PROCEDURES MANUAL

EYE BANK ASSOCIATION OF AMERICA®

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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, 06/17, 06/19, 10/19, 06/20, 06/21, 06/23.

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.	4. See EBAA Medical Standards section C2.000.
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.	6. To ensure that Medical Directors stay current and knowledgeable about the EBAA Medical Standards and regulations.
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.	7. See EBAA Medical Standards section C1.200
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.	9. To ensure active participation and approval by the medical director on technical policies and procedures.
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.	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:

1. FDA regulations 21 CFR 1271 Human Cells, Tissue, and Cellular and Tissue – Based Products
2. EBAA Medical Standards
3. CDC Principles of Biosafety
4. Biosafety in Microbiological and Biomedical Laboratories—6th Edition (cdc.gov)
5. OSHA standards for bloodborne pathogens (BBP, 29 CFR 1910.1030) and personal protective equipment (PPE, 29 CFR 1910 Subpart I)
6. Danneffel, M. B. (1997). Ch. 32 structure and function of eye banks. In J. H. Krachmer, M. J. Mannis & E. J.
7. Holland (Eds.), *Cornea, fundamentals of cornea and external disease* (pp. 463-467). St. Louis: Mosby.
8. Heck E. (2005) Ch. 31 Structure and function of eye banks. In Krachmer, Mannis, Holland (Eds) Cornea,
9. Fundamentals Diagnosis and Management. (pp 407-409), Philadelphia: Elsevier.

Glossary:

1. Biosafety Level 2 (BSL-2)- designated for areas where the presence of an infectious agent may be unknown when handling human blood, body fluids, or tissues. Primary hazards in a BSL-2 laboratory include accidental percutaneous or mucous membrane exposures, exposure of non-intact skin, or ingestion of infectious materials.
2. Contamination- The adulteration of a product during processing (with pathogens, chemicals, allergens, or foreign objects) so that it is no longer wholesome and safe, therefore potentially rendering the finished product unsafe to transplant.
3. Cross contamination- personnel, utensils and maintenance tools that transfer a pathogen or foreign object from one donor to another.
4. Relocation- the action of an eye bank moving and establishing itself into a new place.
5. Pest control management program - a plan in place to eliminate and/or manage pests (e.g., insects, rodents etc.) at the eye bank that may contribute to contamination or cross contamination.
6. Critical Equipment- Equipment required to be able to log in tissue, maintain records, generate procedures, evaluate tissue, or process tissue on a regular basis.

Materials needed:

1. Room with limited access, i.e., locked door

2. Sink with a drain and running water
3. Adequate counter space
4. Adequate stable electrical source
5. Storage space for supplies and instruments
6. Appropriate space for tissue processing
7. Pest Control Management Program

Procedure	Rationale
1. The eye bank laboratory must be large enough to carry out the volume of eye banking functions performed and to accommodate the number of personnel working at any given time.	• See EBAA Medical Standards C3.100 Eye Bank Laboratory. • FDA regulations 21CFR1271.190 (a) Facilities-General
2. The eye bank must divide the facility into separate or defined areas of adequate size for each operation that takes place at the eye bank, or you must establish and maintain other control systems to prevent improper labeling, mix-ups, contamination, cross-contamination, and accidental exposure of tissue to communicable disease agents.	• FDA regulations 21CFR1271.190 (c) Facilities – Operations • EBAA Medical Standards C3.100 Eye Bank Laboratory
3. The EBAA office must be notified (in writing) within 30 days of the relocation, laboratory expansion or addition of a satellite to an eye bank.	• EBAA Medical Standards C3.000 Facilities refer to EBAA accreditation board policy and proc section E1.400
4. The eye bank must maintain the facility in a good state of repair. Facility should have appropriate lighting, ventilation, plumbing, drainage, and access to sinks and toilets that are adequate to prevent the introduction, transmission, or spread of communicable disease.	• FDA regulations 21 CFR 1271.190 (a) Facilities-General • EBAA Medical Standards C3.100 Eye Bank Laboratory
5. The facility must ensure that pests (vermin/rodents, insects etc.) are absent to prevent contamination or cross-contamination.	• 21CFR 1271.190 Facilities • Pest Control Requirement as per Biosafety in Microbiological and Biomedical Laboratories 6th edition • Biosafety in Microbiological and Biomedical Laboratories Appendix G—Integrated Pest Management (IPM). • Pest control services will prevent contamination and cross contamination by eliminating the presence of insects and rodents inside the eye bank.

6. The facility must have a door that can be locked, to ensure limited access to eye bank personnel only.	• EBAA Medical Standards C3.100 Eye Bank Laboratory • Best safety practices
7. The eye Bank must maintain the facility in a clean, sanitary, and orderly manner, to prevent the introduction, transmission, or spread of communicable disease.	• 21 CFR1271.190 (b)(1) Facilities-cleaning and sanitation • EBAA Medical Standards C3.100 Eye Bank Laboratory
8. The eye bank must dispose of sewage, trash, and other refuse in a timely, safe, and sanitary manner.	• 21CFR1271.190 (b) (2) Facilities-cleaning and sanitation
9. The eye bank must establish and maintain procedures for the facility cleaning and sanitation. These procedures must assign responsibility for sanitation and must describe in sufficient detail the cleaning methods to be used and the schedule for cleaning the facility.	• 21CFR1271.190 (d)(1) Facilities-Procedures and Records
10. The eye bank must document and maintain the laboratory cleaning and sanitation performed for the floors, counters, and cabinets. Records must be retained for 3 years after its creation.	• 21CFR1271.190 (d) (2) Facilities-Procedures and Records. 3 years record retention only applies to the cleaning of the facility. All other cleaning related activities, such as equipment cleaning must be kept for 10 years.
11. The laboratory area at the eye bank where blood is handled, or where the tissue is processed should be considered a biosafety level 2 (BSL-2) area. This area must be properly identified with a biohazard sign at the entrance of the area.	• Refer to CDC Principles of Biosafety. Biosafety in Microbiological and Biomedical Laboratories 6th edition or the eye bank country's specific regulations.
12. The BSL-2 is designated for areas where the presence of an infectious agent may be unknown when handling human blood, body fluids, or tissues. Primary hazards in a BSL-2 laboratory includes accidental percutaneous or mucous membrane exposures, exposure of non-intact skin, or ingestion of infectious materials.	• Refer to CDC Principles of Biosafety. Biosafety in Microbiological and Biomedical Laboratories or your country's specific regulations. • Refer to the OSHA Bloodborne Pathogen Standard 2 for specific required precautions. • OSHA standards for bloodborne pathogens (BBP, 29 CFR 1910.1030) and personal protective equipment (PPE, 29 CFR 1910 Subpart I) • https://www.osha.gov/bloodborne-pathogens/worker-protections
13. The eye bank laboratory must also have sufficient grounded outlets from a stable electrical source.	• EBAA Medical Standards C3.100 Eye Bank Laboratory.

	• Any equipment that would be damaged by power fluctuations requires surge protection.
14. The eye bank must adequately control the environmental conditions where these conditions could reasonably be expected to cause contamination or cross-contamination of the tissue or equipment, or accidental exposure of tissue to communicable disease agents.	• FDA 21 CFR 1271.195 Environmental Control and Monitoring
15. The eye bank must monitor and maintain the temperature and humidity of any area where equipment, supplies and reagents are stored according to manufacturer's specifications.	• FDA 21 CFR 1271.195 Environmental Control and Monitoring • EBAA Medical Standards G1.000

C3.200 Equipment, Maintenance and Cleaning

Purpose:

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

Reference:

1) FDA regulations 21 CFR 1271 Human Cells, Tissue, and Cellular and Tissue – Based Products
2) EBAA Medical Standards
3) FDA Guidance - Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)
4) National Institute of Standards and Technology https://www.nist.gov/
5) Occupational Safety and Health Administration Sta 1910.1030 (d)(2)(x)
6) Association for the Advancement of Medical Instrumentation ANSI/AAMI ST79: 2020: A1,A2,A3,A4
7) EBAA Accreditation Board. Final Temperature Probe White Paper. August 2011
8) EPA - Environmental Protection Agency

Glossary

1) **ISO Class 5 Laminar Flow** - Class 100 (ISO 5) laminar flow hoods particle count should not exceed a total of 100 particles per cubic foot of a size 0.5 micron and larger. A major part of a laminar flow hood is a HEPA filter. The ISO 5 Hoods for laboratory applications can provide either horizontal or vertical air streams; Vertical Laminar Flow Hoods are recommended for applications where the process generates vapors, solvents, chemicals or other fine powders
2) **Class II, Type A2 Biosafety Cabinet** - provides personnel, product, and environmental protection through filtered air, laminar or unidirectional air, and a motor blower. Room air is drawn in through the front grill of the cabinet.
3) **Cleaning agent** - removes dirt, dust, crumbs, and germs from surfaces or objects.

4) **Disinfecting agent** - uses chemicals to kill germs on surfaces.

5) **EPA approved disinfectants** -Environmental Protection Agency is governmental agency that protects people and the environment from significant health risks, sponsors and conducts research, and develops and enforces environmental regulations. It approves all cleaners and disinfectants that make claims over the killing of specific microorganisms. Hospital grade designation are EPA approved. Refer to EPA website for full list.

6) **National Institute of Standards and Technology (NIST**) - It was founded in 1901 and is now part of the U.S. Department of Commerce. NIST is one of the nation's oldest physical science laboratories. that provides the national standards to measure time, temperature, fluids, distance, energy, among others.

7) **IQ (Installation qualification)** – Document that describes the installation verification of an equipment together with all of its ancillary and sub systems following manufacturer's instructions. This protocol should verify that all manufacturer's installation requirements are met. These verifications must include but not limited to electrical/utilities requirement, environmental requirement, verify equipment name plate, purchasing document verification, calibration verification, and any software and communication verification.

8) **OQ (Operational qualification)** – Document that describes the manufacturer's intended use operation verification of an equipment. This verification must be done according to manufacturer's instructions and specifications including all ancillary and sub systems of the unit. These verifications must include but not limited to SOP and Operating Manual training, and Accuracy/precision verification. This is usually tested without the product.

9) **PQ (Performance qualification)** – Document that describes the verification of the equipment's performance used during the processing of an ocular tissue. This verification is usually done to show that a unit is suitable to be used to validate a tissue process.

10**) Process Validation** - establishing by objective evidence that a process consistently produces a result or product meeting its predetermined specifications. This study shows that a specific tissue process, after procurement, does not introduce other contaminants to the tissue and cause harm to the recipient.

11) **Verification** - means confirmation by examination and provision that an objective parameter or action is accurate / true when compared to a known outcome.

Materials and Equipment needed:

1) ISO Class 5 Laminar Hood or Class II, Type A2 Biosafety Cabinet or Processing Room
2) Refrigerator with temperature recording device
3) Slit lamp biomicroscope
4) Specular microscope
5) Cleaning, Use, Calibration and Maintenance logs
6) Equipment Service Documentation (Documentation for Calibration, Preventive Maintenance, Certification)
7) Specular microscope, or equivalent
8) Processing Microscope used for DMEK processing
9) Sterilizer (e.g., Autoclave), (optional)
10) Incubator, (optional)
11) Centrifuge (optional)
12) Hospital grade / EPA-registered cleaning and or disinfecting agent

Procedure	Rationale
1) Every eye bank or satellite must have the proper equipment to safely and appropriately evaluate and/or process ocular tissue.	• Best practice
2) The equipment must be suitably located and installed to facilitate operations, cleaning, and maintenance of the unit.	• 21CFR.1271.200 Equipment (a) - General • 21CFR.1271.200 Equipment (d) - Inspections
3) The equipment must be used according to the manufacturer's recommendation and the equipment operating manual must be readily available for users.	• Unit must be operated as per the manufacturer intended use.
4) All equipment must be calibrated/certified (as applicable) and / or serviced for preventive maintenance at least annually. Refer to table 1 below.	• 21 CFR.1271.200 Equipment - (c) Calibration of equipment
5) The eye bank must ensure that the equipment used to verify a unit's parameter (temperature, speed, humidity etc.) must be calibrated, when applicable, before use. The calibration of the equipment that verifies the parameter's accuracy should be traceable to accepted known / standards (e.g., National Institute of Standards and Technology or other as defined by their country's regulatory agency if eye bank resides outside of the US). If a third party is contracted to perform the calibration, then the eye bank must ensure that the contractor's instruments are calibrated before use. The Eye Bank is still responsible for ensuring that the services provided are adequate and in compliance with applicable requirements.	• FDA Guidance - Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) 2011 Section X. Equipment - G. What equipment Calibration must I perform? • EBAA Medical Standards C3.200 Equipment, Maintenance and Cleaning • http://www.nist.gov/), or the manufacturer's supplied or recommended standard. • 21 CFR 1271.200 Equipment • 21CFR1271.150 CGTP requirements (c) Compliance with applicable requirements (1) Manufacturer's arrangements - (ii) and (iii)
6) The eye bank must generate and maintain procedures for each piece of equipment describing the use, cleaning, sanitizing, and maintenance of the equipment. The calibration and preventive maintenance of the equipment must be described in the procedure if the eye bank performs these activities. The schedules for these activities must be established and included in their respective SOP.	• FDA Guidance - Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) Section X. Equipment - F. What Procedures and Schedules Are Required for Equipment? • 21 CFR 1271.200 Equipment (b) Procedures and schedules

7) The equipment must be cleaned and disinfected using a hospital grade / EPA registered cleaning and/or disinfecting agent. The reagent selected must follow the equipment manufacturer's recommendation to avoid the equipment to be damaged.	• www.epa.gov/pesticide-registration/selected-epa-registered-disinfectants • EBAA Medical Standards C3.200 Equipment, Maintenance and Cleaning • EBAA Procedural Manual- C3.200 Equipment, Maintenance and Cleaning – Materials Needed section.
8) The records for the equipment maintenance, cleaning, sanitizing, calibration, and other activities performed can be maintained in hard copy logs or electronically. If records are stored electronically, they must be backed up.	• 21CFR.1271.270 Records – (b) Records management system (c) Methods of retention. • FDA Guidance - Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) 2011 X Equipment - I. What Records Related to Equipment Must I Keep? XIX Records C. What are acceptable methods of Record Retention?
9) The eye bank must maintain detailed records of the use of equipment, including ocular tissue ID processed with that equipment, the person(s) performing the work, and the dates of entries.	• 21CFR1271.270 Records – (a) General • 21CFR1271.200 Equipment (e) - Records
10) The eye bank may have another establishment perform all activities previously described under a contract, agreement, or other arrangement. However, the eye bank is responsible for ensuring that the services provided are in compliance with applicable regulatory agencies and EBAA requirements.	• 21CFR1271.150 CGTP requirements – (c) Compliance with applicable requirements (1) Manufacturer's arrangements (ii) and (iii)
11) All equipment records must be retained for a minimum of ten years from the date of transplantation/implantation, distribution or whichever is latest.	• 21CFR1271.270 Records (b) Records management system (d) Length of retention • EBAA Medical Standards M1.000 Eye Bank Records M1.100 Length of Storage • FDA Guidance - Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells,

	Tissues, and Cellular and Tissue-Based Products (HCT/Ps) - 2011 III - E. Do I Have to Follow CGTP Requirements if My HCT/Ps Are Also Regulated as a Biological Product, Drug, or Device?
12) When applicable, equipment must be properly qualified (IQ, OQ, PQ) before use as suggested in table 1.	• FDA Guidance - Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) 2011 Section X. Equipment - B. Do I Have to Qualify or Certify Equipment (Installation Qualification, Operational Qualification, Performance Qualification)?
13) Any automated, mechanical, electronic, or other equipment used for inspection, measuring, or testing must be capable of producing valid results.	• 21CFR1271.200 Equipment (a) General
14) A non-conformance related to an equipment must be documented and investigated as a deviation/nonconformance and corresponding corrective action must be applied.	• EBAA Procedures Manual Section G1.070 Deviation Investigation and Reporting Procedure
15) The Eye Bank, including its satellites, require specific equipment to be able to store, evaluate and process ocular tissue. Tissue processing must be performed in an environment that meets EBAA Medical Standard E1.200. Specific examples are as follows:	• EBAA Medical Standard E1.200 Processing and Preservation and C3.200 Equipment, Maintenance and Cleaning
A. An ISO 5 / Class 100 Biosafety Cabinet or Laminar Flow Hood	• FDA Guidance - Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) 2011 Section IX. Environmental Control and Monitoring Section C. Is Environmental Monitoring Required? Section E. How Often Should I Perform Environmental Monitoring?
1) Is required when processing tissue for surgical purposes.	
2) Must be certified before use, when relocated and at least annually thereafter. A viable and non-viable count should be performed as part of the annual certification.	
3) Unit must be cleaned and disinfected before use and between tissue from different donors.	• 21 CFR 1271.195 Environmental Control and Monitoring
4) Environmental Monitoring must be performed on a regular basis.	
B. Clean Room (Class 100/ISO 5) (optional)	• FDA Guidance - Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) 2011
1) May be used instead or BSC/Laminar flow hood when processing tissue for surgical purposes.	
2) Must be certified before use and at least annually	

thereafter. A viable and non-viable count should be performed as part of the annual certification.	Section VIII. Facilities C. Is it Necessary to Perform Different Operations in Separate Areas Within a Facility?
3) When an eye bank uses a clean room to process tissue, the room must be certified before use.	• EBAA Medical Standards E1.200 Processing and Preservation
4) The equipment that provides the HEPA filtered air to the room must be certified before validation.	• 1271.195 Environmental Control and Monitoring • https://isocleanroom.co.uk/blog/iso-5-defining-cleanroom-classification-guidelines/
5) Environmental monitoring must be performed regularly.	
6) The area in the room where tissue processing is performed must be cleaned and disinfected between tissue from different donors.	
C. A refrigerator	
1) Is required when storing media and tissue for surgical purposes.	• EBAA Medical Standards Section C3.200 Equipment, Maintenance and Cleaning
2) Must have a temperature display that can be verified without opening the refrigerator. The refrigerator's temperature must be recorded daily to ensure that the temperature remains within 2 – 8 ^{0} C. Temperature probe must reflect the temperature of the stored tissue under normal storage conditions.	• 21CFR1271 Subpart C Donor Eligibility 1271.60 What quarantine and other requirements apply before the donor - eligibility determination is complete? (a) Quarantine (b) Identification of HCT/Ps in quarantine. • https://restoresight.org/wp-content/uploads/2023/02/Final-Temp-Probe-White-Paper-8-2011-JD.pdf
3) The refrigerator must have instrumentation or a temperature monitoring device that records the temperature 24 hours a day, 7 days a week. If using a temperature chart recorder, the graph paper must be changed as prescribed by the cycle it covers, i.e., daily, weekly, or monthly. Alternatively, Electronic monitoring. The recording pen should never print over the same time period twice.	• EBAA Medical Standards Section C3.200 Equipment, Maintenance and Cleaning
4) The refrigerator alarm system must be tested at least annually.	• EBAA Medical Standards Section C3.200 Equipment, Maintenance and Cleaning
5) The inside of the refrigerator must be cleaned periodically with a hospital grade / EPA registered cleaning solution.	• Routine cleaning of the tissue storage area is essential for infection control and to prevent transfer of microorganisms.
6) The refrigerator must be solely used for the storage of tissue; tissue storage solution and respective processing supplies.	• OSHA Occupational Safety and Health 1910.1030 (d)(2)(x)

