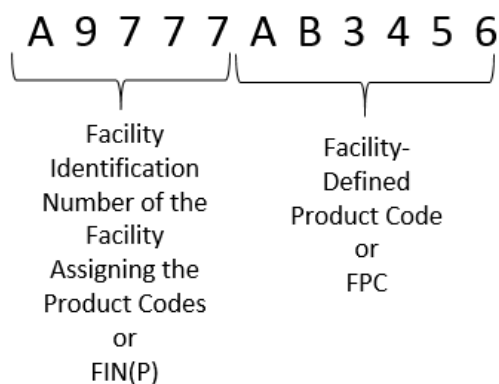
3.4 Processing Facility Information Code [Data Structure 033]

Data Structure 033 identifies the facility that assigned the Product Code (usually a processing facility). It is used when the facility that assigned the Product Code is not the same facility that assigned the DIN.

The Processing Facility Information Code contains two elements:

- A 5-character Facility Identification Code. While this is the same code as used within the first element of the DIN, it is abbreviated as FIN(P) to indicate it identifies the facility that assigned the Product Code. Information about obtaining a FIN(P), and the reference table for its interpretation, are the same as a FIN and are described in 3.1.1.
- A 6-character Facility-Defined Product Code. This code may be used to specify a catalog or other number that identifies the product within its system. The FPC shall not be used to create uniqueness for the product. The processing or labeling facility may choose to publish reference tables for use by the organizations receiving the product. If a value is not required, the default value 000000 (zeroes) shall be used.

Figure 5 Example of Data Content for Data Structure 033



3.5 Compound Message [Data Structure 023]

The compound message data structure allows multiple data structures to be combined into a single data string to be used in 2-D symbols and other newer technology delivery systems. Because EBAA has chosen to use 2-D symbols on the labels of ocular tissue shipped internationally, eye bank software must be able to code and decode information in this data structure.

Structure: =+aabbb

Element	Length	Type
=	1	data identifier, first character
+	1	data identifier, second character
aa	2	numeric {0–9}
bbb	3	numeric {0–9}

The five-character data content string **aabbb** shall be encoded and interpreted as follows:

aa shall specify the number of ISBT 128 data structures that follow;

bbb shall be either:

- all zeroes – indicating this is an undefined message, i.e. only the number of data structures is identified, but not what each one is
- a three-digit number referencing an entry in an ICCBBA maintained table that specifies the sequence of the data structures within a compound message. See Table W2, [RT017] ICCBBA-Specified Compound Messages described in the *ISBT 128 Standard Technical Specification (ST-001)*. The reference table is found on the ICCBBA Website.

Rules for constructing compound messages:

1. A compound message shall comprise a string of ISBT 128 data structures (excluding nationally-defined structures), beginning with the Compound Message [Data Structure 023].
2. Data structures shall be combined with no intervening characters and each data structure shall begin with its data identifier characters.
3. The string shall only contain ISBT 128 data structures (excluding nationally defined structures).
4. The number of data structures following the Compound Message Data Structure shall be indicated in element aa of the Compound Message Data Structure.

5. If the sequence of the message is unspecified, the Compound Message Data Structure shall have elements bbb set to zeroes and element aa shall be set as specified in Rule 4.
6. If an ICCBBA-specified sequence is used, the reference number of the selected message from Table RT017 shall be included in element bbb of the Compound Message Data Structure. The order of the data structures shall be that shown on Table RT017 for the reference number selected.

Reading software should be able to interpret both unspecified sequence and specified sequence compound messages. The software should always verify the integrity of the data string, including checking that the correct number of data structures appears and, when specified sequence messages are used, that the sequence of data structures is correct. Data should only be interpreted if the integrity of the relevant data structures has been confirmed.

A full list of specified sequence compound messages is found in Table W2, [RT017] ICCBBA-Specified Compound Messages on the ICCBBA Website. Requests for additional entries should be submitted to the ICCBBA office (tech.manager@iccbba.org).

3.6.2 Flexible Date and Time

As the use of ISBT 128 spread from blood to other MPO, it became clear that many more types of time (e.g., cross-clamp time, date/time of preservation, date/time of death) might be needed. Rather than create a different data structure for each type of time, a new data structure was created that supported not only multiple types of time, but also supported encoding Coordinated Universal Time (UTC).

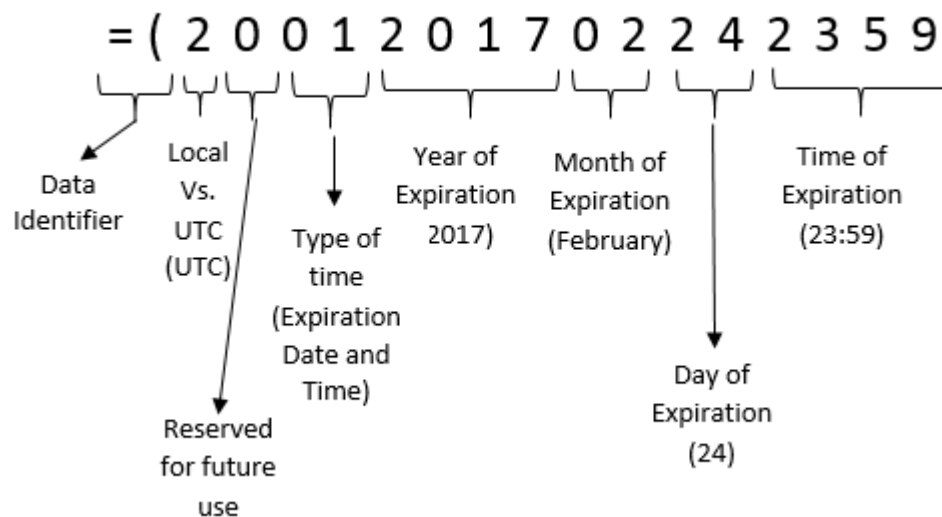
The first character of the data content indicates if the time is local (encoded as a 1) or UTC (encoded as a 2). The second character is reserved for future use. The third and fourth characters indicate the type of date and time (Expiration is 01, Collection/Recovery is 02, Production/Processing is 03, Cross Clamp is 04, Preservation is 05, and Death of Donor is 06). Additional types of time may be added for use with this data structure as they are needed.

See Figure 7.

Guidance for the use of this data structure is described within *Implementation Guide: Use of Flexible Date and Time [Data Structure 031]* (IG-024).

This data structure may be used in place of other date and time data structures or may be used when a specific type of date and time data structure does not exist (e.g., time of death).

Figure 7 Example of Flexible Date and Time [Data Structure 031]



4 Label Design

The following description applies to information required by the EBAA and the ISBT 128 Standard. It does not include all of the regulatory requirements for labeling. It is the responsibility of the eye bank to ensure regulatory and other standards requirements are met. Regulatory requirements take precedence over any guidance provided in this document.

The EBAA has decided to use 2-D symbols rather than linear bar codes. This section will therefore discuss only the use of 2-D symbols.

4.1 Information Requirements

4.1.1 ISBT 128 Label Requirements

The ISBT 128 label area must have a white background.

The minimum information content to ensure traceability shall be:

1. The electronically-readable DIN and Product Code [Product Description Code and Division Code (Pack) Code]
2. The eye-readable DIN, flag characters (rotated 90° clockwise) and the boxed manual entry check character
3. The text “Product Code:” and the eye-readable Product Code [Product Description Code and Division Code (Pack) Code]
4. The eye-readable description of the product (Class, and as space permits, Attributes)
5. The electronically- and eye-readable Facility Identification Number of the processing facility [the FIN(P)], if the facility that assigned the Product Code is different from the one that assigned the DIN.

Eye Banks that do not distribute tissue internationally are not required to use electronically-readable information on their labels. In this situation, item 1 and the requirement for electronically-readable information in item 5 (above) do not apply.