7) The refrigerator must have clearly segregated labeled areas for quarantined tissue, surgical tissue awaiting distribution, and research/training tissue.	• EBAA Medical Standards Section C3.200 Equipment, Maintenance and Cleaning Section I1.000 Storage • Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) 2011 Section XVII. Storage (1271.260) A What storage area activities must I control?
8) The eye bank must have a contingent plan established in the event the refrigerator malfunctions or there is a power failure.	• FDA 21CFR1271.260 Storage

E. An incubator – (optional)

1) The use for the unit must be properly established for warming tissue or growing microorganisms. The unit must solely be used for the established purpose. The eye bank must never use an incubator for dual purpose (growing microbes and warming up tissue) to prevent cross contamination.	• 21CFR.1271.200 Equipment (a) General
2) The incubator must be regularly cleaned / disinfected. Spills inside the incubator must be immediately cleaned and the unit disinfected.	• 21CFR.1271.200 Equipment (a) General (b) Equipment – Procedures and Schedules
3) The unit must have a temperature display so that the temperature can be verified without opening the unit's door.	• EBAA Medical Standards Section C3.200 Equipment, Maintenance and Cleaning

F. Specular microscope

1) Must be used to determine the cell density of the corneal disk tissue before it is distributed for transplantation.	• EBAA Medical Standards Section F1.000 Tissue Evaluation and F1.200 Endothelial Cell Density and Pachymetry
2) Images must be properly identified with tissue ID number.	• 21CFR1271.200 Equipment - (e) Records

G. OCT (optional) Optical Coherence Tomography

1) Pachymetry is required if an eye bank processes tissue for DSAEK and ALK. An OCT may be used to determine the corneal disc thickness.

2) If an OCT is used for this purpose, the unit must be cleaned, maintained, and annually verified.

- EBAA Medical Standards

  Section F1.000 Tissue evaluation

H. Centrifuge (optional)

1) Required if the eye bank centrifuges the donor's blood for serological testing.

2) All blood spills must be cleaned as described in respective eye bank's procedure.

- OSHA standards for bloodborne pathogens (BBP, 29 CFR 1910.1030) and personal protective equipment (PPE, 29 CFR 1910 Subpart I)

I. Sterilizer (optional)

1) It is required when the eye bank sterilizes their own instruments.

2) The sterilizer must be certified by a qualified vendor on a regular basis as determined by the eye bank.

3) The sterilizer must be cleaned as often as recommended by the manufacturer.

4) Acceptable parameters criteria for each load run must be established and described in the unit's standard operating procedure. Each load run must meet these acceptable criteria before considering the instruments sterile.

5) Certain physical indicators must be used during sterilization to ensure the unit is operating properly and that the load was sterilized (see respective procedure C3.300 Instruments, Cleaning and Maintenance)

- Refer to C3.300 Instruments, Cleaning and Maintenance for specific instructions.

J. Slit Lamp –

1) Is required when ocular tissue evaluation is performed by the eye bank.

2) Used to determine eye abnormalities / diseases as well as the presence of foreign bodies in the eye.

3) Records must be properly identified with tissue ID # and maintained for 10 years.

- EBAA Medical Standards
  Section F1.100 Slit Lamp Examination

K. Operating Microscope –

1) Required if the eye bank needs an augmented view of the tissue while processing (e.g., DMEK)

2) Must be cleaned and disinfected before use.

Table 1 Equipment Qualification, Calibration, and Preventive Maintenance Recommendations

Equipment	Equipment Uses	Qualification Required (IOPQ)	Recommended cleaning	Calibration, Preventive Maintenance (PM), Certification
Refrigerator	Tissue, reagent, and supply storage	Optional –thermal mapping performed before initially used.	Follow manufacturer's recommendation or at a minimum, Monthly	Temperature verification and PM
Refrigerator's temperature chart recorder	Same as refrigerator	Not required	N/A	Temperature verification and PM
Refrigerator's temperature monitoring device	Same as refrigerator	Recommended	N/A	Temperature verification and PM
Class II Biosafety type A2 or ISO 5 Laminar Flow / clean bench	Tissue Processing	Required	Before and after every Donor tissue processed	Certification, with viable and non-vial particle count
Clean Room (optional)	Tissue Processing	Required	Daily and between donors	Certification with viable and non-viable particle count and PM
Specular Microscope	Tissue Evaluation	Required	At a minimum, Monthly	Calibration and PM
Optical Coherence Tomography (OCT)	Tissue Evaluation	Not Required	At a minimum, Monthly	Calibration and PM
Sterilizer (optional)	Instrument sterilization	Required	At a minimum, Monthly	Calibration and PM
Centrifuge	Blood separation for serology testing	Not Required	At a minimum, Monthly	Speed verification and PM
Incubator	Tissue warming	Required	At a minimum, Monthly	Temperature verification and PM
Slit Lamp	Tissue Examination	Not Required	At a minimum, Monthly	Annual PM
Operating Microscope	Tissue Processing	Not Required	Before and after use	None

C3.300 Instruments: Cleaning, Disinfection, Maintenance, and Sterilization

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:

1. 21CFR1271 Human Cells, Tissues, and Cellular and Tissue-Based Products
2. Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)
3. ANSI/AAMI ST79:2017 & 2020 Amendments A1, A2, A3, A4 (Consolidated text) Comprehensive guide to steam sterilization and sterility assurance in health care facilities
4. ASCRS-ASORN Special Report, *Recommended Practices for Cleaning and Sterilizing Intraocular Surgical Instruments, (Feb 16,2007)*
5. www.ascrs.org/upload/ASORNSpecialTaskForceReport.pdf, 4/3/07.
6. Philips, N. F. (2013). Ch. 18 Sterilization. In S. Schrefer, & L. Wilson (Eds.), *Berry & Kohn's operating room technique* (Twelfth ed.) (pp. 303-327). St. Louis: Mosby.
7. Phillips, N. F. (2013). Ch. 17 Decontamination and Disinfection. In S. Schrefer, & L. Wilson (Eds.), *Berry & Kohn's operating room technique* (Twelfth ed.) (pp. 285-301). St. Louis: Mosby.
8. Phillips, N. F. (2013). Ch. 14 Surgical Microbiology and Antimicrobial Therapy. In S. Schrefer, & L. Wilson
9. (Eds.), *Berry & Kohn's operating room technique* (Twelfth ed.) (pp. 233-251). St. Louis: Mosby.

Glossary

1. ***IFU*** – Information for use provided by the manufacturer. These instructions include cleaners/disinfectants compatibility with the metals or alloys that instruments are made of. It also includes sterilization parameter limits.
2. ***Biological indicator (BI)-*** Biological sterilization process indicator device intended for use by a health care provider to accompany products being sterilized through a sterilization procedure and to monitor adequacy of sterilization. The device consists of a known number of microorganisms, of known resistance to the mode of sterilization, in or on a carrier and enclosed in a protective package. Subsequent growth or failure of the microorganisms to grow under suitable conditions indicates the adequacy of sterilization.
3. ***Positive biological indicator control-*** Biological indicator, from the same lot as a test biological indicator, which is left unexposed to the sterilization cycle and then incubated to verify the viability of the test BI.
4. ***Bowie-Dick test- Dart removal test*** Diagnostic test of a dynamic-air-removal in a steam sterilizer.
5. ***Challenge test pack-*** Pack used in qualification, installation, and routine quality assurance testing of sterilizers. See also **process challenge device.**
6. ***Chemical indicators (CIs)-*** Devices used to monitor the presence or attainment of one or more of the parameters required for a satisfactory sterilization process or used in specific tests of sterilization equipment.

a. ***Type 1 (process indicators):*** chemical indicators intended for use with individual units (e.g., packs, containers) to indicate that the unit has been exposed to the sterilization process and to distinguish between processed and unprocessed units.

b. ***Type 2 (Bowie-Dick test indicators):*** chemical indicators intended for use in a specific test procedure (e.g., the Bowie-Dick test used to determine if air removal has been adequate in a steam sterilization process).

c. ***Type 3 (single critical process variable indicators):*** chemical indicators designed to react to one of the critical variables and intended to indicate exposure to a sterilization process at a stated value of the chosen variable.

d. ***Type 4 (multicrltical process variable Indicators)*****:** chemical indicators designed to react to two or more of the critical variables and intended to indicate exposure to a sterilization process at stated values of the chosen variables.

e. ***Type 5 (integrating indicators)*****:** chemical indicators designed to react to all critical variables, with the stated values having been generated to be equivalent to, or exceed, the performance requirements given in the ANSI/AAMI/ISO 11138 series for Bis.

f. ***Type 6 (emulating indicators)*****:** chemical indicators designed to react to all critical variables of specified sterilization cycles, with the stated values having been generated from the critical variables of the specified sterilization process. ANSI/AAMI/ISO 11140-1 refers to these indicators as cycle verification indicators.

NOTE: FDA recognition of chemical indicators is limited to Type 1 process indicators; Type 2 indicators for use with special tests; and Type 6 emulating indicators (ANSI/ AAMI/ISO 11140-1:2014).

7. ***Critical Water (distilled, reverse osmosis or deionized water)*** Water that is extensively treated (usually by a multistep treatment process that could include a carbon bed, softening, deionization [DI], and reverse osmosis [RO] or distillation) to ensure that the microorganisms and the inorganic and organic material are removed from the water; a final submicron filtration could also be part of the treatment process. This water is mainly used for the final rinse or for steam generation.

8. ***Decontamination-*** Process of cleaning and disinfecting soiled medical products (e.g., instruments/devices) to render them safe for handling and to the extent necessary for subsequent processing.

9. ***Disinfection-*** Process that kills pathogenic and other microorganisms by physical or chemical means. NOTE-Disinfection destroys most recognized pathogenic microorganisms but not necessarily all microbial forms, such as bacterial spores. Disinfection processes do not ensure the margin of safety associated with sterilization processes.

10. ***Distilled water-*** Water that has been heated to the boiling point, vaporized to remove nonvolatile impurities. Cooled, condensed into a liquid condensate, and collected so that no impurities are reintroduced.

11. ***Deionized Water*** – water that has had ions removed. In water they appear as dissolved mineral salts.

12. ***Equipment qualifications (IOPQ) –***

    a. **Installation Qualification (IQ) -** Process of obtaining and documenting evidence that equipment has been provided and installed in accordance with its manufacturer's specifications.

b. **Operational Qualification (OQ) -** Process of obtaining and documenting evidence that installed equipment operates within predetermined limits when used in accordance with its operational procedures.

c. **Performance Qualification (PQ)** - Process of obtaining and documenting evidence that the equipment, as installed and operated in accordance with operational procedures, consistently performs in accordance with predetermined criteria and thereby yields product meeting its specification.

13. ***EPA* -** Environmental Protection Agency.
14. ***Event-related sterility maintenance*:** Sterility maintenance that is not based on expiration dating but rather on factors such as the quality of the packaging material, the storage conditions, the methods and conditions of transport, and the amount and conditions of handling.
15. ***Exposure time*-** Period for which the process parameters are maintained within their specified tolerances. In a steam sterilization process, exposure time is the period during which items are exposed to saturated steam at the specified temperature.
16. ***Sterilization*-** Validated process used to render a product free from viable microorganisms.
17. ***Sterilizer*:** Apparatus used to sterilize medical devices, equipment, and supplies by direct exposure to the **sterilizing agent.**
18. ***Validation*:** Documented procedure performed to obtain, record, and interpret the results required to establish that a process will consistently yield product complying with predetermined specifications.

Materials needed:

1. Soiled Instruments
2. Instrument Cleaner
3. Instrument Disinfectant
4. Instrument lubricant
5. Sterilizer

Procedure	Rationale/ Requirement Reference
An eye bank that cleans, decontaminates, and sterilizes instruments must have a standard operating procedure (SOP) that clearly describes these activities. Must include if the acceptable criteria were met for each sterilization run.	• 21CFR1271 Human Cells, Tissues, and Cellular and Tissue-Based Products – Part .200 Equipment
The eye bank must establish procedures to track instruments that were used on particular donors and tissue processing as well as instruments that are cleaned and sanitized together.	• Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)
The eye bank must comply with the ANSI/AAMI ST79 standard.	X. Equipment (1271.200) E. Are there Special Considerations for Cleaning and Sanitizing Equipment at Risk for Transmissible Spongiform Encephalopathy Contamination?

Procedure	Rationale/ Requirement Reference
The eye bank must maintain detailed records of the use of instruments, including ocular tissue ID processed with that instrument, the person(s) performing the work, and the dates of entries.	• 21CFR1271.270 Records – (a) General • 21CFR1271.200 Equipment (e) - Records

Procedure	Rationale/ Requirement Reference
1.1 Designate a separate room or area for the decontamination of reused instruments. This area should be separate from the clean designated area and sterilization area. The decontamination area should include functionally separate areas for; 1.1.1 Receipt and processing of contaminated items that require terminal sterilization after decontamination, 1.1.2 Receipt and processing of contaminated items for which the decontamination process incorporates disinfection procedures (i.e., terminal sterilization is not required), 1.1.3 Receipt and processing of equipment (e.g., powered equipment) that require manual disinfection after cleaning. 1.1.4 Workflow pattern that allows items to move progressively from being contaminated to being safe to handle, whether manually (i.e., a pass-through window) or via mechanical cleaning equipment.	• ANSI/AAMI ST79: • 3.3.6.1 - Decontamination area/room. • 3.2.2 Functional Workflow patterns Note: Separating "clean" and "dirty" areas limits environmental contamination and, therefore, the amount of bioburden on devices to be sterilized. Adherence to these functional design recommendations helps contain potential contaminants within a particular portion of the decontamination area and thus helps prevent cross- contamination or recontamination.
1.2 When using a cart to transport contaminated and sterilized instruments, you must segregate and designate areas within the cart for contaminated, disinfected, and sterilized instruments.	• ANSI/AAMI ST79: 3.3.6.1 Decontamination are/room
1.3 Separate soiled, in-use bottles of detergents, disinfectants, and other such supplies from extra supplies in storage so that personnel not wearing PPE can acquire the supplies for other areas without being exposed to contaminated items.	• Same as above
1.4 The Laboratory should have a separate sink for regular hand washing.	• ANSI/AAMI ST79: 3.3.6.1 Decontamination area/room

1.5 Traffic patterns should be designed to facilitate movement of personnel, equipment, and supplies into and out of defined areas within the sterile processing area. The sterile processing area design should include two designated areas that are defined by the activities performed in each area:

1.5.1 Unrestricted areas: These areas include locker rooms, break rooms, meeting rooms, offices, and sterilizer service access rooms. Street clothes are permitted in these areas. The specific areas where food and drink are permitted (e.g., break rooms, meeting rooms, offices) should be identified in the facility's policies and procedures.

1.5.2 Restricted areas: Areas in which decontamination, preparation and packaging, sterilization processing, sterile storage, and distribution are carried out. Personnel in the restricted areas should wear PPE attire and cover head and facial hair. Only authorized personnel and visitors accompanied by authorized personnel should be admitted to this area.

- Rationale: Personnel and visitors can carry microorganisms into processing areas, thus increasing the potential for environmental contaminants in these areas. It is important to protect personnel and visitors from the microorganisms present on contaminated items being processed in the decontamination area.
- NOTE: It is recommended that the sterilizer should be located in an area where the floor, walls and ceiling can withstand high levels of humidity.
- ANSI/AAMI ST79: 3 Design Considerations 3.2 Work area design and functional - 3.2.3 Traffic Control

1.6. Any connecting doors and pass-through windows should remain closed. In some instances, it might not be possible to physically separate the decontamination area from the clean work area, therefore a procedural barrier separation may be used to prevent splashing, the production of aerosols, and the contamination of clean items and work surfaces.

This work practice promotes the changing of PPE when personnel complete decontamination activities and perform clean (e.g., high-level disinfection) activities.

The ventilation and air-handling systems should move air from the clean side of the room to the decontamination side of the room and not the reverse.

- ANSI/AAMI ST79: 3.3.6.1. Decontamination area /room – refer to Note.

1.7. Decontamination side or area should include:

1.7.1 Storage of PPE, cleaning supplies, record-keeping, and cleaning verification supplies.

1.7.2 Trash containers for nonregulated waste (paper towels, wrappers

1.7.3 OSHA or EPA compliant containers for regulated waste (blood and body substances); containers for collection for devices for third-party reprocessing and sharps.

1.7.4 Ultrasonic cleaning devices, automatic washer accessories (e.g., ultrasonic cleaning solution, detergents, loading baskets, carts, and equipment).

1.7.5 Attached solid counters or adjacent work surfaces on which to place the soiled and clean items separately; and are large enough to allow a tray or container basket of instruments to be placed flat for pretreatment or manual cleaning.

1.7.6 May have two-section sinks available for soaking and rinsing prior to cleaning.

1.7.7 When designing this area, consider worktables that are made of non-porous materials (e.g., stainless steel).

- ANSI/AAMI ST79: 3.3.6.1.2 Space considerations

1.8 Always wear PPE, including protective clothing, head cover, gloves, mask, and eye while cleaning and decontaminating reusable instruments.

- Observe Standard Precautions to protect against transmission of bloodborne pathogens (HIV and hepatitis) and other infectious diseases.

1.9 Place contaminated instruments in a biohazard bin.

1.10 Follow detergent and instrument manufacturers' IFU to ensure proper use of the detergent and to ensure compatibility with the instruments.

- ASCRS-ASORN Special Report, Recommended Practices for Cleaning and Sterilizing Intraocular Surgical Instruments, (Feb 16,2007)

Procedure	Rationale/ Requirement Reference
1.11 Quality and volume of water should be used as specified by manufacturer's directions for use (IFU) for suspension of detergents and for cleaning and rinsing instruments. The IFU for many intraocular instruments require or recommend critical water for most cleaning steps.	• Same as above
1.12 Instruments designated for single use only should not be reused. Single-use devices do not include instructions for reuse or reprocessing. The FDA actively regulates third-party and hospital re-processors of single-use devices according to FDA guidance.	• Same as above
1.13 Instruments: Manual cleaning processes	• ASCRS-ASORN Special Report, Recommended Practices for Cleaning and Sterilizing Intraocular Surgical Instruments, (Feb 16,2007) - General Principles of Cleaning and Sterilizing Intraocular Surgical Instruments
1.13.1 Brushes used for cleaning should be designed for cleaning medical instruments.	
1.13.2 Cleaning tools such as syringes and brushes should be discarded after each use. If brushes are reused, they should be designed for reuse and they should be cleaned and high-level disinfected or sterilized, preferably after each use, or at least once daily.	
1.13.3 Cleaning solutions should be discarded after each use.	
1.13.4 Transfer the instruments to a designated basin or sink. Soak instruments in an EPA registered disinfectant according to manufacturers' guidelines/ directions.	• Same as above
1.13.5 When flushing is used as part of a cleaning technique, the effluent should be discharged into a sink or separate basin, so the fluid is not reused. Discharge of the effluent with minimal splash and aerosolization.	• Same as above
1.14 If an ultrasonic cleaner is used:	• ANSI/AAMI ST79: 7.6.4.4 Ultrasonic cleaning equipment • ASCRS-ASORN Special Report, Recommended Practices for Cleaning and Sterilizing Intraocular Surgical Instruments, (Feb 16,2007) – 9 If ultrasonic cleaner is used
1.14.1 Ensure that gross soil has been removed prior to placement in the ultrasonic cleaner.	
1.14.2 Check the manufacturer's IFU of instruments to identify instruments that should not be subjected to ultrasonic cleaning.	
1.14.3 An ultrasonic unit designated for cleaning medical instruments should be used.	
1.14.4 Ultrasonic machines must be emptied, cleaned, disinfected, rinsed, and dried at least daily and preferably after each use.	

1.14.5 Unless specified otherwise by the ultrasonic's manufacturer, cleaning should be peformed with an EPA-registered, facility-approved disinfectant and followed by critical or tap water rinse sufficient to fully remove the cleaning agent. If not contraindicated by the manufacturer, final rinse with 70% to 90% ethyl or isopropyl alcohol is recommended and unassociated with risk for fire.	• Same as above
1.14.6 The machine should be dried completely with a lint-free cloth.	
1.14.7 Refilling should occur immediately prior to use.	
1.15 Rinsing Instruments	• ASCRS-ASORN Special Report, Recommended Practices for Cleaning and Sterilizing Intraocular Surgical Instruments, (Feb 16,2007) – 11. Rinsing
1.15.1 Follow the manufacturer's IFU for selecting the appropriate type of rinse water for the equipment. Unless otherwise specified by the manufacturer's IFU, critical water should be used for the final rinse of instruments.	
1.15.2 Rinsing should provide flow of water through and/or over instruments, with effluent discarded as it is used so only debris-free water is used for rinsing.	
1.15.3 Agitation in a basin of water should not be used as a final rinse.	
1.16 Drying Instruments	• ASCRS-ASORN Special Report, Recommended Practices for Cleaning and Sterilizing Intraocular Surgical Instruments, (Feb 16,2007) – 12 Drying
1.16.1 Instruments should be dried thoroughly to avoid rusting. Use forced or compressed air to dry. The compressed air, preferably, should be filtered and free of oil and water.	
1.16.2 Once the instruments are completely dry, place them in a designated bin and transfer them to the clean work area.	

2.0 Clean Work Area

Procedure	**Rationale/ Requirement Reference**
2.1 The area/room used for the preparation and assembly of instruments and other items to be sterilized should be physically separated from the decontamination area/room. If physical separation of these areas/rooms are not possible, the clean work area/room should be thoroughly cleaned and decontaminated before used for preparation and assembly tasks.	• ANSI/AAMI ST79: 3.3.6.2 Clean work area/room
2.2 The clean work area/room should include:	• Same as above

2.2.1 Storage for head covers and gowns.

2.2.2 Detergents (not used in the decontamination area) and towels.

2.2.3 Monitoring and Record keeping Supplies (sterilization process monitoring devices, logbooks)

2.2.4 Packaging materials and preparation supplies (e.g., cotton balls, gauze dressing, tip protectors).

2.2.5 Incubators for Bioindicators.

2.2.6 Instrument storage and repair boxes.

2.2.7 Transfer carts.

2.2.8 Processing tables of non-porous materials.

2.2.9 Station for instrument lubrication

2.2.10 Testing equipment.

2.2.11 Battery rechargers.

2.2.12 Handwashing stations.

- Rationale: Lint and airborne particles can carry micro-organisms. A relatively lint-free environment is also important to the comfort and safety of employees. Providing adequate space for supplies and equipment and designing the layout to facilitate the flow of work through the various steps of preparation contributes to the efficiency and accuracy of the sterile processing staff.

2.3 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.

NOTE: DO NOT USE THE INSTRUMENT IF RUST IS PRESENT.

- ASCRS-ASORN Special Report, Recommended Practices for Cleaning and Sterilizing Intraocular Surgical Instruments, (Feb 16,2007) – 7.6.4.5 Verification of the cleaning process – see Rationale.

2.4 Lubricate instruments as per manufacturer's IFU.

- Protects instruments against rusting, staining, and corrosion.

2.5 Package or wrap instruments for sterilization and note the expiration date if applicable 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.

- 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).

2.6 Reusable 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.

2.7 Package separately for sterilization or include within enucleation instrument tray.

- EBAA Procedural Manual June 2021 – C3.300 Instruments, Cleaning and Maintenance – 11.

Procedure

Rationale/ Requirement Reference

3.0 Sterilization Area

- ANSI/AAMI ST79; 3.3.6.3 Sterilization Area

3.1 Should be located within the clean work room/area.

3.2 Instruments should flow from the preparation and packaging area to the sterilization area and then onto sterile storage or distribution.

3.3 Allow space for all methods of sterilization; the staging and loading of sterilizer carts; the storage of long, heat-resistant gloves, sterilizer cleaning supplies, and record-keeping supplies; and hand-washing stations.

3.4 Provide a holding area for load cooling on sterilizer carts.

3.5 Sterilizers should be located in a restricted-access area and not in high-traffic areas or near any potential sources of contamination, such as scrub sinks, clinical sinks or hoppers, wash sinks, or containers for the disposal of linen and trash.

3.6 Air intake or return ducts should not be located in the area designated for cool-down. The temperature in the sterilizer access area should not exceed that specified in the sterilizer manufacturer's written IFU.

3.7 Sterilizer must be qualified before use, A sample of the qualification is provided in Appendix 3.	• Current Good Tissue Practice (CGTP) and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) Section X. Equipment – • What Are the General Equipment Requirements? • Do I Have to Qualify or Certify Equipment (Installation Qualification, Operational Qualification, Performance Qualification)?
3.8 Collect the qualification information and verify that the unit has met all expected results and acceptance criteria. The eye bank must validate the sterilization process based on the acceptable results obtained during the unit's qualification.	
3.9 Use the load configurations established in the Performance Qualification when sterilizing instruments on a regular basis.	• 21CFR1271.270 Records – (a) General
3.10 Once the unit has been properly qualified (IOPQ), then is ready to be used to sterilize the instruments. Maintain the qualification documentation for at least 10 years.	
4.0 Sterile Storage	• ANSI/AAMI ST79; 3.3.6.4 Sterile Storage
4.1 The sterile storage room should be located adjacent to the sterilization area, preferably in a separate, enclosed, limited-access area.	
4.2 Closed or covered cabinets are preferable for high-traffic areas. Open or wire shelving is suitable for confined storage areas, provided that proper attention is given to traffic control, area ventilation, and housekeeping. Storage areas should be designed to protect sterile items and their packaging from damage	
Procedure	**Rationale/ Requirement Reference**
5.0. Sterilizer Cleaning and Maintenance	
The autoclave must be cleaned as often as recommended by the manufacturer using an EPA – registered cleaning and disinfecting agent. All cleaning and maintenance records must be kept for 10 years and readily available for site inspection.	• 21CFR1271.270 Records – (a) General
5.1 Chemical indicators or sterilization process indicators must be placed inside each instrument tray or wrapped kit/pouch. Indicators should be placed in an area that is the most difficult for the sterilant to penetrate.	• The term “chemical indicators” includes process indicators, chemical integrators, and air removal 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.
5.2 All articles to be sterilized must be wrapped in materials that meet recommended sterilization standards (See ANSI/AAMI ST79). 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.	• Terminally sterilized items should be wrapped appropriately and labeled with expiration information. IUSS should not be used as a substitute for sufficient instrument inventory.

5.3 Place steam indicator tape on the outside of each package. A lot number and expiration date must be designated and labeled on each item sterilized.

- External indicators are used to differentiate processed from non-processed items, not to establish whether adequate sterilization has taken place.

5.4 Document the date, lot number, load contents, the exposure time and pressure, operator name, and whether a biological indicator test was used and the test results for each sterilization cycle.

5.5 Annual certification/calibration/ preventive maintenance to verify the temperature, pressure and time must be conducted and documented.

5.6 Monitor the efficiency of the sterilization process at least once each week, but preferably daily, or as determined during the qualification process of the unit with a reliable biological indicator that employs spores of established resistance 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.

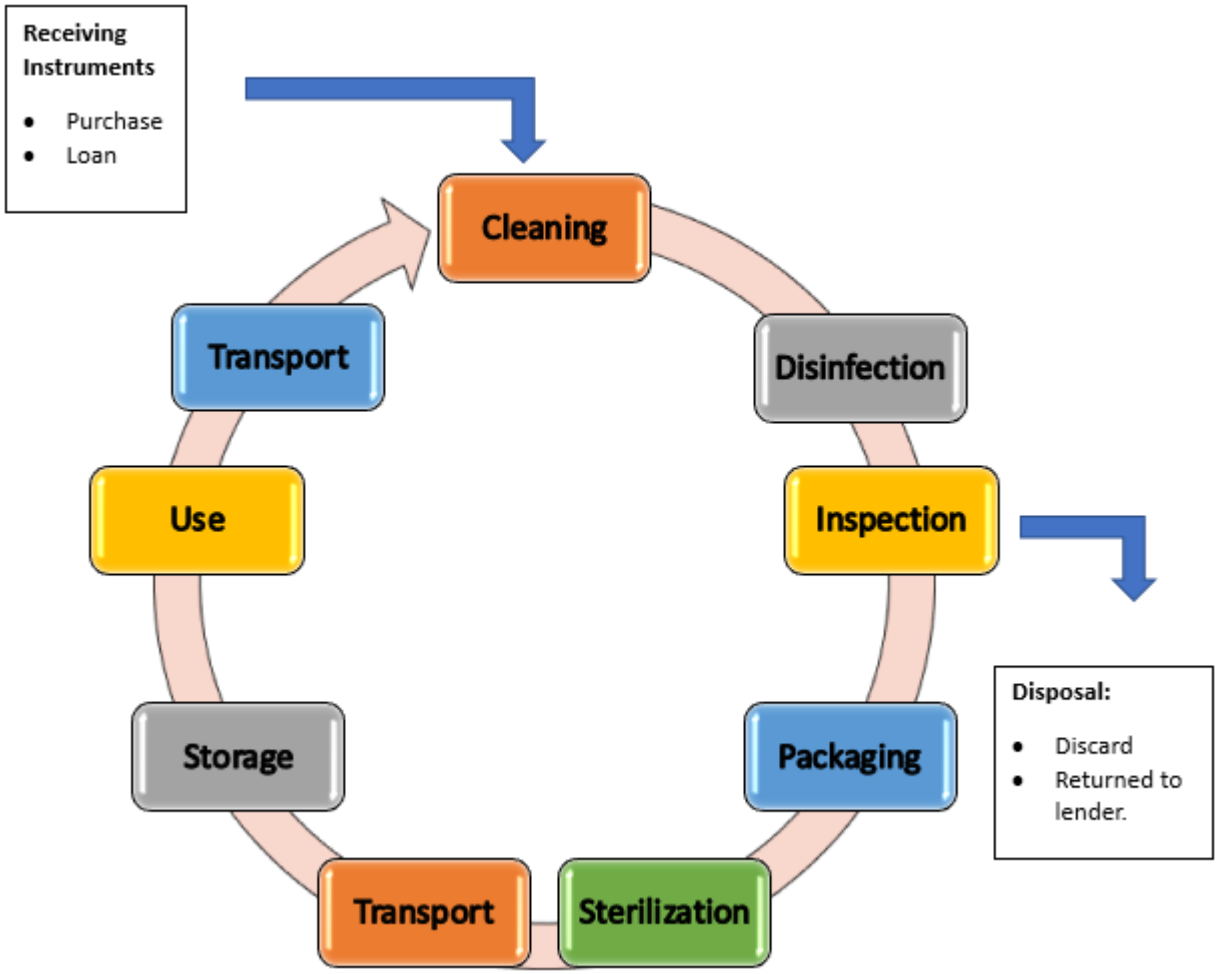
- 2021 EBAA Procedural Manual, June 2021 C3.200 Equipment, Maintenance and Cleaning 5(G)

5.7 Biological-indicator test packs shall be used during initial installation testing of steam sterilizers and following any malfunctions, major repairs, or relocation. Biological-indicator test packs should also be used routinely in sterilization loads at least weekly, but preferably daily.