4.1.2 Additional EBAA Label Requirements

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 the source eye bank
2. ISBT 128 tissue identifier. The ISBT 128 tissue identifier includes the Donation Identification Number (DIN), Product Code, and Processing Facility Information Code (if applicable).
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. If the Product Code and Donation Identification Number are not assigned by the same entity, then the label must include the Processing Facility Identification Code [FIN(P)].
6. Expiration date of tissue, in the international format (YYYY-MM-DD).
7. A statement that the tissue is intended for single patient application only
8. A statement that the tissue is not to be considered sterile unless the tissue has been subjected to a validated process to ensure sterility.
9. Type of storage solution
10. ISBT 128 data structures within Data Matrix 2-D symbols on ocular tissue products distributed internationally effective January 2, 2017

Short and intermediate term preserved tissues:

- Date and time of donor's death (YYYY-MM-DD HH:MM)
- Date and time of initial corneal/scleral preservation (YYYY-MM-DD HH:MM)

4.2 Electronically-Readable Information

Data Matrix 2-D symbols should be used. Symbol specifications shall follow ISO/IEC 16022:2006(E) and additional requirements found in the *ISBT 128 Standard Technical Specification* (ST-001). Information shall be encoded within an ISBT 128 Compound Message data structure. See *Use of Data Matrix Symbols with ISBT 128* (IG-014) for more information about the encoding of information within a Data Matrix symbol.

4.3 Eye-Readable Information

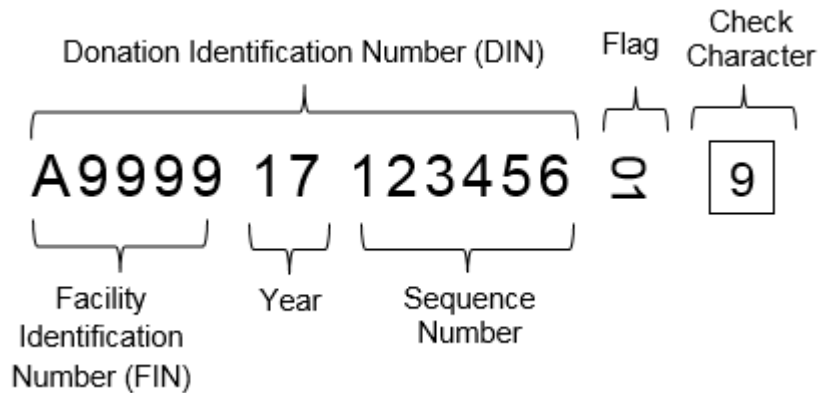
Minimum font sizes are determined by the printer used and readability. Typically, font sizes below 6 cannot be used because distinguishing between an “o” and an “e” becomes difficult.

4.3.1 Donation Identification Number [001]

The DIN shall be printed using a sans serif typeface. A national authority should determine how it should be displayed. In the US and Canada, the DIN is printed by having spaces before and after the year code to facilitate ease of reading:

A9999 17 499999

The text presentation of the DIN does not include the first character of the data identifier. It includes the second character of the data identifier because it is also a part of the data content. See Figure 8.

Figure 8 Text Presentation of DIN

The flag characters may be used to convey specific information other than the unique identification of the product and shall be distinguished from the Donation Identification Number [see *ISBT 128 Standard Technical Specification (ST-001)*].

There are three types of flag characters (Types 1, 2, and 3). See *ISBT 128 Standard Technical Specification (ST-001)* for more information. Only two (Types 1 and 2) are used in the US. When Type 1 or Type 2 flag characters are used they shall be printed as either:

- **Numeric Presentation:** The two-digit values of flags “ff” shall be printed rotated 90° clockwise to make them visually different from the Donation Identification Number.
- **Non-numeric Presentation:** A graphical icon or other representation of the value of “ff”, e.g., for flag “07” printing an icon showing a small test tube.

4.3.2 Product Descriptions [Data Structure 003]

Class name shall be printed on the label. The Class name shall be printed as it appears in the *Standard Terminology for Medical Products of Human Origin (ST-002)*.

Where space permits, Attributes text shall be printed on the label (except default Attributes). The text for Attributes shall appear as in Table 3. If an Attribute does not appear in Table 3, please contact the ICCBBA help desk (email iccbba@iccbba.org) for guidance on appropriate text. Information that cannot be printed on the label shall appear in accompanying documentation.

Product description bar code text should be printed with the Class name in larger print than Attribute(s).

Table 3 Text Associated with Attributes

Attribute Group	Attribute Variable	Instructions for Printing Text	Text (or example text when indicated) to Print on Product Label
Corneal Graft	Default: Not applicable or not specified	No text corresponding to the default appears on the label.	
	Anterior and posterior layers	Print the text shown in the next column immediately beneath the Class name "CORNEA".	Anterior and Posterior Layers
	Anterior layer	Print the text shown in the next column immediately beneath the Class name "CORNEA".	Anterior Layer
	Bowman Layer	Print the text shown in the next column immediately beneath the Class name "CORNEA".	Bowman Layer
	Corneal button	Print the text shown in the next column immediately beneath the Class name "CORNEA".	Corneal Button
	Corneal ring	Print the text shown in the next column immediately beneath the Class name "CORNEA".	Corneal Ring
	Corneoscleral disc	Print the text shown in the next column immediately beneath the Class name "CORNEA".	Corneoscleral Disc
Corneal Graft	Laser shaped	Print the text shown in the next column immediately beneath the Class name "CORNEA".	Laser Shaped

Attribute Group	Attribute Variable	Instructions for Printing Text	Text (or example text when indicated) to Print on Product Label
	Posterior layer	Print the text shown in the next column immediately beneath the Class name "CORNEA".	Posterior Layer
	Split cornea	Print the text shown in the next column immediately beneath the Class name "CORNEA".	Split Cornea
Anatomical Position	Default: Not specified	No text corresponding to the default appears on the label.	
	Left		Left
	Right		Right
Storage State	Default: No information provided	No text corresponding to the default appears on the label.	
	Ambient storage	Print the storage temperature range on the affixed label or in the accompanying documentation.	Example text: Room Temperature
	Cryopreserved	Print the storage temperature range on the affixed label or in the accompanying documentation.	Example text: ≤-120 C
Storage Stage	Freeze dried		Freeze Dried
	Frozen	Print the storage temperature range on the affixed label or in the accompanying documentation.	Example text: ≤-25 C

Attribute Group	Attribute Variable	Instructions for Printing Text	Text (or example text when indicated) to Print on Product Label
	Hypothermic storage	Print the storage temperature range on the affixed label or in the accompanying documentation.	Example text: 2 C – 8 C
	Moist chamber		Moist Chamber
	Organ culture	(This term is not used in North America.)	
Storage Solution	Default: Not specified	Print the brand name of the storage solution after the Class name. Note: For the Storage Solution Attribute group, select the Default (Not Specified).	Example text: CORNEA in OPTISOL-GS
	Albumin	Print “In Albumin” after the Class name.	Example text: CORNEA in Albumin
	Antimicrobial solution	Print the name of the antimicrobial solution on the affixed label after the Class name.	Example text: CORNEA in Polytrimethoprim or in Ciprofloxacin
Storage Solution	Cryoprotectant medium	(This term is not used in North America.)	

Attribute Group	Attribute Variable	Instructions for Printing Text	Text (or example text when indicated) to Print on Product Label
	Ethanol	<p>In addition to printing “in Ethanol” after the Class name on the affixed label, print the concentration (%) of ethanol on the affixed label or in the accompanying documentation.</p> <p>Note: The word “Ethanol” does not have to be printed twice if the concentration is printed on the label,</p>	<p>CORNEA in Ethanol</p> <p>Example text: 100% Ethanol</p>
	Glycerol (high conc)	Print “in Glycerol” after the Class name.	Example text: CORNEA in Glycerol
	No storage solution		No Storage Solution
	Nutrient medium	(This term is not used in North America.)	
	Recombinant albumin	Print the name of the solution on the affixed label after the Class name.	Example text: CORNEA in 20% rHSA
	Saline	Print “in Saline” after the Class name.	Example text: CORNEA in Saline
Endothelial Cell Density	Default: No information provided	No text corresponding to the default appears on the label.	
Endothelial Cell Density	Information provided	(No information needs to be printed. The endothelial density should be provided in accompanying documents.)	

Attribute Group	Attribute Variable	Instructions for Printing Text	Text (or example text when indicated) to Print on Product Label
Pathogen Reduction	Default: No information	No text corresponding to the default appears on the label.	
	No pathogen reduction		Not Sterile
	Pathogen reduced: method NS		Pathogen reduced
	Radiation sterilization		Radiation sterilization
Transport Solution	Default: Not specified	No text corresponding to the default appears on the label.	
	Dextran		Dextran
Portion	Default: Not specified	No text corresponding to the default appears on the label.	
	Eighth	Print text shown in the next column immediately below the Lamellar Preparation Attribute, if present. If the Lamellar Preparation attribute is not present, it should appear immediately below the Class "Sclera" or the Corneal graft attribute.	Eighth
Portion	Half	Print text shown in the next column immediately below the Lamellar Preparation Attribute, if present. If the Lamellar Preparation attribute is not present, it should appear immediately below the Class "Sclera" or the Corneal graft attribute.	Half

Attribute Group	Attribute Variable	Instructions for Printing Text	Text (or example text when indicated) to Print on Product Label
	Part, NS	Print text shown in the next column immediately below the Lamellar Preparation Attribute, if present. If the Lamellar Preparation attribute is not present, it should appear immediately below the Class "Sclera" or the Corneal graft attribute.	Partial
	Quarter	Print text shown in the next column immediately below the Lamellar Preparation Attribute, if present. If the Lamellar Preparation attribute is not present, it should appear immediately below the Class "Sclera" or the Corneal graft attribute.	Quarter
Portion	Sixth	Print text shown in the next column immediately below the Lamellar Preparation Attribute, if present. If the Lamellar Preparation attribute is not present, it should appear immediately below the Class "Sclera" or the Corneal graft attribute.	Sixth
	Third	Print text shown in the next column immediately below the Lamellar Preparation Attribute, if present. If the Lamellar Preparation attribute is not present, it should appear immediately below the Class "Sclera" or the Corneal graft attribute.	Third

Attribute Group	Attribute Variable	Instructions for Printing Text	Text (or example text when indicated) to Print on Product Label
	Whole	Print text shown in the next column immediately below the Lamellar Preparation Attribute, if present. If the Lamellar Preparation attribute is not present, it should appear immediately below the Class "Sclera" or the Corneal graft attribute.	Whole
Whole Eye Type	Default: Not applicable or not specified.	No text corresponding to the default appears on the label. Default: No information provided	
	Content Removed	Print text shown in the next column immediately below the Class "Whole Eye".	Content Removed
Lamellar Layer Preparation	Default: Not applicable or not specified	No text corresponding to the default appears on the label.	
	Laser	Print text shown in the next column immediately below the Corneal Graft Type Attribute.	Laser
Lamellar Layer Preparation	Manual Dissection	Print text shown in the next column immediately below the Corneal Graft Type Attribute.	Manual Dissection
	Microkeratome	Print text shown in the next column immediately below the Corneal Graft Type Attribute.	Microkeratome

Attribute Group	Attribute Variable	Instructions for Printing Text	Text (or example text when indicated) to Print on Product Label
Ocular Tissue, Non-Clinical	Default: Does not apply because tissue is for clinical use or, if for non-clinical use, type of non-clinical tissue is not encoded.	No text corresponding to the default appears on the label.	
	Aqueous Humor	Print text shown in the next column immediately below the Class name "OCULAR TISSUE, NON-CLINICAL"	Aqueous Humor
	Cornea	Print text shown in the next column immediately below the Class name "OCULAR TISSUE, NON-CLINICAL"	Cornea
	Iris	Print text shown in the next column immediately below the Class name "OCULAR TISSUE, NON-CLINICAL"	Iris
	Lens	Print text shown in the next column immediately below the Class name "OCULAR TISSUE, NON-CLINICAL"	Lens
	Optic nerve	Print text shown in the next column immediately below the Class name "OCULAR TISSUE, NON-CLINICAL"	Optic nerve
	Posterior part	Print text shown in the next column immediately below the Class name "OCULAR TISSUE, NON-CLINICAL"	Posterior part
	Retina	Print text shown in the next column immediately below the Class name "OCULAR TISSUE, NON-CLINICAL"	Retina

Attribute Group	Attribute Variable	Instructions for Printing Text	Text (or example text when indicated) to Print on Product Label
	Vitreous Humor	Print text shown in the next column immediately below the Class name "OCULAR TISSUE, NON-CLINICAL"	Vitreous Humor

4.3.3 Dates [Data Structures 004, 005, 006, 007, 008, 009, 031]

Dates shall be printed in compliance with ISO 8601-2004 extended format.

Expiration Date:

2017-03-17

Times shall be printed based on a twenty-four hour clock with a colon placed between the hours and minutes.

The UTC, if desired, shall be printed beneath the local time in parenthesis with the designation "UTC". Italics may also be used to clearly differentiate UTC from local time. For example:

Expiration Date/Time:

2017-01-15 15:15 EST
(2017-01-15 20:15 UTC)

4.3.4 Text Not Associated with Electronically-Readable Information

Text not associated with electronically-readable information includes such things as warnings (e.g., "Single patient use only" and "Not sterile") and information not included within the ISBT 128 Product Description Code (e.g., the specific type of commercial storage solution). This text may appear on the label as space permits.

5 Label Examples

5.1 Examples of labels when the facility that assigned the DIN is the same as the facility that assigned the Product Code.

Figure 9 Cornea Label



GENERIS EYE BANK Any Street, Anywhere, Worldwide  A9999 17 345621  Product Code: V0004000	CORNEA in Optisol-GS Left Expiration Date: 2017-01-18 Date Time of Death: 2017-01-04 12:16 Date Time of Preservation: 2017-01-04 14:29 See Product Insert
SINGLE PATIENT USE ONLY NOT STERILE Storage: 2 - 8 C	

Figure 10 Cornea, Anterior and Posterior Layers



GENERIS EYE BANK Any Street, Anywhere, Worldwide  A9999 17 345678  Product Code: V0006000	CORNEA in Life4C Anterior and Posterior Layers Right Expiration Date: 2017-01-18 Date Time of Death: 2017-01-04 12:16 Date Time of Preservation: 2017-01-04 14:29 See Product Insert
SINGLE PATIENT USE ONLY NOT STERILE Storage: 2 - 8 C	

Figure 11 Partial Sclera





GENERIS EYE BANK Any Street, Anywhere, Worldwide  A9999 17 345639  Product: V0015002, Pack 2	SCLERA in Ethanol Partial Left Expiration Date: 2019-02-04 Date Time of Death: 2017-02-04 14:25 Date Time of Preservation: 2017-02-04 16:54 See Product Insert
SINGLE PATIENT USE ONLY NOT STERILE Storage: Room Temperature	

Figure 12 Whole Sclera

GENERIS EYE BANK Any Street, Anywhere, Worldwide  A9999 17 345657  Product: V0069000	SCLERA in Ethanol Whole Sclera Right Expiration Date: 2019-02-04 Date Time of Death: 2017-02-04 14:25 Date Time of Preservation: 2017-02-04 16:54 See Product Insert
SINGLE PATIENT USE ONLY NOT STERILE Storage: Room Temperature	

5.2 Examples of labels when the facility that assigned the DIN is not the same as the facility that assigned the Product Code.