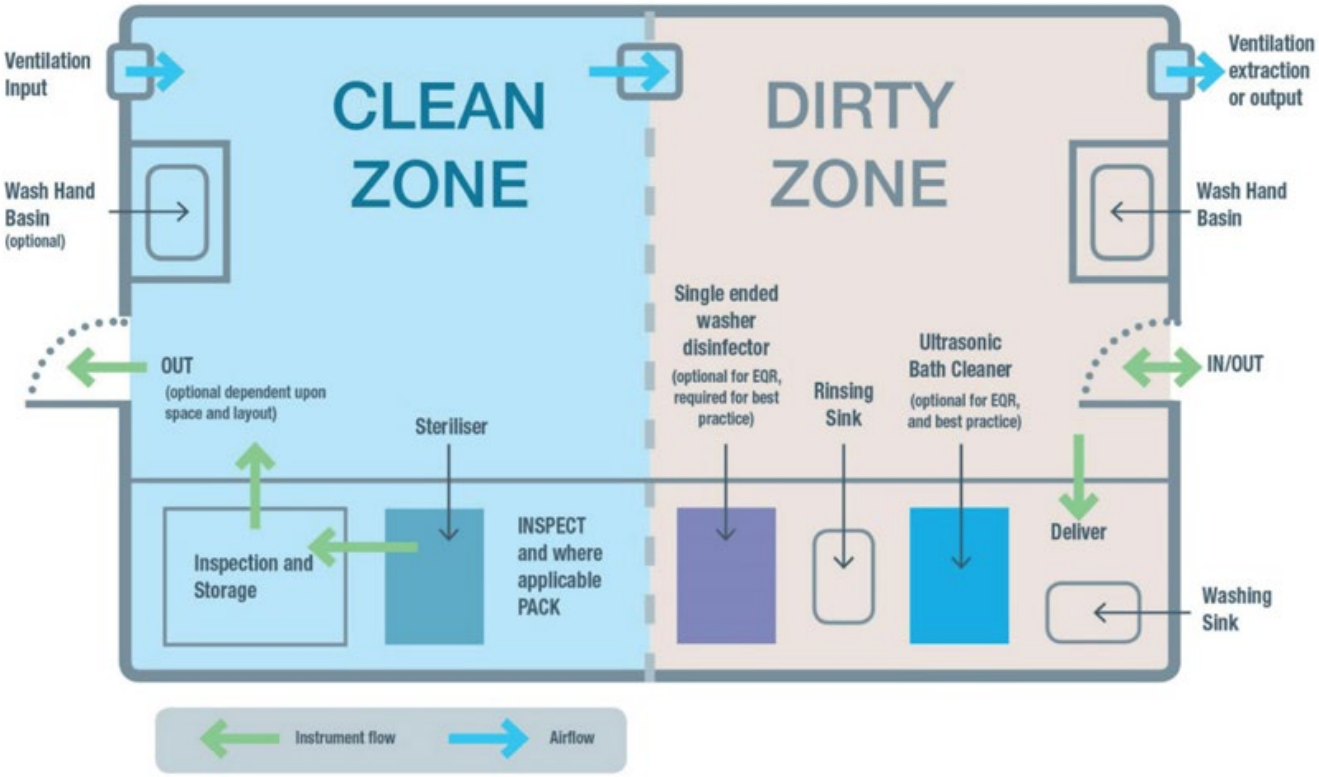
- The condition of the equipment, the expertise of the sterilization operator, and other factors determining success or failure of a steam sterilization cycle may vary. The less frequently a sterilizer is used, the greater the opportunity for an unnoticed problem that could affect sterilization. Biological-indicator test packs provide a useful means to monitor the efficiency of sterilization practices.

5.8 An eye bank that uses any other sterilizer must follow manufacturer's requirements and recommendations. The unit must be properly qualified (IOPQ) before use. The eye bank must properly determine which indicators to use for each run and the corresponding acceptable criteria that ensures that the run met such criteria.

Appendix 1: Workflow Diagram



Appendix 2: Example of Decontamination and Clean Areas in the Same Room



Appendix 3: Sterilizer Qualification Overview

E. Sterilizer Qualification (IOPQ)

E1. If an autoclave is used by an Eye Bank, the unit must be properly qualified (IOPQ) before use.

E2. You must include expected results and acceptance criteria for the section to be considered "pass or fail".

E3. Example of the qualification of the unit is described below:

E3.A Installation qualification (IQ) the following at minimum should be verified:

a) Purchase documentation verification must ensure that all paperwork from receipt matches unit being installed.

b) Equipment SOP verification (can be a draft) and other SOP's related to the qualification.

c) User manual review verification.

d) Environmental /installation Verifications (room humidity and temperature)

e) Utilities Verification (Electrical and water requirements)

f) If Unit comes with Software, a Communication Verification between unit and computer must be done.

E3.B Operation Qualification (OQ) verify:

a) Calibration verification – unit must be calibrated before this verification is performed.

b) Instrumentation qualification – Digital display must be verified.

c) Manufacturer's operation specification verification. Run unit empty and ensure that the unit reached expected temperature and pressure as described in the unit's operation manual. The eye bank should determine the heat distribution inside the unit. To determine if the unit has any spot inside the chamber that does not reach the temperature/ pressure at the established time. Map the chamber using previous results to establish time, temperature, and pressure.

d) Place a bioindicator (BI) and chemical indicators (CI) in different areas inside the unit as previously indicated. Map results and conclude if there is an area inside the unit that the BI fails to meet acceptable criteria.

E3.C. Performance Verification (PQ)

a) Verify different load configurations (small, medium and/or fully loaded configurations) to determine which configuration allows the heat/steam to be distributed in an effective manner.

b) Ensure that the configurations are well described including front view and top view. To simplify, Include photos.

c) Place the chemical indicators and bio-indicators where the heat might be hard to reach.

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.	7. Documents the dates of implementation, reviews and updates. See EBAA Medical Standards section C3.400.
8. Number all pages. Create a Table of Contents.	8. It will make referencing a section easier.
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.	10. See EBAA Medical Standards section C3.400.
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.	11. Promotes visibility and availability of pertinent policies and procedures to staff. Required by FDA sec. 1271.180.
12. Review the manual at least annually to identify any needed updates.	12. Maintains eye bank's practice in compliance with current standards and regulations. Required by EBAA Medical Standards C3.400.
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.	14. To document the staff's' comprehension of the policies and procedures.
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.	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 scapels/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.	12. An incident report should be completed indicating the treatment offered or action taken, as appropriate.
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.	13. It has been determined by CDC and OSHA that 1:10 dilution of sodium hypochlorite is very effective against HIV and HBV.
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	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:

Albiar, E. (1988). The impact of AIDS on corneal transplantation. *Insight (American Society of Ophthalmic Registered Nurses), 13*(1), 12, 16.

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Bialasiewicz, A. A., & Jahn, G. J. (1987). Screening for potentially pathogenic agents in cornea donors. *American Journal of Ophthalmology, 103*(1), 104-105.

Bohnke, M., & von Domarus, D. (1983). Hepatitis B surface antigen in a donor's eye. *Graefe's Archive for Clinical and Experimental Ophthalmology = Albrecht Von Graefes Archiv Fur Klinische Und Experimentelle Ophthalmologie, 220*(2), 84-86.

Caron, M. J., & Wilson, R. (1994). Review of the risk of HIV infection through corneal transplantation in the United States. *Journal of the American Optometric Association, 65*(3), 173-178.

Duffy, P., Wolf, J., Colins, G., DeVoe, A.G., Streeten, B., & Cowen, D. (1974) Letter: Possible person-to-person transmission of Creutzfeldt-Jakob disease. *New England Journal of Medicine*, 290(12), 692-693.

Gandhi, S. S., Lamberts, D. W., & Perry, H. D. (1981). Donor to host transmission of disease via corneal transplantation. *Survey of Ophthalmology, 25*(5), 306-311.

Gottesdiener, K. M. (1989). Transplanted infections: Donor-to-host transmission with the allograft. *Annals of Internal Medicine, 110*(12), 1001-1016.

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Hogan, R. N., & Cavanagh, H. D. (1995). Transplantation of corneal tissue from donors with diseases of the central nervous system. *Cornea, 14*(6), 547-553

Javadi, M. A., Fayaz, A., Mirdehghan, S. A., & Ainollahi, B. (1996). Transmission of rabies by corneal graft. *Cornea, 15*(4), 431-433.

Khalil, A., Ayoub, M., el-Din Abdel-Wahab, K. S., & el-Salakawy, A. (1995). Assessment of the infectivity of corneal buttons taken from hepatitis B surface antigen seropositive donors. *The British Journal of Ophthalmology, 79*(1), 6-9.

Koenig, S. B. (1999). Ch. 102 donor age. In F. S. Brightbill (Ed.), *Corneal surgery: Theory, technique & tissue* (3rd ed.) (pp. 875-881). St. Louis: Mosby.

Lam, D. S. (1995). Corneal transplantation and infectious hepatitis. *The British Journal of Ophthalmology, 79*(11), 1057.

Lee, H. M., Naor, J., Alhindi, R., Chinfook, T., Krajden, M., & Mazzulli, T. et al. (2001). Detection of hepatitis C virus in the corneas of seropositive donors. *Cornea, 20*(1), 37-40.

O'Day, D. M., & Khoury, J. M. (1999). Ch. 101 donor tissue selection. In F. S. Brightbill (Ed.), *Corneal surgery: Theory, technique & tissue* (3rd ed.) (pp. 869-875). St. Louis: Mosby.

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Raber, I. M., & Friedman, H. M. (1987). Hepatitis B surface antigen in corneal donors. *American Journal of Ophthalmology, 104*(3), 255-258.

Reinhart, W. J. (1997). Ch. 36 medical standards for eye banking. In J. H. Krachmer, M. J. Mannis & E. J. Holland (Eds.), *Cornea, fundamentals of cornea and external disease* (pp. 485-492). St. Louis: Mosby.

Salame, N., Viel, J. F., Arveux, P., & Delbosc, B. (2001). Cancer transmission through corneal transplantation. *Cornea, 20*(7), 680-682.

Sugar, J., & Mannis, M. (1997). Grafting and the risk of hepatitis transmission: Is there reason to be cautious? Are we cautious enough? *Cornea, 16*(2), 123-124.

Wagoner, M. D., Dohlman, C. H., Albert, D. M., Lavin, P., Murphy, A., & O'Neill-Dryja, M. (1981). Corneal donor material selection. *Ophthalmology, 88*(2), 139-145.

Zakov, Z. N., Dohlman, C. H., Perry, H. D., & Albert, D. M. (1978). Corneal donor material selection. *American Journal of Ophthalmology, 86*(5), 605-610.

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

well as the groin and behind the knees. Covered in E1.000	
AA. A review of all available records shall be performed by technical staff prior to recovery.	AA. To verify initial screening information and rule out potentially hazardous or contraindicated tissue for surgical use.
1) Medications, including antibiotics, should be recorded.	1) Antibiotics may be an indicator that the donor had an infection.
2) Temperature or temperature range over last 48 hours, noting any variations.	2) Elevation of temperature or hypothermia can be related to factors associated with an infectious process or altered metabolic or neurologic function.
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.	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) 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.	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) 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).	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) Notation of the interval between death, enucleation, excision and preservation.	6) See EBAA Medical Standard D1.500.
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.	4. See EBAA Medical Standards section K1.000.

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: 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.	4. Cause of death by “gross findings” will generally not include histology. Final autopsy reports should be obtained and reviewed when available.

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.	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) Consent/authorization may be obtained by any individual designated by his/her employing institution to present the option of eye donation to the family.	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) Consent/authorization must be witnessed in accordance with state law.	3) One or two additional witnesses may be required. Consult your state and local law.
4) Consent/authorization must clearly indicate permission for the ocular tissue donated. The next-of-kin should be	4) Permission for ocular tissue donation should provide the prospective donor's next-of-kin sufficient understandable information and

informed of the various recovery options and the factors that influence which will occur.

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.

opportunity to consider whether or not to agree to such donation. It should also minimize the possibility of coercion or undue influence.

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.

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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 recovery paperwork and note the time that cooling of the ocular tissue began.	5. This information should be used to evaluate the suitability of the corneal tissue for surgical use.

E1.000 Recovery, Open-Container Processing and Preservation

Reference:

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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:

Alp, B. N., Elibol, O., Sargon, M. F., Aslan, O. S., Yanyali, A., Karabas, L., Talu, H., & Caglar, Y. (2000). The effect of povidone iodine on the corneal endothelium. *Cornea*, 19(4), 546-550.

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Lindquist, T. D., Maxwell, A. J., Miller, T. D., Win'E, T. L., Novicki, T., Fritsche, T. R., Iliakis, B., & Montoya, M. M. (2011). Preparation of Corneal Donor Eyes Comparing 1% Versus 5% Povidone-Iodine. *Cornea* 30(3), 333-337.

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Nash, R. W., Lindquist, T. D., Kalina, R. E., (1991). An evaluation of saline irrigation and comparison of povidone-iodine and antibiotic in the surface decontamination of donor eyes. Archives of Ophthalmology. 109(6). 869-872.

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Materials Needed:

1. Sterile Supplies:

Sterile ophthalmic irrigating solution; e.g. normal saline or balanced salt solution
Sterile 5% povidone-iodine 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
1. Ensure appropriate supply before traveling to donor site. 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.	1. To assure sterility of instruments and supplies.

2. Verify consent for ocular tissue removal. 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 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.	2. To verify whether consent is for whole eyes or corneas only and that consent is valid prior to removal of any ocular tissue.
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.	3. To verify the accuracy of all reported information.
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.	4. To verify the accuracy of all reported information.
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.	5. To protect the eye bank technician from potential exposure to infectious disease.
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	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

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).	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. Draw a blood sample. 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.	7. To obtain the serum necessary for EBAA and FDA required serology testing.
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.	8. To prevent the introduction, transmission, and spread of communicable disease. See FDA sec. 1271.190.
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.	9. To ensure a clean area for set up of the sterile field.
10. Prepare the donor.	
A. Elevate the donor's head if this has not already been done.	A. To prevent pooling of blood in the orbital area which could lead to excessive bleeding, swelling, and bruising post ocular tissue removal.
B. Gently open each eye-lid and thoroughly	B. To remove debris, microorganisms and

irrigate the corneal and conjunctival sac of each eye following the procedure approved by the eye bank medical director. The procedure must include 2 rinses with a 5% povidone-iodine (PI) solution that covers the entire corneal surface, conjunctiva, lids, and lashes. The contact time for each application must be between 2 and 5 minutes and the PI shall be irrigated between applications. 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 should be given to rinse PI solutions and antibiotics from each eye with sterile ophthalmic solutions such as sterile saline within reasonable time limits.

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, a 5% povidone-iodine solution shall contact all ocular tissue intended for transplantation twice between the time of the donor's death and tissue preservation. The concentration (5%), volume of solution, and the duration of ocular surface exposure (2-5 minutes) to the solution shall be specified in the eye bank's operating procedures and approved by the Medical Director.

C. Clean the orbital area and surrounding skin, using alcohol or gauze moistened with water.

C. To remove gross blood, dirt, or debris from the donor's skin.

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.

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.

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 excision, set up the vials or chambers containing corneal preservation medium adjacent to your sterile field, but not touching the field.	A. Develop a sterile conscience to protect the sterile field from inadvertent contamination.
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).	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. Don sterile sleeves using aseptic technique. Double glove if this is your eye bank's policy. Powdered gloves should not be used.	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. Don sterile sleeves by slipping on and over gloved hands.	D. If double gloving, the second pair of gloves is donned after the sterile gown or sleeves.
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	12. The drape(s) provides the technician with

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.

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.	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	Set up the sterile right and left eye jars. Check instruments to be sure none are missing or damaged.	2. Ensure all necessary supplies/instruments are present prior to beginning the aseptic recovery
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.	3. This provides access to the eye during the enucleation procedure.
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^{o} around the cornea.	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	Insert the closed scissors under the conjunctiva and perform a blunt dissection.	5. To facilitate access to the ocular muscles.

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.	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 the muscles. The sclera is thinnest underneath the insertion sites of the ocular muscles. Do not traumatize the cornea during this procedure.
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.	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. 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.	8. The globe will be completely removed from the socket after this step.
9. Secure the eye in a sterile eye jar that can be sealed from the environment. Using a dental 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.	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. 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).	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.
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	A. Gently remove drapes so as not to damage the donor's skin or accidentally remove eyebrow or eyelashes.
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.	B. To restore the appearance of the donor. Minimal or gentle manipulation of the eyelids will help decrease post-mortem discoloration and swelling.
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.	C. These procedures may be developed in consultation with your local funeral directors, hospitals, and skin or tissue bank(s).
D. Leave the donor's head elevated.	D. Promotes blood and fluid to drain away from the face to reduce bleeding and swelling.
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.	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. 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.	F. The non-sterile labels are added to the jars after-sterile handling of the exterior is completed.
G. Record information about the enucleation in the donor's medical record according to your eye bank's policy.	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.	I. These procedures may be developed in consultation with your local funeral directors, hospitals, and skin or tissue bank(s).

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.

K. Disposable instruments should be discarded as 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.

L. Be sure that used non-disposable instruments are marked as biohazardous during transport.

M. Transport the eyes to the eye bank as soon as possible.

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, 5% povidone-iodine 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
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 2 applications of povidone-iodine, followed by a normal saline or balanced salt solution rinse. The povidone- iodine solution concentration must be 5%.	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 twice 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.	2. Performing a procurement culture is at the discretion of the eye bank's medical director.
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.	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.
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.	5. Take care not to touch cornea with the solid blade eye speculum when placing it under the eyelid.
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.	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. 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.	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.	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. 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).	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. 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.	10. The risk of endothelial trauma or corneal contamination is greatest at this stage of the excision process.
11. Cultures of the incision site may be taken at this time, per your eye bank's policy.	11. Culturing is performed at the discretion of the eye bank medical director.
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.	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.	13. To avoid stretching or folds leading to potential loss of endothelial cells. To avoid contamination of the ocular tissue.
14. Continue to hold the cornea by the scleral rim with the small-toothed forceps, transfer it to a labeled storage medium container. The preloosened 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.	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. Examine the posterior chamber for a crystalline lens.	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.
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.	A. Sharps are disposed as soon as possible to decrease the risk of exposure to contaminated sharps.
B. Remove drapes. Insert eye caps. Close the eyelids and remove all remaining prep solution with gauze and water or alcohol.	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. Leave the donor's head elevated.	C. Promotes blood and fluid to drain away from the face to reduce bleeding and swelling.
D. Record information about the excision in the donor's medical record according to your eye bank's policy.	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.