The FIN(P) appears beneath the Product Code on the left side of the label. The full name of the processor may appear on the label as shown in Figure 14 (see lower right portion of the label), but this is not required and may not be possible given the size of the label.

Figure 13 Cornea Label with FIN(P)

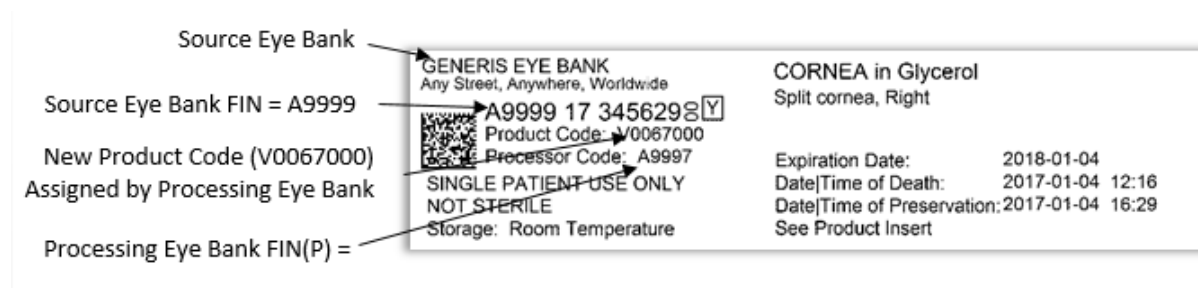
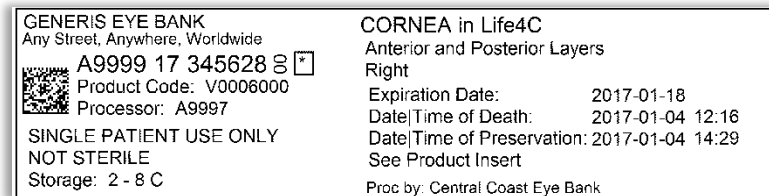
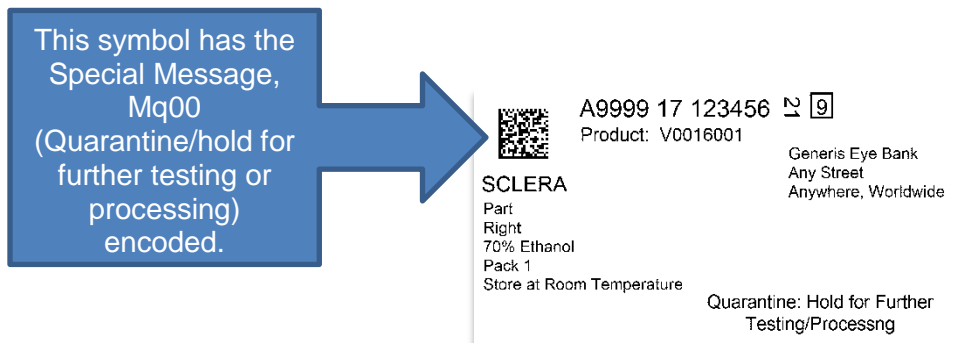


Figure 14 Cornea, Anterior and Posterior Layers with FIN(P)



5.3 Example of In-Process Label

Figure 15 In-Process Label Example



6 Re-Labeling

Facilities may receive and re-label products from other organizations. If products are re-labeled then:

- The DIN [Data Structure 001] should not be changed.
- The Product Code [Data Structure 003] shall be changed when the product is modified into a product that has a different Product Description Code or is divided such that a different Division (Pack) Code is needed.
- If a new Product Code is assigned, a Processing Facility Information Code [Data Structure 033] shall be changed or added. It shall correspond to the facility that assigned the Product Code that is on the label.

Facilities that re-label shall ensure that all products are labeled uniquely. This requires the use of the Processing Facility Information Code if an eye bank receives tissue from a recovery organization that supplies tissues to multiple eye banks. This is important to ensure each tissue is uniquely identified. For example, a recovery organization assigned the DIN A9997 17 345639 to a donation. It then sent scleral tissue to two eye banks, A and B.

Bank A created:

DIN: A9997 17 345639

Product Code: V0020002 (SCLERA|Ambient storage|Ethanol|Part, NS)

Processing Facility Information Code: A9998000000

Bank B created:

DIN: A9997 17 345639

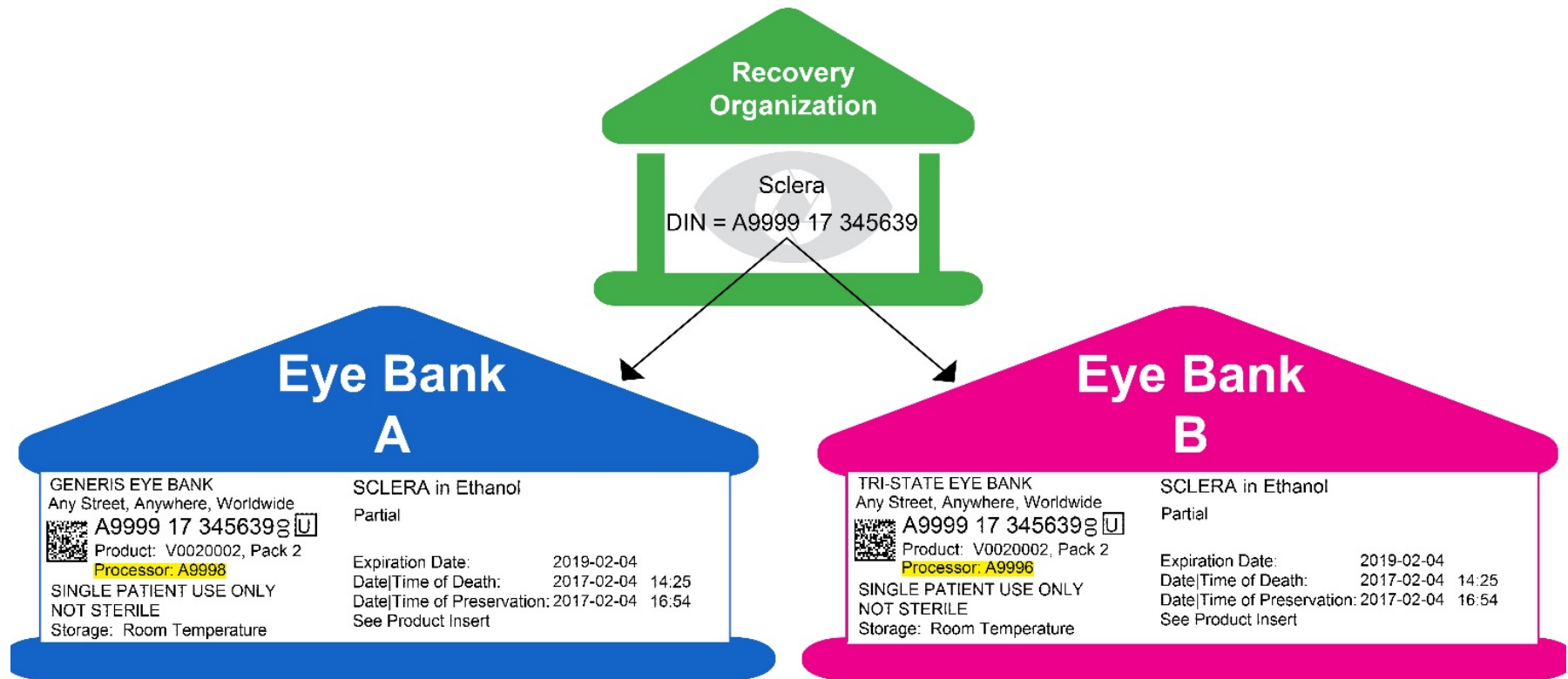
Product Code: V0020002 (SCLERA|Ambient storage|Ethanol|Part, NS)

Processing Facility Information Code: A9996000000

The DIN and Product Codes are identical (A9997 17 345639 and V0020002). The codes only vary by the 5th character in the Processing Facility Information Code. Thus this code is essential to support traceability of the tissue.

See Figure 16.

Figure 16 Use of Processing Facility Information Code to Create Uniqueness



7 Software Developers Information

7.1 Data Structures

Software must support all essential ISBT 128 data structures needed for tissue traceability or are required by other Standards and Regulations. These are:

- Data Structure 001 (Donation Identification Number)
- Data Structure 003 (Product Code)
- Data Structure 005 (Expiration Date and Time)
- Data Structure 033 (Processing Facility Information Code)

Additionally, since EBAA has chosen to use Data Matrix, software must also support Data Structure 023 (Compound Message).

Other data structures that may also be useful for eye banks are:

- Data Structure 002 [Blood Groups (ABO and Rh)] – used for special messages
- Data Structure 007 [Collection (or Recovery) Date and Time]
- Data Structure 009 (Production Date and Time) which may be used to convey the date/time of preservation.
- Data Structure 031 (Flexible Date and Time) which may be used to convey any date and time, including the date/time of death
- Data Structure 029 (Dimensions) which at some point may be used to convey endothelial cell density

See the *ISBT 128 Standard Technical Specification (ST-001)* for more information about data structures.

7.2 Order of Product Description Attributes on the Label

While often Attributes are printed in the order the Attribute group appears in the ISBT 128 Product Description Code Database, this is not appropriate for ocular tissues. Attributes shown in **Table 4** are printed in the order shown.

Table 4 Order of Attributes

Attribute Group	Location on Label
Corneal Graft	Immediately beneath the Class name "CORNEA".
Whole Eye Type	Immediately below the Class "WHOLE EYE".
Lamellar Layer Preparation	Immediately below the Corneal Graft Type Attribute.

Attribute Group	Location on Label
Portion	For CORNEA: <ul style="list-style-type: none"> • Immediately below the Lamellar Preparation Attribute, if present. • If the Lamellar Preparation attribute is not present, immediately below the Corneal graft attribute. For SCLERA: Immediately below the Class name "SCLERA".
Type of Non-Clinical Tissue	Immediately beneath the Class name "OCULAR TISSUE, NON-CLINICAL".

7.3 Facility Identifiers

Facility identifiers within an ISBT 128 code [e.g., the FIN within Data Structure 001 and the FIN(P) within Data Structure 033] serve to uniquely identify products. They shall not be used to determine which organization played a particular role in producing a tissue. For example, the FIN within the DIN identifies the organization that assigned the DIN. No further interpretation of the role of that organization (e.g., recovery organization, source bank, or processor) shall be made. If a particular role of an organization is to be captured in facility records, a separate field shall exist. That means, for example, if the facility wants to capture the source eye bank as part of its records, that information should be captured in a separate field from the DIN.

The organization that supplied the tissue shall be recorded in the receiving facility's records. This information might not be on the label (either in electronically- or eye-readable format), but would be available from documents shipped with the tissue.

8 Abbreviations

DIN	Donation Identification Number
EBAA	Eye Bank Association of America
EBTAG	Eye Bank Technical Advisory Group
FDA	Food and Drug Administration
FIN	Facility Identification Number
FIN(P)	Facility Identification Number of the Processing Facility
FPC	Facility Defined Product Code
ICCBBA	International Council for Commonality in Blood Banking Automation
MPHO	Medical Products of Human Origin
PDC	Product Description Code
UTC	Coordinated Universal Time
WHO	World Health Organization



Guidance Document for Investigating and Reporting Adverse Reactions to the EBAA

Version 4

July 2019

Guidance Document for Investigating and Reporting Adverse Reactions to the EBAA

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INTRODUCTION

The EBAA initiated an adverse reaction reporting system in 1990. EBAA Medical Standard M1.500 requires each distributing establishment to seek postoperative outcome information between three and six months after transplant. MS G1.000 requires the investigation and reporting of adverse reactions to the EBAA for review by the Medical Review Subcommittee of the Medical Advisory Board. Reporting of adverse reactions was redesigned in 2004 for online use, utilizing the EBAA Online Adverse Reaction Reporting System (OARRS). OARRS enables easy reporting of adverse reactions, surgery, microbiological results, tissue-mate status, tissue source, transportation and comments.

The EBAA Medical Advisory Board (MAB) approved a number of significant changes to the OARRS system: (a) In June 2012, the MAB voted to standardize the surgical procedure and cause of death

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categories to match the statistical report; (b) OARRS was updated to capture the Genus and species of any culture positive organism; (c) In June 2013, the MAB voted to harmonize our adverse reporting categories with the European SOHO V&S (Vigilance and Surveillance of Substances of Human Origin) categories, recognized by the World Health Organization (WHO) Project NOTIFY; (d) A data element was added in OARRS to delineate between domestic and internationally-placed tissue.; (e) The MAB voted in November 2013 to add a new reporting category called “Early Regraft” for regrafts prior to 8 weeks. These changes necessitated a major revision of the Guidance Document for Adverse Reaction Reporting to the EBAA, previously published in 2009.

OARRS was updated in 2017 in response to member requests and a review by the Medical Review Subcommittee with the following changes: (a) The tissue ID fields were enlarged to accommodate both the DIN and Product Code; (b) Malignancy was added as a separate adverse reaction category; (c) PDEK was added to the listing of procedures; (d) a question was added to capture whether tissue was preloaded into an inserter by the processor; (e) a question was added to capture whether the storage solution was changed after processing. If yes, the system collects the lot & expiration date.; and (f) OARRS was updated to ask about antifungal supplementation.

The OARRS system was revised again in 2019 to update the coding and security of the reporting system, and version 4 of this guidance reflects those changes.

OARRS may be accessed through the following link: [OARRS](#)

The Medical Review Subcommittee is responsible for reviewing adverse reaction submissions once they are complete. Officially, the subcommittee’s charge is to: review adverse events and document their occurrence; and monitor the efficacy of medical standards and their effectiveness regarding disease transmission. The subcommittee develops outcome measures to monitor areas for performance and outcome improvement. This subcommittee reports directly to the Medical Advisory Board.

GENERAL GUIDANCE FOR INVESTIGATING ADVERSE REACTIONS

Reports of adverse reactions may be received by any entity performing an eye banking function. However, the source eye bank is ultimately responsible for coordinating adverse reaction investigations. The source bank must notify all entities involved in the recovery, processing, storage, final distribution, tissue evaluation, and donor eligibility determination of the results of the investigation. Each of the involved entities must participate in the investigation and maintain documentation of the adverse event and results of the investigation forwarded to it by the source bank.

Here is a typical scenario for investigating a reported adverse reaction:

1. Surgeon reports an adverse reaction to the Distributing Eye Bank
2. Distributing Eye Bank notifies Source Eye Bank (unless same entity); Source Eye Bank coordinates investigation.
3. Quarantine other ocular tissue not yet transplanted from same donor and investigate status of mate tissue.