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.

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.

H. Disposable instruments should be discarded as sharps in a sharps container.

I. Rewrap non-disposable instruments for return to the eye bank or for cleaning and sterilization by the facility if necessary.

I. Be sure that used non-disposable instruments are marked as biohazardous during transport.

J. Transport the corneas to the eye bank as soon as possible.

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 *Standard Precautions* 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^{o} 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.

10. Inject or transfer blood slowly and carefully into tube to prevent hemolysis.

11. Use ***Standard Precautions***. Do not recap needle. Discard into appropriate sharps container.

11. See procedure C3.600.

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.

14. Freezing will hemolyze the cells and make it virtually impossible to obtain serum.

15. Transport specimen to laboratory

15. Ship blood and tissue according to your state and federal guidelines.

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

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.

    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
5 % 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. Place a 5% povidone-iodine solution container near the eye jars and medium vials, 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 5% povidone-iodine solution for 2 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 between povidone-iodine applications 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). Per EBAA medical standards, a 5% povidone-iodine solution shall contact all ocular tissue intended for transplantation twice between the time of the donor's death and tissue preservation.

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

13. 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.

14. 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. T
p

15. 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.

16. Record the method and date of storage on the tissue report form.

17. 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.

15. 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
5% povidone-iodine solution
2 vials corneal storage medium
2 sterile corneal containers (e.g. corneal viewing chambers)
2 mini tipped culturettes (if cultures are performed by 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
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.	1. Minimizes the risk of contamination by providing a decontaminated work surface. Allows laminar flow to be established.
2. Don appropriate protective apparel consistent with the biological safety cabinet being used. 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.	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.
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. Place a 5% povidone-iodine solution container near the eye jars and medium vials, according to your eye bank's policy.	5. Antibiotic or antiseptic application to the whole eye prior to corneal excision reduces the microbial population. Refer to EBAA Medical Standard E1.110. A 5% povidone-iodine solution shall contact all ocular tissue intended for transplantation twice between the time of the donor's death and tissue preservation.

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.

8. This is used to hold the eye during the corneal removal.

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.

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

10. Soak or irrigate the eye using a 5% povidone-iodine solution for 2 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 between povidone-iodine applications over a metal instrument pan or a moisture impermeable drape.

10. Studies have shown that whole globe immersion is superior to irrigation for removal of microbes (see reference list). Per EBAA medical standards, a 5% povidone-iodine solution shall contact all ocular tissue intended for transplantation twice between the time of the donor's death and tissue preservation.

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^{o} around the cornea using small-toothed forceps and iris or tenotomy scissors, leaving about 2mm of conjunctiva evenly around the cornea.

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. 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.	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.
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.	15. Perforation of the choroid causes vitreous leakage, which may collapse the globe including the anterior chamber. This would compromise the corneal endothelium.
16. Extend the scleral incision 360^{o} 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.	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. Keep the incision parallel to the limbus to 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.	17. Scleral rim width is important because some surgical corneal holding devices require a minimum 3 mm rim while other 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 peritomy. Use of a scoring trephine may help to achieve consistent rim sizes.
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.	18. The risk of endothelial trauma and cell damage is greatest at this stage of the excision process.
19. A culture of the incision site may be performed at this time, per your eye bank's policy.	19. Culturing is performed at the discretion of the eye bank medical director.

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.	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. 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.	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. Examine the posterior chamber for crystalline lens.	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).
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 according to each eye bank's policies and procedures.	25. See procedures I1.000 and J1.000.
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 / clean 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.

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. See EBAA Medical Standards C3.300.
28. 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 for 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 making 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**
1. Establish guidelines which deem outcomes from processing as acceptable or not- acceptable, including, but not limited to:	
a. Target and/or minimum/maximum stromal bed thickness.	a. To identify desired thickness post-cut.
b. Post-processing endothelial cell count.	b. To ensure adequate cell viability following surgery.
c. Uniformity of cut.	c. To ensure transplant adheres properly.
d. Absence of perforation.	d. Perforated cornea would indicate traumatized tissue.
2. Select appropriate donor tissue (cornea or whole globe).	2. To ensure suitable tissue is identified and used.

3. Clean work area with a disinfectant where processing will occur and document cleaning.	3. To minimize the risk of contamination by providing a decontaminated work surface.
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 flow hood 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.	
10. Set up microkeratome system and run appropriate system checks according to manufacturer's recommendations.	10. To ensure equipment functions properly prior to use.
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.	11. To determine initial corneal measurements.
12. For corneal tissue, use an anterior chamber:	12.
a. Place cornea on artificial chamber, taking care not to fold cornea, induce stress lines, or traumatize the endothelium.	a. The risk of endothelial trauma and cell damage is greatest at this stage (and step "l" below) of the lamellar processing.
b. Center tissue.	b. To ensure cut is central to help promote an

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

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.

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

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 Ster-
ile 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 tomanufacturers' 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.	3. To set up a sterile field.
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.

7. Avoid contamination of tissue or damage to the corneal endothelium during this step.

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.

8. This is particularly important if transferring from Optisol to MK, etc., which is essential information for tissue used for refractive keratoplasty (epikeratoplasty.)

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.

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 Ster-

ile 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 Arti-
ficial anterior chamber

Non-Sterile Supplies

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

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

3. Turn on femtosecond laser and perform appropriate warm up procedure.	3. Perform in accordance with laser manufacturer's recommendation, to ensure equipment functions properly prior to use.
4. Don appropriate attire and personal protective equipment consistent with surgical environment (e.g. operating room).	4. To prevent exposure to open wounds, non-intact skin, or mucus membranes such as in the nose or eyes.
5. Carefully check and confirm the laser parameters and settings desired by the trans- planting surgeon for the corneal tissue. Set laser according to these parameters.	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. With approved decontaminant, clean work area and surfaces where processing will occur and document.	6. To minimize the risk of contamination by providing a decontaminated work surface.
7. Using aseptic technique, establish sterile field(s). Aseptically present all sterile items to the field as needed for the procedure.	7. To ensure all necessary supplies are delivered to the sterile field in an aseptic manner.
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.	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.	9. Have all necessary supplies ready for processing to minimize the length of time the cornea is out of the container and exposed.
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.	10. To determine initial corneal measurements.
11. For corneal tissue, use an artificial anterior chamber:	11.
a. Place cornea on artificial chamber, taking care not to fold cornea, induce stress lines, or traumatize the endothelium.	a. High risk of endothelial trauma and cell damage at this stage.
b. Center tissue.	b. To ensure dissection is central to help promote a uniform graft thickness.
c. Secure helmet.	c. To keep cornea in place during processing.
d. Tighten cornea into place.	d. To ensure cornea is securely positioned between piston and helmet.
e. Pressurize the chamber.	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.	f. Mark cornea as per surgeon's request. Beware the potential toxicity ink (e.g. gentian violet) on the endothelium.
g. Lower the laser head and applanate sterile contact lens onto the cornea.	g. Ensure that applanation is complete and centered onto the cornea.
h. Emit the laser.	h. Allow laser to run its full cycle. Take care not to move laser or surgical table during emission.
i. Using fine forceps and a fine blunt instrument perform detachment of cleavage plane to loosen stromal adhesions and tissue bridges.	i. Take care not to damage cap/button and to inspect for damage tissue.
j. If needed, perform depth and diameter measurements of anterior cap and/or posterior stroma.	j. To verify the target stromal bed/cornea button thickness and the target diameter of the graft was achieved.
k. If needed, replace and center the cap. Ensure cap is secure.	k. Replacing the cap limits the exposure of stromal lamellae to storage media, slowing edema.
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.	l. High risk of endothelial trauma and cell damage is greatest at this stage of processing.
12. Place corneal tissue into sterile media solution and container.	12. To maintain tissue viability and to provide storage of the tissue.
13. Label container.	13. Ensure tissue is appropriately identifiable.
14. Perform above procedure for mate tissue, if desired.	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. Perform a post-processing slit lamp and specular microscopy (if required) evaluation of the 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 Medical 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.

Giebel, A.W., Price F.W. (2009). Descemet's Membrane Endothelial Keratoplasty (DMEK): The Bare Minimum. In F.W. Price & M.O. Price (Eds.) DSEK, what you need to know about endothelial keratoplasty (pp. 119-146). Thorofare: Slack.

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

Kruse F, Laaser K, Cursiefen C, et al. (2011). A Stepwise Approach to Donor Preparation and Inser- tion Increases Safety and Outcome of Descemet Membrane Endothelial Keratoplasty. *Cornea*; 30:580-587.

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McCauley M, Price F, Price M. (2009). Descemet Membrane Automated Endothelial Keratoplasty, Hybrid Technique Combining DSAEK Stability with DMEK Visual Results. *J Cataract Refract Surg*;35:1659-1664.

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.

Studeny P, Farkas A, Vokrojova M, et al. (2010). Descemet Membrane Endothelial Keratoplasty with a Stroma Rim (DMEK-S). *Br J Ophthalmol*;94(7):909-914.

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 Sinskey 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 flow hood 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.	
10. Continue to the following steps according to method selected: • Femtosecond/microkeratome – Step 11-12 • Pneumatic dissection – Step 13 • Peeling dissection – Step 14	10. Different methods may be utilized to obtain the graft. The pneumatic and peeling dissection technique does not utilize microkeratome or femtosecond laser.
11. Perform an anterior lamellar resection with either a microkeratome or femtosecond laser.	11. Refer to E1.222 if utilizing a microkeratome and E1.225 if utilizing a femtosecond laser.
12. Begin preparing Descemet's Membrane graft.	
a. Anterior cap should remain detached.	a. Allows for access to posterior stroma.
b. Inject air in to posterior stroma to detach Descemet's Membrane and obtain approximately a 6-8 mm central bubble for DMAEK tissue.	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. Coat endothelium with viscoelastic.	c. Protects endothelial cells during manipulation of tissue.
d. Use 15 degree blade and Anwar scissor to cut and remove posterior stroma.	d. This step is not performed if tissue is a DMEK graft. Use of trypan blue assists in visualization during processing.
e. Use air to elevated Descemet's Membrane and re-attach anterior stromal cap.	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.	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. Once the needle is approximately 2mm from the limbus and properly positioned, inject air.	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. Once the bubble is achieved, do not push air vigorously. The bubble may be expanded with gentle pressure.	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. Once the bubble has been achieved, measure the size with a caliper in order to ensure adequate graft size.	d. Take care not to touch the membrane while measuring the size of the bubble.
e. Deflate the bubble by piercing the anterior stroma with scissors or a sharp blade.	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. Optional step. Stain DM with trypan blue and rinse with BSS.	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.	a. Use non-particulating surfaces and sponges when possible.
b. Score the DM at the limbus.	b. Care must be taken to minimize tears and minimize the depth of scoring to just beyond DM.
c. Place a few drops of trypan blue on the endothelium to stain the tissue .	c. This aids visualization of the exposed membrane at the limbus.
d. Rinse the trypan blue with BSS and fill the endothelial side with a few drops of corneal storage solution.	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. Optional step: seat the cornea in a suction block to aid handling of the tissue.	e. This will allow for easier manipulation of the membrane.
f. Stain the DM with trypan blue and rinse with BSS.	f. Aids visualization of any damage induced by the procedure.
g. Begin peeling the membrane from the scored edge using tying forceps.	g. If the membrane begins to tear, stop the peeling from that location and begin at another location.
h. Continue peeling until the membrane is freed as much as required to provide a large donor area for the surgeon.	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
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.	1. Sclera must be preserved using aseptic technique, the same as when preserving corneal tissue for transplantation.
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.	2. See procedures E1.200.
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.	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.
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.	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.
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.	5. Running scissors between the sclera and choroid layers helps to gently separate the choroid layer from the scleral wall and facilities a clean dissection of the intraocular material.
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.	6. Facilitates complete removal of all tissue or particulate material. Antibiotic soak loosens any remaining tissue fragments and reduces the microbial flora.

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.	7. Due to the dehydration of the scleral tissue, re-shaping becomes difficult, even after soaking in sterile normal saline prior to surgery.
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.	10. Prevents contamination of ocular tissue by leakage or evaporation (for alcohol preservations). Break in seal indicates tampering and potential contamination.
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.	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.
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.	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., Beurerman, 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
1. Cryopreservation • Donor corneas may 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.	• 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.
2. Glycerin • Donor corneas may be stored in glycerin for a period of time validated by the eye bank, and not to exceed the expiration date of the medium or container.	• If an eye bank elects to use glycerin methods, a detailed policy and procedure shall be included in the eye bank's written policies and procedures manual.
3. Irradiated • Donor corneas may be irradiated E-beam or Gamma and stored in albumin for a period of time validated by the eye bank, and not to exceed the expiration date of the storage medium or container.	• If an eye bank elects to use irradiation methods, a detailed policy and procedure shall be included in the eye bank's written policies and procedures manual.
4. Organ Culture • Donor corneas may be preserved for longer periods, i.e., 1 month or more, using organ culture techniques. These preservation methods are more complicated than preservation in short or medium-term corneal storage medium and are not common in the U.S. at present. Organ culture is reported to be the preservation method of choice in the United Kingdom and some western European countries.	• If an eye bank elects to use organ culture methods, a detailed policy and procedure shall be included in the eye bank's written policies and procedures manual.

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 clear zone measurement: Expressed in millimeters, the diameter of the clear central cornea free of arcus only
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
Clear zone: Measurement of diameter (in millimeters) of the clear central cornea, free of neovascularization, pterygia, arcus, or other stromal anomalies
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
Corneoscleral size measurement: Expressed in millimeters, the size of the entire corneoscleral disc between its narrowest and widest aspects
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
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
Keratic precipitates: Inflammatory cells found on the endothelium
Polymegathism: Variations in endothelial cell size with some cells appearing larger than normal
Rim size measurement: Expressed in millimeters, the width of the scleral rim at the narrowest and widest

points

Scar measurement: General depth, location and size of a scar. A scar is an aberration of a cornea, primarily visualized in the stroma, representing past surgery, injury or infection

Slit lamp biomicroscope: A binocular microscope with varying magnification settings attached to a light source with varying intensity settings

Stress lines: Evidence of corneal endothelial stretching that appears as a streak or a line in a linear fashion (e.g., snail tracks)

Striae: Grayish white lines within the stromal layer which are caused by swelling between layers of the corneal stromal collagen

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

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. For a preserved corneal evaluation DO NOT OPEN the storage container.	7. This prevents excessive drying and possible contamination of corneal epithelium. 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^{o} to 20^{o} angle of incidence and then moved to scan the entire cornea.	9. To properly evaluate and see endothelium, the angles indicated must be observed.
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.	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. Make notations on the donor information form regarding the evaluation and what was observed during initial evaluation.	11. After preserving ocular tissue, the initial evaluation may differ from final 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.	12. It is important to record quality of ocular tissue when determining whether it is suitable for surgery. See the attached table for recommended minimum standards for surgical suitability by surgery type.
13. Evaluate and record the minimum information below:	13. 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 F1.100.
A. Measurement of arcus clear zone	A. Clear zone measurements are acknowledged to impact surgical suitability determination more significantly for surgery types utilizing the anterior corneal segment. Eye banks are encouraged to provide a measurement free of neovascularization, pterygia, arcus or other stromal anomalies if that measurement may responsibly improve or otherwise clarify surgical suitability determination.
B. Measurement of any scars	B. A scar should be described by a few consistent parameters (e.g. “shallow anterior,” “full-thickness”) to ensure effective communication between the eye bank and transplanting surgeon or another importing entity.
C. Measurement of rim size and corneoscleral size	C. Rim width and corneoscleral size are important for surgical preparations requiring

	artificial anterior chambers (the scleral rim serves as the gasket on these devices) and in surgeries where the periphery or stem cells are used (e.g. KLA).
D. Folds or striae, noting severity E. Presence or absence of epithelial defects, and amount F. Presence or absence of guttata change and amount G. Presence or absence of stress lines H. Presence or absence of polymegathism or pleomorphism and amount I. Evidence of any technical problems in removal J. Presence of any infiltrates or foreign bodies	
14. 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.	14. Document each slit lamp examination of tissue intended for transplant.