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4. Source Eye Bank contacts surgeon (or designates Distributing Eye Bank to contact surgeon) to determine whether pre-existing/pre-disposing conditions, intraoperative complications, or possible sources of contamination may have influenced outcome. (See EBAA Adverse Reaction Inquiry Sample Form) If pre-existing or pre-disposing conditions exist, the Source Eye Bank Medical Director must determine if further investigation is necessary (see examples below).
5. Source Eye Bank initiates and coordinates investigation to review records produced by its staff, as well as records produced by the Recovery Establishment, Processing Establishment, Storage Establishment, and others involved with the tissue before it was distributed to the consignee.
6. Source Eye Bank submits to Medical Director a summary of records reviewed (including donor information form and tissue evaluation form), information obtained from transplanting surgeon (include post-op report, inquiry information), and mate status. Medical Director contacts surgeon for further follow up if necessary.
7. Medical Director establishes imputability, the likelihood that the adverse reaction in the recipient can be attributed to the tissue. Only Possible, Likely/Probable or Definite/Certain graft-transmitted adverse reactions are reportable via OARRS.
8. Source Eye Bank notifies all entities involved in the recovery, processing, storage, final distribution, tissue evaluation, and donor eligibility determination of the results of the investigation.
9. EBAA reporting is required within 30 days of the first report to an eye bank, via the OARRS website https://oarrs.restoresight.org/banks/sign_in.
10. If the adverse reaction involved a communicable disease and there is a reasonable possibility that the tissue caused the response, the bank which made the tissue available for distribution must report to the FDA within 15 days of the initial receipt of the information. The FDA MedWatch mandatory reporting form (Form FDA-3500A) should be used to report adverse reactions involving a communicable disease if it: a) is fatal; b) is life-threatening; c) results in permanent impairment of a body function or permanent damage to body structure; or d) necessitates medical or surgical intervention, including hospitalization.

Imputability Level Explanation (Adapted from SOHO V&S Guidance) *

Level of Attribution	Description	OARRS Reportable?
Not Assessable	Insufficient data for imputability assessment	No
Excluded	Conclusive evidence beyond reasonable doubt for attributing adverse reaction to alternative causes	No
Unlikely	Evidence clearly in favor of attribution to alternative causes	No
Possible	Evidence is indeterminate	Yes
Likely, Probable	Evidence in favor of attribution to the tissues/cells	Yes
Definite, Certain	Conclusive evidence beyond reasonable doubt for attribution to the tissues/cells	Yes

*Any systemic infection in a recipient due to a relevant communicable disease agent or disease (RCDAD) must be reported regardless of level of attribution.

FIVE TYPES OF ADVERSE REACTION INVESTIGATIONS

1. Graft Failure

Graft failure may occur early or late. Reportable graft failures are those that occur early and that conform to the criteria for Primary Graft Failure or Early Regraft listed below. Grafts that have been clear for a period of time after surgery and then fail are not reportable as adverse reactions under the Graft Failure category.

Criteria to determine Primary Graft Failure:

- Corneal edema present from the time of keratoplasty **and**
- Does not clear after eight weeks **and**
- No known operative or postoperative complications or underlying recipient conditions that would explain the biologic dysfunction

Criteria for determining Early Regraft:

- Corneal edema present from the time of keratoplasty **and**
- Does not clear prior to the time of regraft **and**
- No known operative or postoperative complications or underlying recipient conditions that would explain the biologic dysfunction **and**
- Regrafted in less than eight weeks
- In endothelial keratoplasty cases this may include failure of graft to attach, despite confirmation of correct graft orientation (e.g. by S-stamp)

Guidance for investigating reports of graft failure:

- Review storage conditions
- Review recovery records
- Review processing records
- Review mate status
- Review potential operative contributing factors.

Examples: Endothelial trauma, chamber collapse, intracameral injection of toxic or preservative containing fluids, Toxic Anterior Segment Syndrome (TASS), known intraoperative Descemet trauma, prolonged vitrectomy,

For endothelial keratoplasty: tissue manipulation intraoperatively (e.g. upside down), re-bubbling, surgeon experience is less than ten cases, poor surgeon cut, presence of anterior chamber IOL, incision size, number of folds, insertion/folding technique, use of forceps, dislocation.

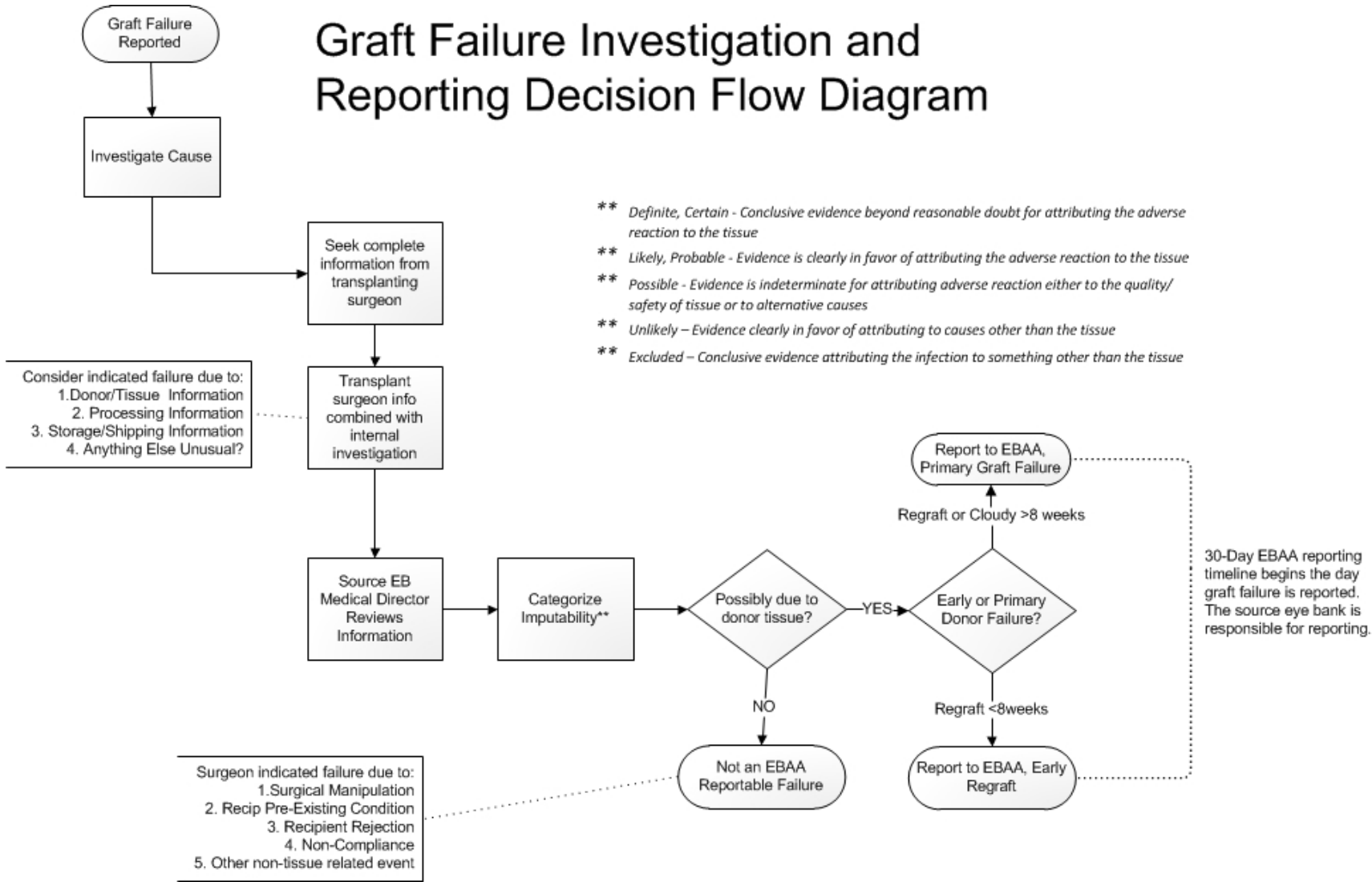
- Review potential recipient contributing factors.

Examples: Persistent epithelial defect, persistent elevated IOP, marked post-operative inflammation, choroidal hemorrhage, IOL dislocation, flat anterior chamber, ocular surface

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disease, recurrence or persistence of pre-operative infectious keratitis, persistent wound leak.