Recommended Mimimum Standards for Surgical Suitability by Surgery Type						
These are recommended minimum standards. Ultimately tissue suitability is left to the discretion of the tranpslanting surgeon.						
	Epithelium	Stroma	Descemet's	Endothelium	Rim and C/S Size	Other
PK	Any condition of epithelium is acceptable. Pterygium must be outside of intended graft area.	No infiltrates. No evidence of prior refractive surgery affectingintended graft area. No laser photoablation surgical history. Foreign bodies, neovascularization, penetrating scars, or anterior scars of visual significance must be outside of indended graft area.	No Descemet's membrane detachment or tears within intended graft area.	No evidence of endothelial dystrophy.	N/A	No history of Down Syndrome or evidence of ectastic dystrophy.
ALK	Any condition of epithelium is acceptable. Pterygium must be outside of intended graft area.	No infiltrates. No evidence of prior refractive surgery affectingintended graft area. No laser photoablation surgical history. Foreign bodies, neovascularization, penetrating scars, or anterior scars of visual significance must be outside of indended graft area.	Any condition of Descemet's membrane is acceptable.	Any condition of endothelium is acceptable.	N/A	No history of Down Syndrome or evidence of ectastic dystrophy
DSEK/DSAEK	Any condition of epithelium is acceptable.	No infiltrates. No Foreign bodies or penetrating scars within the indended graft area.	No Descemet's membrane detachment or tears within intended graft area.	No evidence of endothelial dystrophy.	Corneoscleral disc size and rim size should be suitable for mounting on anterior chamber for processing.	N/A
DMEK	Any condition of epithelium is acceptable.	No infiltrates. No foreign bodies.	No Descemet's membrane tears within intended graft area.	No evidence of endothelial dystrophy.	Must be sufficient for intended use.	N/A
KLA	Any condition of epithelium is acceptable.	No infiltrates.	Any condition of Descemet's membrane is acceptable.	Any condition of endothelium is acceptable.	Conjunctiva must be intact over sufficient portion of rim.	No history of melanoma or metastatic cancer of a solid organ. Conjunctival and limbal area must be free of evidence of disease or dystrophy. Rim portions may be concidered from mated pairs.
K-Pro	Any condition of epithelium is acceptable. Pterygium must be outside of intended graft area.	No infiltrates. No evidence of prior refractive surgery affecting intended graft area. Foreign bodies or anterior scars of visual significance must be outside of intended graft area.	Any condition of Descemet's membrane is acceptable.	Any condition of endothelium is acceptable.	N/A	N/A
Long-Term Cornea Preservation /Other	Pterygium must be outside of intended graft area.	No infiltrates.	Any condition of Descemet's membrane is acceptable.	Any condition of endothelium is acceptable.	Must be sufficient for intended use.	N/A
Sclera	Any condition of epithelium is acceptable.	No infiltrate on corresponding cornea.	Any condition of Descemet's membrane is acceptable.	Any condition of endothelium is acceptable.	N/A	No history of melanoma or metastatic cancer of a solid organ.

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 hand-book 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:

Endothelial cell density: The average calculated number of endothelial cells per square millimeter
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 aiding in the analysis of the size, shape and density of endothelial cells
Stress lines: 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.

General Limitations:

Specular microscopy is limited in its ability to perform an overall assessment of the cornea or corneal endothelium due to: a) the lighting angle and magnification are specialized to view endothelium only; b) clear specular imaging can only be achieved in an annular region between the center and periphery; c) it is incapable of cross-sectional viewing or useful microscopy in other layers; and d) the efficacy of automated algorithms to calculate cell density is reduced as image clarity reduces (primarily a function of both magnification, cellular deturgescence, and location on the cornea).

Additional Functions:

Some newer specular microscopes now enable a diffuse-lighting view of an endothelium for better observation of endothelial topography. The last two generations of specular microscopes have enabled pachymetry via graduated zoom synchronized to linear distance, measured in microns, to measure the distance between epithelium and endothelium**.**

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 specular image 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. Specular image should ideally be flat or with minimal folds, in focus, free of debris and RBC (if possible), and adequately warmed. Note: Allowing additional warming time may assist in resolving image quality issues. The more cells or fields analyzed, the more representative it will be of the whole corneal endothelium. The best specular images are found the central/peri-central area. 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 and/or multiple fields should be captured, counted, and/or averaged. The algorithm type should be "Center Method" or "Variable Frame" (these methods have been validated by the manufacturers). 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 overall shape of the area to be analyzed (variable frame = traced area defines shape, center method = bordering cells define shape) should be smooth and without "tentacles, peninsulas, or long points." Do not count or include in the area to be analyzed the following: cells where you are unable to see the complete cell borders; overlapping cells (if including multiple frames), or cell drop out (guttae).

6. In the case of corneal tissue that is prepared for PK or EK, 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.	

F1.400 Pachymetry Measurement

Purpose:

To describe the procedure for in-container measurement of corneal thickness of the donor cornea using optical coherence tomography or specular microscopy.

Reference:

Rosenwasser, G.O.D., & Nicholson, W.J. (2003). Evaluation of the Donor Cornea. *Introduction to eye banking: a handbook and atlas*. (1st ed.) (pp. 71)

Definition of terms:

Pachymetry of the cornea: A measurement of thickness of a cornea or corneal segment (e.g. graft thickness of posterior layers processed for DSAEK).

Optical Coherence Tomography: An imaging technique that uses low-coherence light to capture micrometer-resolution, two- and three-dimensional images from within optical scattering media.

Materials needed:

Optical Coherence Tomography (OCT) system that is configured for eye banking with image display and capturing capability or Specular Microscope.

Labeled corneal tissue in storage viewing chamber containing medium

Option: Computer-based image capture system with the ability to produce a hard copy and adequate backup.

Optical Coherence Tomography

Set up:

The labeled viewing chamber containing the medium and cornea is placed in the OCT adaptor for cornea viewing chambers. The OCT system 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 OCT 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 may be obtained as soon as possible before processing.	1. This will allow more accurate evaluation of the corneal thickness. Pachymetry of the cornea varies significantly under varied conditions of hydration.
2. Position viewing chamber in adaptor holding bracket with anterior of cornea facing the camera. Position the Cornea Illuminators (light sources) toward the viewing chamber to illuminate the cornea for examination. Position camera of the OCT close to the viewing chamber until it almost touches the viewing chamber. Do not allow camera to touch the surface of the viewing chamber. This may damage the camera.	2. Basic laboratory technique should be observed at all times.
3. Start the scan process by moving the camera until the cornea image is in focus. The image of the desired scanned region should be in or nearly in the target zone. Adjust scan beam to target zone and orientation with joystick.	3. The entire cornea should be included in the scan. The OCT system scans multiple images of the cornea at different angles allowing the system to analyze the average thickness of the particular location of the cornea.
4. Adjust image quality/scan strength. Capture and save the scan to the image recording system. Include pertinent donor data on the OCT image to identify it as per your eye bank's SOP.	4. OCT image scans 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.
5. Analyze the scan to determine corneal thickness.	5. Transplantable corneas may be established by the individual eye bank's medical director.
6. After obtaining OCT images, the ocular tissue should immediately be returned to the refrigerator. Try to minimize the duration that the cornea is at room temperature.	6. Ocular tissue preserved in corneal storage medium and maintained at optimal temperature will enhance cell viability.
7. Record the OCT evaluation according to your eye bank's policy in the ocular tissue information form.	

Specular Microscopy

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 the cornea to reach normal room temperature. The most optimal evaluation may be obtained as soon as possible before processing.	1. This will allow more accurate evaluation of the corneal thickness. Pachymetry of the cornea varies significantly under varied conditions of hydration.
2. Position chamber in holding well of microscope. With the adjustment knob of the magnifying lens, lower the magnifying lens until it almost touches the 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.
3. Begin slowly raising the magnifying lens or cornea until cornea endothelial cells come into focus	3. If cells are not visible at first, scanning for bright lights can put you in a better position for illumination of cells.
4. Push the reset button to zero the counter.	4. Setting counter to zero allows the beginning of measurement at the endothelium.
5. Begin slowly raising the magnifying lens or cornea until cornea epithelial cells come into focus.	5. The counter will show the distance between the endothelium and epithelium.
6. After obtaining the measurement, the ocular tissue should immediately be returned to the refrigerator. Try to minimize the duration that the cornea is at room temperature	6. Ocular tissue preserved in corneal storage medium and maintained at optimal temperature will enhance cell viability.
7. Read and record the value on the display according to your eye bank's policy on the ocular tissue information form.	7. Transplant corneas may be established by the eye bank's medical director.

G1.000 Quality Assurance

Purpose:

To outline how to establish a Quality Assurance Program in order to provide uniformly safe, high quality products for surgical use.

Definition of terms:

1. **Acceptance criteria -** the product specifications and acceptance/rejection criteria, such as acceptable quality level and unacceptable quality level, with an associated sampling plan, that are necessary for making a decision to accept or reject a lot or batch (or any other convenient subgroups of manufactured units).
2. **Audit -** documented review of procedures, records, personnel functions, equipment, materials, facilities, and/or vendors to evaluate adherence to the written SOP, standards, or federal, state and/or local laws and regulations
3. **Complaint -** Any written or oral communication concerning dissatisfaction with the identity, quality, packaging, durability, reliability, safety, effectiveness, or performance of a product.
4. **Donor Screening -** Action for looking at the donor's relevant available documents to determine if a patient can become a potential donor.
5. **Distribution of the tissues -** process of preparing tissue for shipment to consignee.
6. **Facilities -** Area at the eye bank where the ocular tissue is received and/or processed.
7. **Manufacture** - any or all steps in the recovery, processing, storage, labeling, packaging, or distribution of any human cell or tissue, and the screening or testing of the cell or tissue donor.
8. **Process control -** A system of checks and balances incorporated into standard operating procedures involving critical operations to prevent errors.
9. **Quality Assurance –** Assures regulatory agencies, consignees and patients that quality requirements will be fulfilled by using systematic activities implemented in an organization therefore instills confidence that the organization will provide a safe product.
10. **Quality Assurance Program** – denoted as QAP, is a program that: 1) defines the policies and environment required to meet standards of quality and safety and, 2) provides confidence that the processes and tissue consistently conform to requirements for quality. Dimensions of QA may include quality control, auditing and process control, standards for personnel, facilities, procedures, equipment, testing and recording keeping activities. (EBAA). This comprehensive Program prevents recurrence of errors or accidents.
11. **Quality Control –** Its part of the QAP that focuses in fulfilling quality requirements through an operational technique and activity.
12. **Qualification -** The method of establishing confidence that equipment, reagents, and ancillary systems are capable of consistently operating within established limits and tolerances. Process performance qualification is intended to establish confidence that the process is effective and reproducible.
13. **Quarantine** the storage or identification of an HCT/P, to prevent improper release, in a physically separate area clearly identified for such use, or through use of other procedures, such as automated designation.
14. **Relevant communicable disease agent or disease** a communicable disease or disease agent listed as follows: (a) Human immunodeficiency virus, types 1 and 2; (b) Hepatitis B virus; (c) Hepatitis C virus; (d) Human transmissible spongiform encephalopathy, including Creutzfeldt-Jakob disease; and (e) Treponema pallidum.
15. **Tissue recovery -** process to excise ocular tissue.
16. **Tissue processing –** any process performed on tissue after excision.
17. **Validation -** The process of demonstrating a specific process or procedure will consistently produce expected results within predetermined specifications.

Regulatory:

1. EBAA Medical Standards

   EBAA Appendixes

   A. Appendix I: FDA Defined Relevant Communicable Disease Agents and Diseases.
   B. Appendix II: FDA Defined Contraindications to Transplant
   C. Appendix III: Donor Eligibility Determinations
   D. Appendix IV: Testing
   E. Appendix V: Accredited Eye Banks Not Located in the United States

2. FDA Regulations

   A. 21 CFR Part 1271 Human Cells, Tissue, and Cellular and Tissue-Based Products

3. FDA Guidance

   A. Current Good Tissue Practice and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps). December 2011
   B. Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps). August 2007
   C. Validation of Procedures for Processing of Human Tissues Intended for Transplantation. March, 2002
   D. Guidance for Industry: Regulation of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) - Small Entity Compliance Guide. August 2007
   E. FDA 21 CFR Part 207 - Requirements For Foreign And Domestic Establishment Registration And Listing For Human Drugs, Including Drugs That Are Regulated Under A Biologics License Application, And Animal Drugs, And The National Drug Code.

4. AATB Standards for Tissue Bank QA program

Canadian References:

1. CAN/CSA-Z900.1-17 National Standard of Canada. (2017) Cells, tissues and organs for transplantation: General requirements.
2. CAN/CSA- Z900.2.4-17 National Standard of Canada. (2017) Ocular tissues for transplantation.
3. Health Canada (2018) Guidance Document for Cell, Tissue and Organ Establishments. Safety of Human Cells, Tissues and Organs for Transplantation

Materials needed:

a. n/a

Procedure	Rationale/ Medical Standard/ Regulation
1. Eye banks located in the USA must be registered with the Food and Drug Administration. This registration must be renewed yearly. Eye banks must ensure that the registration status is maintained and consistently updated. For eye banks located in other countries additional regulatory requirements specific to that country must be followed. If an eye bank from another country wants to export tissue to the USA, they must register with the FDA and follow FDA requirements as described in 21 CFR 1271.	1a. EBAA Med Stds - B1.000 (5) Active membership 1b. FDA 21 CFR 1271.21 - When do I register, submit an HCT/P list, and submit updates? 1c. FDA 21 CFR 1271.1(b)1 - What is the purpose of this part – Scope
2. All eye banks must have a Quality Assurance Program, hereafter known as the QAP, developed and established at their main facility. This Program must comprise of several programs that will oversee and manage regulatory compliance of the various policies, processes and activities directly related to the screening of the donor, tissue recovery, tissue processing, the distribution of the tissues and any other product that is manufactured at the eye bank. The QA program defines the policies and environment required to meet standards of quality and safety and provides confidence that the processes and tissue consistently conform to requirements for quality. Dimensions of QA may include quality control, auditing and process control, standards for personnel, facilities, procedures, equipment, testing, and record keeping activities.	2a. EBAA Med Stds - G1.000 Quality Assurance and EBAA Appendix V - Accredited Eye Banks Not Located in the United States 2b. FDA 21 CFR 1271.160 Establishment and maintenance of a quality program
3. The main objective of the QAP is to prevent the introduction, transmission and spread of communicable diseases, as well as ensure that the quality of the tissue is acceptable for transplantation.	3a. EBAA Med Stds - E1.200 Processing and Preservation 3b. FDA 21 CFR 1271.160 Establishment And Maintenance of A Quality Program
4. The quality program as required by FDA, must established and maintained procedures related to core GTP requirements as described in the code of federal regulations core current good tissue practices.	4a. EBAA Med Stds – G1.000 Quality Assurance 4b. FDA 21 CFR 1271.150(b) - Core cGTP requirements
5. The Quality Assurance personnel must be individuals within your organization that do not directly oversee or supervise the technical processes or personnel except for those pertaining to QA activities described within this procedure to avoid a conflict of interest.	5a. Best tissue practices

6. A Quality representative or designee must be appointed at the eye bank to establish, oversee, manage and maintain the QAP. The Medical Director and the eye bank's Executive Director, as well as the QA designee will approve the Quality Assurance Program. All three parties will be responsible for approving proper implementations, corrective /preventive actions, adverse reaction determination, deviations, non-conformance outcomes, validations and final disposition of tissues or other products produced at the eye bank that have been compromised. The QA designee should have complete oversight of the technical compliance of the eye bank.

6a. EBAA Med Stds - C1.200 (1) Medical Director aspects

6b. FDA 21 CFR 820 Management Responsibilities

   A. The eye bank's Executive Director and Medical Director are ultimately responsible for:
   B. Actively supporting, cooperating and assisting the QAP and QA personnel.
   C. Ensuring personnel to adhere to the QAP.
   D. Ensuring reportable deviations and recalls are submitted in a timely manner to the FDA and EBAA or any other required regulatory agency as per state/country directives.
   E. Approving technical processes/procedures, equipment qualifications, process validations, technical competencies and implementation of new standards and regulations.
   F. Acting as the liaison between the regulatory and accreditation agencies inspectors and the organization.

6c. EBAA Med Stds - C1.200 (2,3) Medical Director aspects

6d. FDA 21 CFR 1271.47(b) What procedures must I establish and maintain? – Review and Approval

7. The Quality Manager or designee is responsible for:
   A. The establishment, maintenance, implementation and of the QAP to ensure compliance of all approved policies and procedures.
   B. Monitoring implementations and corrective actions ensuring that they are effectively improving.
   C. Acting as the liaison between the regulatory and accreditation agencies inspectors and the organization.

7a. EBAA Med Stds – G1.000 Quality Assurance

7b. FDA 21 CFR 1271.160 Establishment and maintenance of a quality program.

7c. FDA Guidance - cGTP and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) December 2011

8. Ensure that your QAP has imbedded all FDA regulations, EBAA standards, state requirements or eye bank country's requirements as applicable.

8a. FDA 21 CFR 1271.1(b) What is the purpose of this part - Scope

9. The QA system should comprise at a minimum the

following programs:

A. Document Control – manages all standard operating procedures (SOPs) and forms for all technical and quality processes. The Medical Director, eye bank's Executive Director, and the Quality Manager or designee that oversees the QAP must approve each procedure before is implemented. Procedures must be established and maintained for all steps that are performed in testing, screening determining donor eligibility and for all programs in the QAP. Each procedure should be identified with unique numbers for tracking purposes. Any change in a procedure must be performed according to the change control program. Eye bank can use an Excel spreadsheet to maintain the list of procedures and versions. Procedures can also be managed electronically using a qualified, controlled software.	A1. EBAA Med Stds - C3.400 Procedure manual and G1.000 Quality Assurance A2. FDA 21 CFR 1271.160 Establishment and maintenance of a quality program. A3. FDA 21CFR 1271.47 What procedures must I establish and maintain? A4. FDA 21 CFR 1271.180 Procedures
B. Change Control – manages all changes in procedures, processes and evaluates if a change in a process would require revalidation. All changes must be approved by the Medical Director, Eye Bank's Executive Director and QA Manager. Every change in a procedure or form must contain a version/revision number. Each version of the document must be filed and readily available. This program should be controlled solely by one person. Employees including upper management, should not have access to editable documents so that the current version is controlled. Available software for document control are commercially available and can greatly assist in change control.	B1. EBAA Med Stds - E1.220 Cornea B2. FDA 21CFR 1271.225 Process Changes
C. Facilities – describes the cleaning process of the laboratory and where this activity is documented.	C1. EBAA Med Stds - C3.000 Facilities C2. FDA 21 CFR 1271.190 Facilities
D. Environmental Monitoring – describes how the room temperature is monitored as well as how the area where the tissue is aseptically processed is monitored. Must Include the materials and supplies used for monitoring an area and frequency.	D1. EBAA Med Stds – G1.000 Quality Assurance D2. FDA 21 CFR 1271.195 Environmental Control and Monitoring
E. Recovery – describes how to evaluate the recovery site and ensure there are no major issues that would preclude from procuring the ocular tissue. Procedure should describe how to assess and screen the donor's body for recovery, how to perform an aseptic hand scrub, and how to aseptically excise ocular tissue	E1. EBAA Med Stds – E1.100 Recovery E2. FDA 21CFR1271.215 Recovery

F. Processing and Process Controls – describes how to control every ocular process to ensure minimal cross contaminations and errors throughout the process. Describes the verifications needed during the process from receipt of tissue/product to the final disposition.	F1. EBAA Med Stds - E1.200 Processing and Preservation F2. EBAA Med Stds definition of Process Controls
G. Labeling Controls – describes how the eye bank avoids mixing donor labels and verifications that need to be performed to segregate approved tissue from tissue in quarantine to prevent donor mix-ups.	G1. EBAA Med Stds - J1.000 Labeling G2. FDA 21 CFR 1271.370 Labeling
H. Storage – describes how ocular tissue is stored as well as supplies and reagents used in each process are stored according to manufacturer's recommendation.	H1. EBAA Med Stds - I1.000 Storage, C3.300 H2. FDA 21CFR1271.260 H3. FDA Guidance cGTP and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) December 2011 XVII. Storage
I. Donor screening, and donor testing - describes the acceptance criteria used to determine donor eligibility.	I1. EBAA Med Stds - D1.000 Donor Eligibility, I2. D1.120 Screening for FDA Defined Relevant Communicable Disease Agents and Diseases, I3. D1.200 Donor Testing and Appendix II : FDA-defined Contraindications to Transplant I4. FDA 21 CFR 1271.45 Subpart C - Donor eligibility I5. FDA 21CFR1271.50 How do I determine whether a donor is eligible?
J. Tissue Evaluation - describes how tissue is evaluated for suitability determination. This program includes the evaluations that must be performed (such as slit lamp and cell density count) to determine the suitability of the tissue.	J1. EBAA Med Stds - F1.000 Tissue Evaluation
K. Sterilization of Instruments – describes the methods used to sterilize instruments. Validation of the sterilization of instruments must be performed if sterilization is performed in-house. If sterilization is performed by a third party then program must state how each sterilization load is verified to be acceptable for use.	K1. EBAA Med Stds - C3.300 Instruments, Cleaning and Maintenance K2. FDA Guidance cGTP and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue -Based Products (HCT/Ps) (C example 3) and (J). December 2011
L. Deviation Investigation and Reporting – describes how to investigate a deviation and how to report the deviation to an accreditation and regulatory agency.	L1. EBAA Med Stds - G1.000 Quality Assurance L2. FDA 21 CFR 1271.160 Establishment and maintenance of a quality program (b) (6) Deviations
M. Tissue Recalls – describes how to determine if the recipient's surgeon must be notified when a deviation or non-conformance has occurred as well as	M1. EBAA Med Stds - G1.300 Tissue Recall

how to recall tissue from consignee.	M2. FDA 21 CFR 1271.160 (b)(2)(iii) Establishment and maintenance of a quality program M3. FDA 21 CFR 1271.440 Orders of retention, recall, destruction, and cessation of manufacturing
N. Corrective Action and Preventive Action program – describes how to implement and how to verify that the CAPA plan is efficient in preventing the reoccurrence of the deficiency.	N1. EBAA Med Stds - G1.000 Quality Assurance N2. FDA 21 CFR 1271.160 Establishment and maintenance of a quality program.
O. Auditing Internal and external processes – verifies the degree of compliance with the core CGTP requirements. Auditors must be an individual who does not have direct responsibility for the area being audited. This program should describe the specific areas being audited and the scope of that specific audit. This is performed to identify deficiencies within the approved processes. Once deficiencies are identified, corrective actions can be put in place to prevent the deficiency to reoccur. The deficiency may also show if a process needs to be changed or to be re-validated.	O1. EBAA Med Stds - G1.000 Quality Assurance. O2. FDA 21 CFR 1271.160 Establishment and maintenance of a quality program (c) Audits O3. FDA Guidance cGTP and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue -Based Products (HCT/Ps) (C example 3) and (J). December 2011 V. Establishment and Maintenance of a Quality Program J. What Are the Requirements for Performing Quality Audits of Your Establishment?
P. Adverse Reaction Investigation and Reporting – describes how to investigate and determine the root cause of an adverse reaction and how to report it to an accreditation and regulatory agency.	P1. EBAA Med Stds - G1.000 Quality Assurance. P2. FDA 21 CFR 1271.350 (a) Reporting (adverse reactions reports)
Q. Preventive Maintenance and Calibration of Equipment - lists all lab equipment at the eye bank and describes how to manage the contractors that perform calibration and preventive maintenance on critical equipment as well as describes what documents are retained for those activities. Describes how the equipment is used, cleaned, calibrated and/or maintained as a preventive measure.	Q1. EBAA Med Stds - C3.200 Equipment, Maintenance and Cleaning Q2. FDA 21 CFR 1271.200 Equipment
R. Receipt, pre-distribution shipment, and distribution of ocular tissue - describes how to control the tissue chain of custody from receipt to distribution.	R1. EBAA Med Stds - L2.000 Packaging, Sealing and Packing for Transport R2. FDA 21CFR 1271.150(9), Current good tissue practice requirements - receipt, predistribution shipment, and distribution of an HCT/P in 1271.265(a) through (d) R3. FDA 21 CFR 1271.265 Receipt, predistribution shipment, and distribution of an HCT/P R4. FDA 21CFR1271.265(a) Receipt, predistribution shipment, and distribution of an HCT/P - Receipt

S. Equipment Qualification – describes which equipment will be qualified before use by performing an installation, operation and performance qualification (IQ,OQ,PQ). This applies to equipment that might affect the suitability of the tissue.	S1. EBAA Med Stds - Qualification definition S2. FDA 21 CFR 1271.195 (4) Maintenance of Equipment S3. FDA 21 CFR 1271.200 Equipment
T. Process Validation Program – describes which processes are validated, the methodology used in the validation process and testing results conclusion. Describes how to resolve discrepancies during validation.	T1. EBAA Med Stds - Validation definition and T2. E1.200 Processing and Preservation T3. E1.220 Cornea, E1.230 Sclera
U. Supply Management – describes how to qualify the vendors of critical reagent/supplies prior to use. Describes how to maintain the supply and reagents inventory as well as the qualification of each new reagent/supply lot including what documentation is retained for each supply/reagent. Describes how reagents/materials are qualified by physical inspection and by reviewing manufacturer certificates before use.	U1. EBAA Med Stds - C3.300 Instruments and Reagents as well as Vendors definition U2. FDA 21 CFR 1271.210 Supplies and Reagents
V. Qualification of Vendors, Testing Laboratories, Importing Eye Banks and Contractors – describes what are the acceptable parameters used to qualify these entities.	V1. EBAA Med Stds - Audit definition
W. Complaint Program – is any written, oral, or electronic communication that involves a distributed HCT/P that alleges: (1) That an HCT/P has transmitted or may have transmitted a communicable disease to the recipient of the HCT/P; or (2) Any other problem with an HCT/P relating to the potential for transmission of communicable disease, such as the failure to comply with current good tissue practice. (3) As well as any other communication that the eye banks' management deems necessary to be reported and followed up on.	W1. EBAA Med Stds - G1.000 Quality Assurance W2. FDA 1271.160.(b)(2) Establishment and maintenance of a quality program W3. FDA 1271.320 Complaint file W4. FDA Guidance December cGTP and Additional Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) 2011 XXI. Complaint File
X. Training Program – describes how the technical personnel maintains competency as a recovery or process technician	X1. EBAA Med Stds – C2.000 Training, Certification and Competency Reviews of Personnel Performing Tasks Overseen and/or Regulated by the EBAA, FDA, and Other State and Federal Agencies. X2. FDA 21 CFR 1271.170 Personnel X3. FDA 21 CFR 1271.170 (c) X4. FDA Guidance - cGTP and Additional Requirements for Manufacturers of Human Cells,

	Tissues, and Cellular and Tissue-Based Products (HCT/Ps) December 2011 VI. Personnel B.
11. The collected data must be periodically reviewed and evaluated by the executive director, medical director, technical director, or other appropriate individual.	11a. This information serves as the basis for identifying the need for corrective action.
12. You must establish a tracking system to facilitate the investigation of actual or suspected transmission of communicable disease and appropriate corrective action from the donor to consignee or from consignee or final disposition to the donor.	12a. EBAA Med Stds – Tracking definition 12b. EBAA Med Stds - E1.300 Use of Short or Intermediate Term Storage Solution 12c. FDA 21 CFR 1271.290 Tracking
13. Documentation of the eye bank's quality assurance program activities 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.	13a. EBAA Med Stds – G1.000 Quality Assurance 13b. FDA 21 CFR 1271.270 Records

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	***Rationale – Inputs***
1. Using your eye bank's relevant procedure, determine if a CAPA is to be issued	1. There should be a mechanism within your quality system to initiate a CAPA
2. Obtain your eye bank's CAPA form	2. Use an approved and controlled form to document steps taken in this procedure
3. Assign a tracking number to the CAPA	3. Used for traceability and reference
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.)	4. This will ensure the input is clearly documented
5. Define timelines for Containment Action, Root Cause Analysis, Actions Implemented, and Verification of Effectiveness	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	6. The CAPA form will be the central documentation of the incident and associated corrective/preventive actions
Procedure – Define, Assess, & Contain	***Rationale – Define, Assess, & Contain***
1. Record the date that the CAPA was initiated on the CAPA Form	1. Established timeframes will be based on this date
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	2. Clearly document the reason for the CAPA
3. Document, on the CAPA Form, any actions that were immediately taken (prior to documentation on the CAPA form), if applicable	3. Clearly document the immediate response if applicable
4. Perform a *containment action* and document such actions on the CAPA form	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
Procedure – Root Cause Analysis	***Rationale – Root Cause Analysis***
1. Investigate the incident to determine the root cause of the incident	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. Enlist other employees and the Medical Director as necessary to assist with the root cause analysis	2. Use subject matter experts within your organization to have an accurate root cause determined
3. Document the root cause analysis on the CAPA form	3. The Root Cause Analysis will determine the next steps
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	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

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

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 – 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	***Rationale – Review, Approval, and Close***
1. Ensure the CAPA form is complete	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. Attach all objective evidence, notes, and other documentation gathered during the investigation, action, and monitoring steps	2. All referenced documentation should be attached to the CAPA form for easy review
3. Present the CAPA to reviewers specified in your eye bank's procedures; have the reviewers sign & date if approval is given	3. Typically this includes Management and the Medical Director
4. Retain the completed CAPA per your eye bank's record retention procedures	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
Use as much detail as possible. Attach documentation as applicable.

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
Describe the method by which effectiveness will be monitored.

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

Summary, Review, Approval, Closure				
Were the Actions successful?	☐ Yes ☐ No	Is all supporting documentation attached?		☐ Yes ☐ 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

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 Product s (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.	1. FDA Regulation 21 CFR 1271 Human Cells, Tissues, and Cellular and Tissue-Based Products • 21 CFR1271.150 (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. 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.	2. CFR 1271.350 Reporting (b) Functions
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.	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. 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.	4. EBAA MS C1.000 Personnel and Governance C1.100 Director C1.200 Medical Director 4th paragraph
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	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.	6. Current Industry Good Tissue Practice
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.	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. Investigate the probable root cause for the deviation.	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. QA must determine if the deviation was against a core CGTP regulation 1271.150 and follow the attached flow chart.	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 <u>not</u> against a core CGTP and it was <u>not</u> related to tissue, QA together with the executive officers should assign appropriate corrective action and approve the deviation.
12. If deviation was <u>not</u> 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 <u>not</u> 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.	14. FDA regulation 21 CFR 1271.265 Receipt, predistribution shipment, and distribution of an HCT/P (c) Availability for distribution (2)
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 nonconformance cannot be resolved. Submit deviation to FDA and assign appropriate CAPA. Notify EBAA. Approve deviation.	15. CFR 1271.350 Reporting (b) Functions
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.	16. Based on FDA rejection letters rationale.
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.	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. 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.	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:	19. https://www.accessdata.fda.gov

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.
w. Save the summary with the confirmation number.

x. Send a copy of the submission to the EBAA within 10 business days.

19x. EBAA Medical Standard B1.200 Inspections by Other Official Agencies

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.

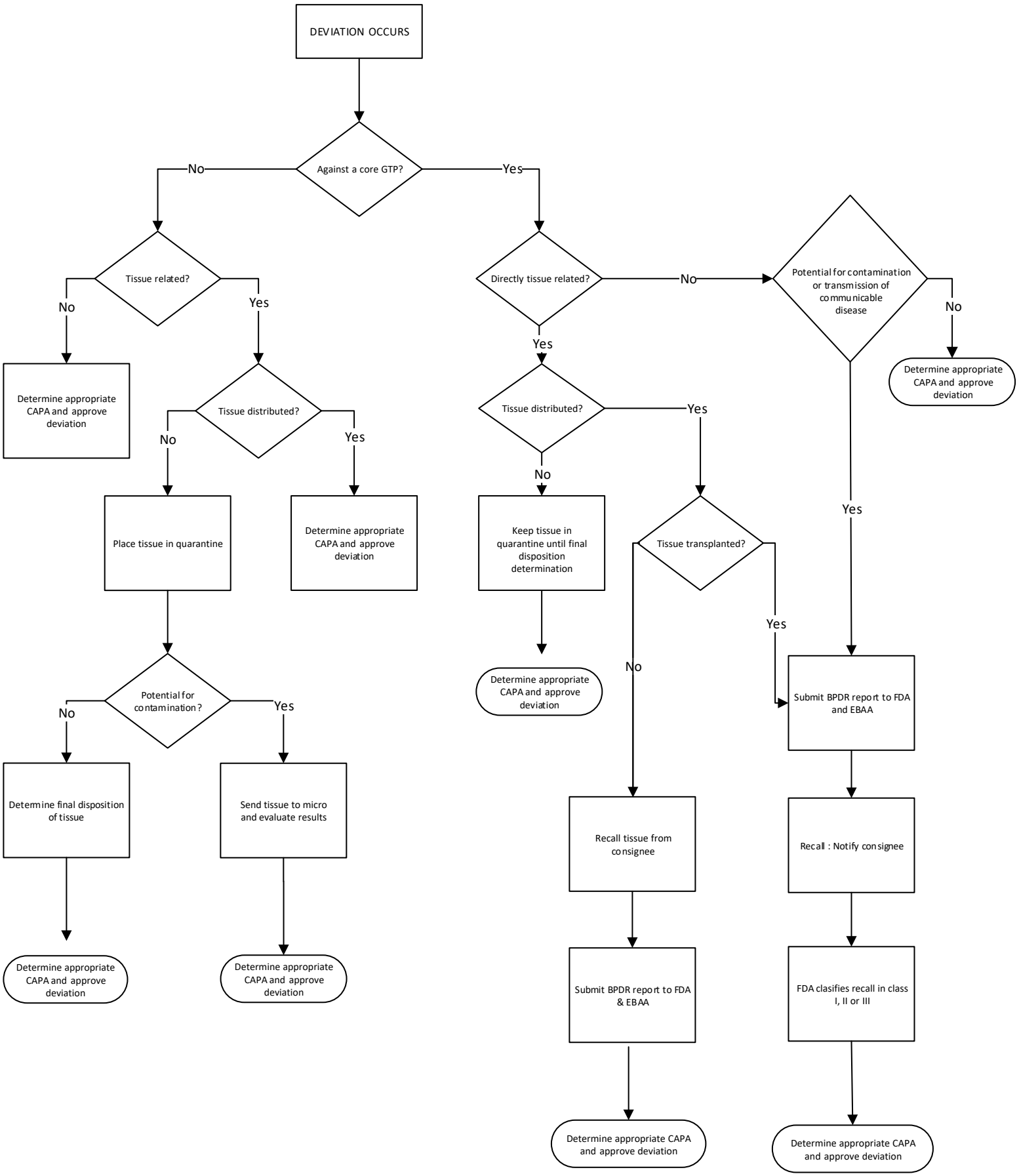
20. EBAA Medical Standard B1.200 Inspections by Other Official Agencies

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.