Graft Failure Investigation and Reporting Decision Flow Diagram



2. Ocular Infections

A graft-transmitted ocular infection exhibits signs and symptoms of infection consistent with the infectious agent (e.g. pain, redness, loss of vision, hypopyon, corneal infiltrates, vitritis, etc.) from, or near, the operative site.

A “**Possible**” graft-transmitted infection is reported when the evidence is indeterminate:

- Surgeon reports an ocular infection believed to be due to donor tissue.
- No pre-implant donor culture was performed.
- No pre-existing or pre-disposing conditions, intraoperative complications, or possible sources of contamination are identified to exclude imputability.

A “**Likely/Probable**” graft-transmitted ocular infection may be attributed to the graft if there is:

- A match between the pre-implant donor and recipient culture findings in a recipient with no known or identified risk factors for the disease.
- A report of graft-associated infection in one or more recipients of tissues from the same donor.
- Evidence of failure to comply with SOP for aseptic technique prior to distribution of tissue.

A “**Definite/Certain**” graft-transmitted ocular infection may be attributed to the graft if there is:

- Confirmation by appropriate laboratory testing (e.g., genotyping, PCR, wet prep) that demonstrates scientific evidence linking the infectious agent in the recipient with donor samples, or
- A report of graft-associated infection with the same organism (genus and species) in two or more recipients of tissues from the same donor. In cases of coagulase-negative staphylococcus where the possibility of contaminants may be considerable from either the donor rim or from the recipient, a matching genus and species (such as *Staphylococcus epidermidis*) may not change a “Likely / Probable assessment to a “Definite / Certain” assessment. The Medical Director would need to make such an assessment.

Note: Only Possible, Likely/Probable and Definite/Certain graft-transmitted ocular infections are to be reported to OARRS

Guidance Document for Investigating and Reporting Adverse Reactions to the EBAA

Guidance for investigating reports of ocular infection:

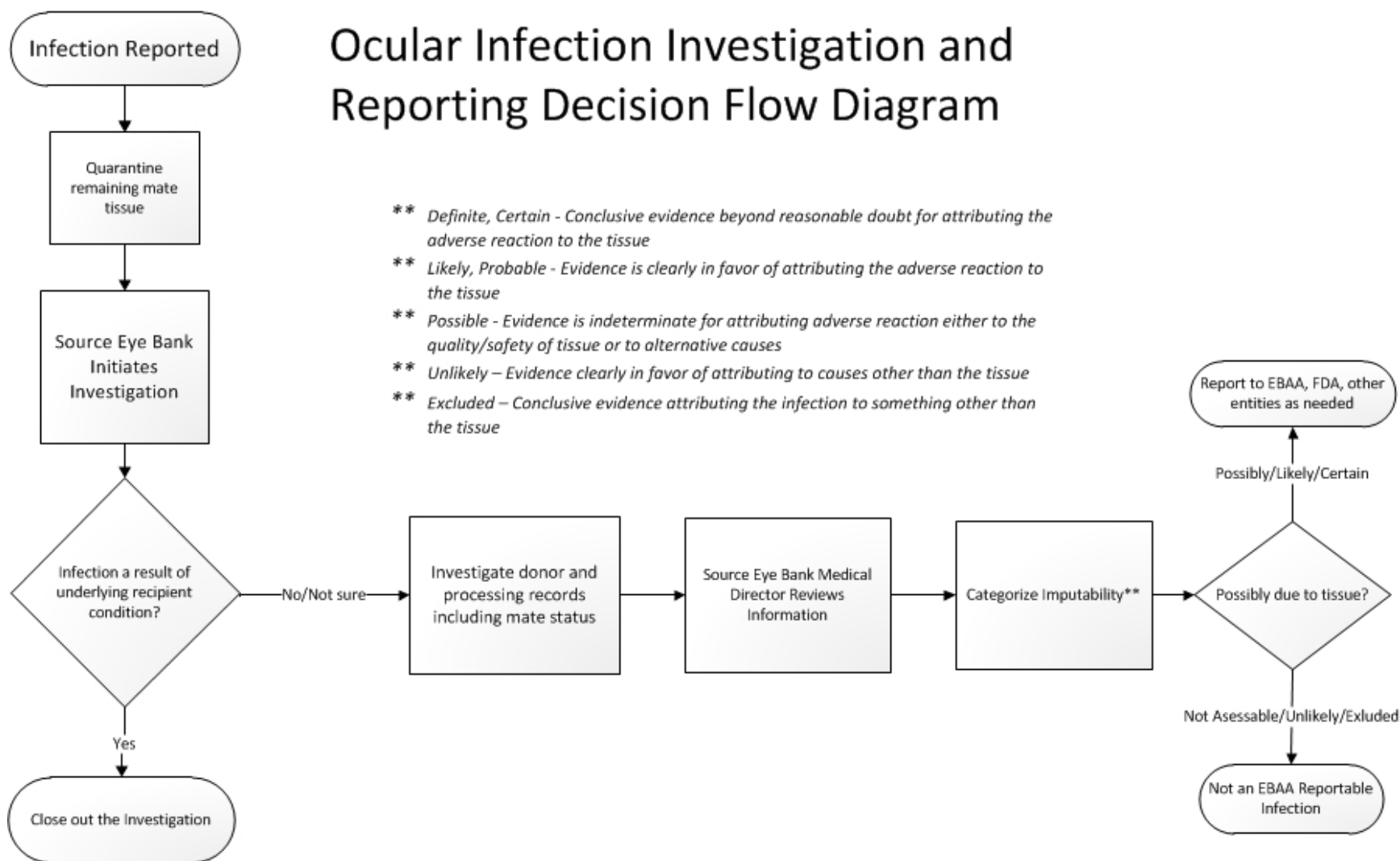
As part of the investigation, review records for possible sources of contamination

Examples: Breaks in aseptic technique during handling of tissue, improper sterilization of instruments, improper maintenance of equipment, contamination or expiration of storage solution, inadequate maintenance of sterile field in tissue preparation

- Review culture results pre and post-op
- Review donor screening records
- Review tissue evaluation
- Review recovery records
- Review processing records
- Review storage conditions
- Review mate tissue status, if applicable
- Review tissue bank donor cultures, if applicable
- Review potential intraoperative contributing factors

The Appendix contains a list of microorganism selections available on the OARRS website.

Ocular Infection Investigation and Reporting Decision Flow Diagram



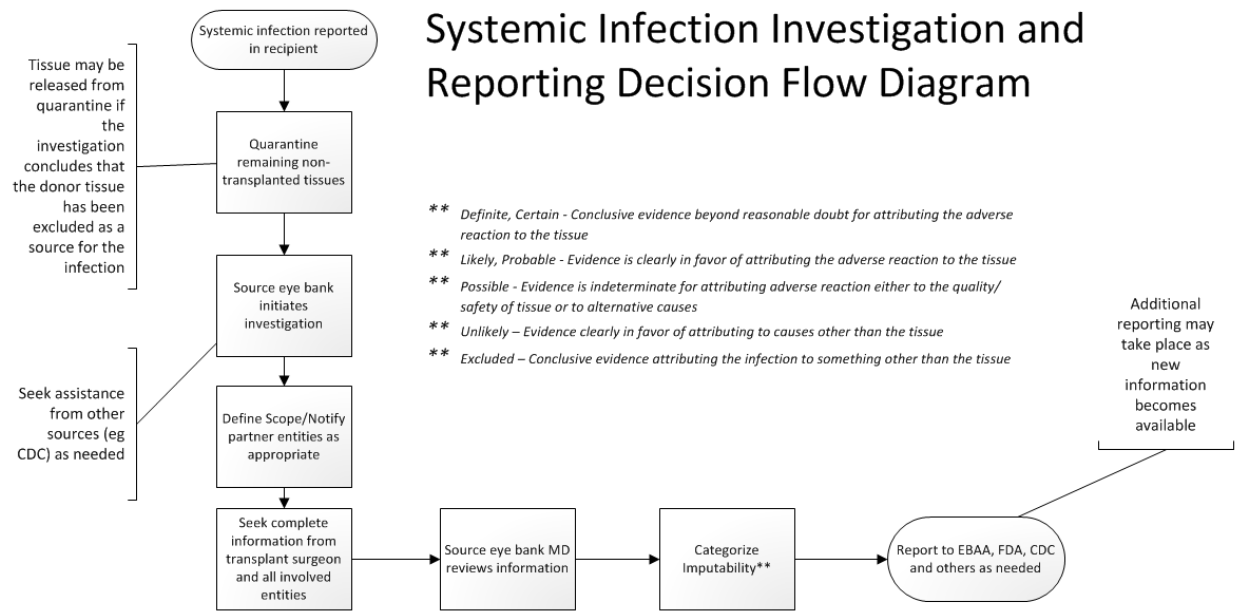
3. Systemic Infection in a Recipient

Any systemic infection due to a relevant communicable disease agent or disease (RCDAD) such as HIV, hepatitis, syphilis, West Nile Virus (WNV), or Creutzfeldt Jakob Disease (CJD) that develops in a recipient, whether or not it is suspected to be due to donor tissue, must be reported to the EBAA. The investigation should include:

- Report to EBAA via OARRS
- Review donor screening records from all sources
- Review serology and NAT infectious disease testing
 - Additional testing on archived serum may be warranted as part of the investigation with the most sensitive testing available
- Review mate recipient status, if applicable
- Contact other known recovery and distributing agencies

If an infection of a systemic nature is determined to be possible, likely/probably, or definitely due to donor tissue, communicate to all entities that recovered organs or received or recovered tissues from that donor.

Reporting may take place before the investigation is complete due to the lengthy investigations that can take place. Investigations may require coordination with the Centers for Disease Control (CDC) Office of Blood, Organ and Other Tissue Safety, FDA, and local health authorities. Other expert help may be required from reference laboratories and infectious disease experts.



4. Corneal Dystrophy

A donor derived corneal dystrophy is a dystrophy diagnosed in a recipient, which may possibly, probably or definitively be derived from the transplanted tissue and may or may not have been present in the tissue at the time of donation. This includes ectatic disease, such as keratoconus, which has been reported to affect 2 cases since 2007.

Tips for investigating a reported corneal dystrophy:

- Review donor records including ophthalmology records, if available
- Review tissue evaluation
- Review mate tissue status

5. Ocular Malignancy

A donor derived ocular malignancy is a malignant disease diagnosed in a recipient, which may possibly, probably or definitively be derived from the transplanted tissue and may or may not have been present in the tissue at the time of donation. Local ocular malignancies are usually related to metastatic disease to the anterior segment of the donor’s eye (e.g. adenocarcinoma and melanoma). These donors typically would be deferred by proper eye evaluation prior to tissue collection. However, if malignancy transmission is reported, detailed investigation and reporting is appropriate, as follows:

- Review of recipients clinical symptoms, test results and any alternative risk factors for the malignancy in the donor’s medical history
- Review tissue evaluation
- Review mate tissue status
- Histological examination and immunohistochemistry to help identify the pathology for comparison of tumors in the donor and recipient(s)

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- Determination of the genetic identity of donor and recipient tumors can provide a high degree of confidence regarding imputability
- The temporal sequence is also an important factor in investigating imputability. Most transmitted tumors appear within the first 14 months after transplantation. Therefore, it is unlikely that an aggressive tumor diagnosed in the recipient five years after transplantation is donor-transmitted

6. Refractive Surgery in the Donor Tissue

Evidence suggestive of prior refractive surgery in the donor tissue inadvertently utilized for full thickness or anterior lamellar keratoplasty is an EBAA-reportable adverse reaction. This significant adverse event (SAE) is reportable through OARRS, regardless of whether the recipient has an adverse outcome, because inappropriate tissue has been released for clinical use. Tissues with a history of refractive surgery knowingly released by the eye bank for tectonic or emergency uses would not be reportable.

DEFINITIONS

Adverse Reaction: 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).

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

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

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.

Distributing Establishment: 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.

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

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

Graft: Tissues prepared for use in transplantation

HIV: An abbreviation for human immunodeficiency virus

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Imputability: The likelihood that a serious adverse reaction in a recipient can be attributed to the tissue or cells applied or that a serious adverse reaction in a living donor can be attributed to the donation process.

OARRS: An abbreviation for Online Adverse Reaction Reporting System.

Processing Establishment: The entity that performs post-recovery tissue preparation.

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.

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.

Recovery Establishment: The 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 U.S. law.

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.

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

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).

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

Guidance Document for Investigating and Reporting Adverse Reactions to the EBAA

REFERENCES

Medical Standards. Eye Bank Association of America. Washington, DC: October 25, 2018.

[Medical Standards – October 25, 2018](#)

SOHO V&S Guidance for Competent Authorities: Communication and Investigation of Serious Adverse Events and Reactions Associated with Human Tissues and Cells. EU Public Health Programme, Project #20091110. January 2013.

<http://www.notifylibrary.org/sites/default/files/SOHO%20V%26S%20Communication%20and%20Investigation%20Guidance.pdf>

NOTIFY: Exploring Vigilance Notification for Organs, Tissues and Cells. Organs, Tissues, & Cells, 2011, November, 14, 3: Suppl. <http://www.notifylibrary.org/sites/default/files/BOOK%20NOTIFY.pdf>

Guidance for Industry: Investigating and Reporting Adverse Reactions Related to Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) Regulated Solely under Section 361 of the Public Health Service Act and 21 CFR Part 1271, March 2016.

<https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/UCM434834.pdf>

USEFUL LINKS

Notify Library

<http://www.notifylibrary.org/>

FDA's HCT/P Adverse Reaction Reporting

<http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/ucm152576.htm>

Form: [Form FDA 3500A - Mandatory Reporting](#) (2/2013)

OARRS Website

https://oarrs.restoresight.org/banks/sign_in

OARRS Organism Listing (Genus and Species)

Bacteria

Achromobacter (formerly Alcaligenes)

Acinetobacter spp.

Citrobacter spp.

Clostridium perfringens

Corynebacterium spp.

Enterococcus species

- Enterococcus faecalis
- Enterococcus faecium
- Other Enterococcus spp.
- Enterococcus unspecified

If known, include Vancomycin resistance in the comments (VRE)

Enterobacter spp.

Escherichia coli

Flavobacterium spp.

Haemophilus influenzae

Klebsiella spp.

Mycobacterium species

- Mycobacterium avium
- Mycobacterium chelonae
- Mycobacterium fortuitum
- Other Mycobacterium spp.

Pseudomonas aeruginosa

Propionibacterium spp.

Serratia marcescans

Staphylococcus species

- Staphylococcus aureus
- Staphylococcus epidermidis / coagulase negative
- Staphylococcus unspecified
- If known, include methicillin resistance in the comments (MRSA)

Streptococcus species

- Streptococcus pyogenes (Group A Strep)
- Streptococcus agalactiae (Group B Strep)
- Streptococcus pneumoniae
- Viridans streptococci (alpha hemolytic)
- Streptococcus unspecified

Stenotrophomonas maltophilia

Fungi

Aspergillus spp.

Candida species

- Candida albicans
- Candida glabrata
- Candida parapsilosis
- Candida tropicalis
- Candida other
- Candida unspecified

Cephalosporium spp.

Curvularia spp.

Fusarium spp.

Penicillium spp.

Yeast – non-specified

Virus

Herpes simplex

Cytomegalovirus

Parasites

Acanthamoeba spp. (if known, add the species to the comments)

Other

REVISION HISTORY

2009

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