21. EBAA Medical Standards

G1.000 Quality Assurance

22. Retain deviation reports for a minimum of 10 years.


DEVIATION OCCURS
Against a core GTP?
No
Yes
Tissue related?
No
Yes
Determine appropriate CAPA and approve deviation
Tissue distributed?
No
Yes
Place tissue in quarantine
Determine appropriate CAPA and approve deviation
Potential for contamination?
No
Yes
Determine final disposition of tissue
Send tissue to micro and evaluate results
Determine appropriate CAPA and approve deviation
Determine appropriate CAPA and approve deviation
Directly tissue related?
No
Yes
Tissue distributed?
Yes
No
Keep tissue in quarantine until final disposition determination
Determine appropriate CAPA and approve deviation
Tissue transplanted?
No
Yes
Recall tissue from consignee
Submit BPDR report to FDA & EBAA
Determine appropriate CAPA and approve deviation
Potential for contamination or transmission of communicable disease
No
Yes
Determine appropriate CAPA and approve deviation
Submit BPDR report to FDA and EBAA
Recall : Notify consignee
FDA clasifies recall in class I, II or III
Determine appropriate CAPA and approve deviation

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.	1. To ensure compliance with CLIA.
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.	
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.	1. To ensure compliance with CLIA.
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.	

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.

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. 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.

2. See EBAA Medical Standards section G1.210. This statement is required regardless of whether the eye bank performs the cultures.

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.

8. See reference list.

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.

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.

12. See step 1-B above.

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.

14. See EBAA Medical Standard G1.210.A.

15. Request that all surgeons who receive ocular tissue report any cases of postoperative infection with a positive corneoscleral rim culture.

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

Procedure	***Rationale***
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. 3rd 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 not become invalidated at the time of testing. (ex; specimen centrifuge and testing timelines).

9. See FDA Guidance Eligibility Determination for Donors of Human Cells, Tissues, and 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 nonreactive for the following infectious agents:

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.

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

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-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.	12. Refer to FDA guidance Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) VI. Donor testing: specific requirements Hepatitis B surface antibody (anti-HBs) test
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.	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. 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.	14. EBAA Medical Standards Appendix 2: FDA contraindications to Transplant, (II) Clinical Evidence (e)
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.	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. 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.	16. See CFR1271.80 (d)(1)
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.	17a. Refer to EBAA Medical Standards C3.200 Equipment, Maintenance and Cleaning, 17b. Refer EBAA Medical Standards I1.000 Storage
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	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)

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 laboratory's official serologic report. File the written or electronic hard copy results with the donor record.	19. Good Eye Bank practices
20. The Eye bank must maintain documentation of results and interpretation of all testing for at least 10 years.	20a. Refer to EBAA Medical Standards M1.100 Length of Storage. 20b. Refer to FDA 1271.55(d)(4)
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.	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.
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.	22. Eye Bank Best Practices
23. If Eye Bank stores blood samples for future testing, they must have a SOP regarding the archiving of blood samples.	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

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. 2. Eye banks sharing donors with affiliated organizations should establish a protocol to receive positive serology results from those affiliated organizations.	3. Refer to EBAA Medical Standard G1.290.

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.

G1.400 Supply Management

Purpose:

To define the procedure by which the eye bank will receive, inspect, and store supplies and/or reagents utilized in eye bank operations, and by which vendors should be qualified.

Definition of Terms:

Critical Supplies: Materials used during the aseptic recovery, processing, and/or storage that will or could be reasonably expected to come in close or direct contact with the donor tissue. Examples include sterile gloves, corneal viewing chambers, corneal storage solution, etc.

COA: Certificate of Analysis

COC: Certificate of Compliance/Conformity

COS: Certificate of Sterility

Non-Critical Supplies: Materials used by the eye bank that will not or are not reasonably expected to come in close contact with the donor tissue. Examples include reconstruction prosthetics, biohazard bags, shipping coolers, etc.

Vendor: An external organization (supplier, contractor, consultant, etc.) who provides critical supplies or services to the eye bank

Regulatory

FDA: 21 CFR Part 1271.210

Materials Needed

Supplies Receiving Log (example at the end of this procedure)
Released Supply Sticker (or other identifier to indicate that a supply is released for use)
Vendor Evaluation Form (example at the end of this procedure)

Procedure – Vendor Qualification

Procedure	***Rationale***
1. Prior to obtaining supplies from a vendor, perform an evaluation of the vendor to determine their ability to meet specified requirements and to establish the type and extent of control to be exercised 2. Document and retain the evaluation on a Vendor Evaluation Form (example attached) 3. Clearly define and document the following:	1. 21 CFR 1271.210(a)

a. Vendor contact information
b. Supplies and/or services provided
c. Requirements and specifications of the products and/or services to be met by the vendor (e.g. sterility requirements, necessary certifications to accompany product, etc.)
d. Any written contract or agreement between the vendor and the eye bank
e. Obtain any relevant certifications and/or registrations

4. If an audit is required, define the type and scope. The audit must be successfully performed prior to vendor approval
5. Retain documentation of references (if provided and checked)
6. Clearly communicate the vendor approval status to the relevant staff at the eye bank to ensure only qualified vendors are used

Procedure – Supplies Inspection and Release

Procedure	***Rationale***
7. All supplies utilized in the eye bank operations (including recovery, processing, and storage) should be listed and classified as Critical or Non-Critical. Include any acceptance criteria and manufacturer requirements for each supply as well as any necessary documentation that must accompany the supply (such as a COA).	7. 21 CFR 1271.210(a)
8. Qualified vendors shall be used to source supplies a. New vendors must be evaluated for compliance with any applicable regulatory requirements prior to ordering/purchasing materials.	8. 21 CFR 1271.210(a)
9. Upon delivery of the supplies, the personnel receiving the supply will place the supply in quarantine until an inspection is complete and the item is released	
10. A designated individual(s) will inspect the supply and pay particular attention to the following:	10. 21 CFR 1271.210(a-b)

a. Is the item received as ordered and does the item and quantity received match that of the original order and/or packing list?
b. Is there any transit or shipping damage?
c. If the item is sterile, are all sterility indicators present and valid?
d. Is there any sign of item contamination or packaging damage?
e. If the item is temperature-sensitive, did the item arrive at the appropriate temperature?
f. Is the item acceptable for the intended use?
g. Is a certificate of analysis, conformity, or sterility present or ordered as required?
h. Other inspection items required by your eye bank (expiration dates, etc.)

11. Upon a successful inspection, document the supply in the Supplies Receiving Log
    a. Ensure the records of the receipt of the supply include: type, quantity, manufacturer, lot number, date of receipt, and expiration date
12. If the item failed inspection, label the item as such and notify the individual who placed the initial order for resolution with the supplier and/or manufacturer
13. Affix a Released Supply identifier to the item
14. Place the supply in the designated appropriate storage location
15. Utilize a First-In/First-Out (FIFO) system for inventory storage unless the item received has an expiration date that is nearer to the current date of the item currently in inventory
16. Store all supplies according to manufacturer's instructions – pay attention to any environmental requirements (such as storage temperature or humidity)

11. 21 CFR 1271.210(d) and C3.300

15. This ensures that the oldest items (those that expire first) are utilized before newer items

Example Supplies Receiving Log with Example Entry

Item	Lot Number	Expiration Date	Quantity Received	Manufacturer	Supplier	Inspected By	Inspection Date	Inspection Pass/Fail
SST Blood Tube	*123456*	*12/12/2022*	*46 Tubes*	*Tube MFG*	*Tubes-R-Us*	*J. Doe*	*12/12/2019*	*Pass*

Example Vendor Qualification Form

VENDOR INFORMATION					
Vendor Name:					
Contact Person:					
Address:					
City:		State:		Zip:	

SUPPLIES OR SERVICES PROVIDED		***CHECK ALL THAT APPLY AND DESCRIBE IN DETAIL***
☐	Supplies:	
☐	Services:	

REQUIREMENTS AND SPECIFICATIONS
LIST ALL REQUIREMENTS AND SPECIFICATIONS OF THE SUPPLIES OR SERVICE PROVIDED. USE ADDITIONAL SHEETS IF NECESSARY.

VENDOR EVALUATION					
Is a written agreement or contract required?	☐ Yes		☐ No		
Is an audit required?	☐ Yes	☐ No	If Yes:	☐ On-Site	☐ Remote
Certifications and/or Registrations: *Obtain copies if checked*					
References Provided?	☐ Yes	☐ No	If Yes, List:		
Describe type and extent of control to be exercised:					
Evaluation Summary:					

EVALUATION RESULTS	
☐ **Vendor is APPROVED**	☐ **Vendor is REJECTED**

Name – Evaluator	**Signature**	**Date**

G1.500 Validation

Purpose:

To provide an overview of what an eye bank needs to validate in accordance with FDA, EBAA and other applicable standards.

Reference:

- FDA regulations 21 CFR 1271 Human Cells, Tissue, and Cellular and Tissue – Based Products
- EBAA Medical Standards

Glossary:

- *Validation*- The process of demonstrating a specific process or procedure will consistently produce expected results within predetermined specifications.
- *Verification*- The confirmation by examination and provision of objective evidence that specified requirements have been fulfilled.
- *Process Validation*- Where the results of processing cannot be fully verified by subsequent inspection and tests, you must validate and approve the process according to established procedures.
- *Documentation*- Providing standard operating procedures to provide general guidance, a process validation master plan that addresses more specific responsibilities, priorities, and schedules, protocols for each specific acceptance criteria, measurements for each validation, then a controlled report for each validation.
- *Software Validation*- Provides objective evidence that the design outputs of a particular phase of the software development life cycle meet all the specified requirements.
- *Installation Qualification (IQ)* - Documented verification that all important aspects of the equipment installation adhere to specifications. Needed when new equipment is installed.
- *Operational Qualification (OQ)*- Documented evidence that the equipment performs in accordance with the system specifications throughout operating ranges. Confirmation Equipment operates per manufacturers specifications.
- *Performance Qualification (PQ)*- Establishing documented evidence that the equipment under anticipated conditions produces results for predefined requirements. Performs as specified.
- *External validation/verification*- Performance of a validation/verification by a contracted third-party supplier.
- *Internal validation/verification*- Performance of a validation/verification by quality personnel.

Materials needed:

- Depends upon what is being validated and what type of validation is being performed.

Procedure	Rationale
15. The following items may be included in the initial validation: a. Validation Report: i. Title – identify the process to be validated. ii. Purpose – the goal of the validation.	Per EBAA Medical Standards, validation is required for: a) Tissue Processing (E1.200) b) Sterilization (C3.300) c) Tissue Storage (E1.200) d) Assessment of Endothelium (F1.000) e) Labeling (J1.000)

iii. System description – description of test methodology, identification of equipment, supplies/reagents, include critical steps and effects on other processes.
iv. Responsibilities – individuals performing the validation.
v. Acceptance/Rejection criteria.
vi. Test Results
vii. Results summary
viii. Review and approval/disapproval

Examples of validations for each, but not limited to:
a) *Tissues Processing*: transfers, rim cut, EK, LSK, environmental monitoring, etc.
b) *Sterilization*: autoclaving, irradiation, ultrasonic cleaning
c) *Tissue Storage*: fridge, freezer, shipping containers, preservation media
d) *Assessment of Endothelium*: specular, slit lamp
e) *Labeling*: statement of sterility if applicable, software validation

b. Installation Qualification/ Operational Qualifications/ Performance Qualification (IQ/OQ/PQ)
i. For facilities or equipment validation

FDA 1271.200 Equipment
EBAA Medical Standard C3.200

c. Cultures:
i. Where there is a risk of contamination/cross-contamination or the introduction of communicable disease, cultures must be obtained.
ii. Establish criteria for acceptable culture results.
iii. Identify steps in the process where contamination/cross-contamination or the introduction of communicable disease could occur and culture.
iv. A validated process should be monitored with in process-cultures being obtained on a regularly scheduled basis.

FDA 1271.220 Processing and Process Controls

16. Changes in validated process:
a. Any change to a validated process must be evaluated, verified or re-validated and documented accordingly.

FDA 1271.225 Process Change
FDA 1271.230 Process Validation

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 ocular tissue in usual manner with source eye bank ISBT 128 Tissue identifiers, plus a label "For Non-Clinical Use Only" and "not for Transplant"	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 the word "BIOHAZARD' or Biohazard legend. A statement indicating the tissue has not been tested and the tissue is potentially hazardous biological material, or some other designation per OSHA requirements.	Label alerts the persons receiving ocular tissue to exercise infectious disease precautions.
4. Attach the label to container, i.e., jar, vial, or viewing chamber in a prominent place.	
5. The ocular tissue should be appropriately stored according to its method of preservation.	5. Consult eye bank's S O P for storage of non-surgical tissue.
6. Distribute ocular tissue according to eye bank's SOP.	
7. Retain distribution records and enclose a physical copy of a tissue information form with tissue. Electronic versions of the tissue report form may be used in place of physical copies when tissue will be used in training or educational events where large amounts of tissue will be used, e.g., wet labs.	

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.	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. 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.	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. 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.	8. To prevent the release of "potentially hazardous" ocular tissue for surgery.
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.	9. Biohazardous material must be disposed of quickly and safely.
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.	10. See procedure H1.

J1.000 Labeling

Purpose:

To outline procedure for labeling of ocular tissue from time of recovery through time of distribution for surgical use, research, and teaching.

Definition of terms:

Intermediate or temporary label: A temporary label applied at time of recovery 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:
Permanent label
Pen
Manual or digital printing device for each type of label.

Procedure	Rationale
1. Each ocular tissue must be in a container labeled with a unique identification.	
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. Upon tissue arrival at the laboratory for final processing and disposition, determine label type needed, based on potential outcomes such as 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 conforming 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 identifiers. ISBT tissue identifiers include 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 international format (YYYY-MM-DD HH:MM).

D. In accordance with EBAA Medical Standard L1.000, all dates shall be written as YYYY-MM-DD HH:MM to harmonize with the ISO 8601 requirements. If space on the label does not permit this information, it must be listed on the Tissue Report Form.

E. Date and time of ocular tissue preservation, in international format (YYYY-MM-DD HH:MM).

E. In accordance with EBAA Medical Standard L1.000. all dates shall be written as YYYY-MM-DD HH:MM to harmonize with the ISO 8601 requirements. If space on the label does not permit this information, it must be listed on the Tissue Report Form.

F. If the cornea has additional processing, clearly indicate this on the label.

G. The following statements:
- tissue intended for single application or single patient use only.
- tissue not considered sterile.

H. Tissue expiration date 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 affix a label containing the word “BIOHARD” or biohazard legend and a statement that tissue is for “Non-Clinical Use Only” and “Not for Transplant.”

5. See EBAA Medical Standards section H1.000, which requires a statement alerting tissue receiver that contents are 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.	2. Availability of materials facilitates efficient communication of needed information and minimizes potential errors.
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.	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. Identify potential receivers of ocular tissue according to eye bank procedures.	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. Distribute ocular tissue, using the procedure established by the eye bank, which may be patient-based or surgeon-based.	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. 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.	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. 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.	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. 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.	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. A re-hydration procedure must be included as a package insert for all sclera preserved in alcohol.	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 pre-served corneas preserved in Optisol-GS, likorol, likorol-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 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.	6. To maximize the vapor barrier function of the 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.
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.	9. See EBAA Medical Standards section L1.200.
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).	10. See EBAA Medical Standards section H1.000.
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.)	

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
1. Use standard good practice when recording eye donor information. A. Write neatly and legibly B. Use proper spelling and grammar C. Use black or blue indelible ink pen D. Use military time (24 hour clock) E. Use authorized abbreviations only F. Record information promptly G. Do not leave blanks on forms	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.
2. Use the following procedure to correct a mistaken entry: 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.	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.
3. Do not tamper with any existing eye bank record. Tampering includes: A. Adding to an existing record by filling in the blanks.	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.myflor-ida.com/MCHQ/Health_Facility_Regulation/Laboratory_Licensure/docs/organ_tissue/AdverseReactionFormPartI.pdf

http://ahca.myflor-ida.com/MCHQ/Health_Facility_Regulation/Laboratory_Licensure/docs/organ_tissue/AdverseReactionFormPartII.pdf

Materials Needed:

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

Procedure	Rationale
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.	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.
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.	2. Some information requested may be difficult to collect. Surgeons should be assured patient identification information would be treated anonymously.
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.

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.

3. The OARRS reporting system summarizes information allowing the EBAA to look for trends that may impact eye banking practice.

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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Implementation Guidance Document

Uniform Donor Risk Assessment Interview Forms

Version 2
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

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TABLE OF CONTENTS

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 **U**niform **D**onor **H**istory **Q**uestionnaire for **O**rgan, **T**issue, and **E**ye 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.

V. REFERENCES

Uniform DRAI - Donor greater than 12 yrs old (current version)

Uniform DRAI – Child donor less than or equal to 12 yrs old (current version)

Uniform DRAI - Birth Mother (current version)

EBAA Eye-Only Uniform DRAI - Birth Mother (current version)

EBAA Eye-Only Uniform DRAI - Child Donor ≤12 years old (current version)

EBAA Eye-Only Uniform DRAI - Donor >12 yrs old (current version)

Uniform DRAI - Requirements Crosswalk Documents (current versions)

AOPO-EBAA-AATB Guidance Document, *Effective Quality Assurance of the DRAI for a Donor >12 years old*, *(current version)*

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Medical Standards, EBAA, Washington, DC, current edition

Minimum Medical Standards, European Eye Bank Association, current edition
http://www.europeaneyebanks.com/article/Minimum%2BMedical%2BStandards%2B%2528Rev1%2529/365

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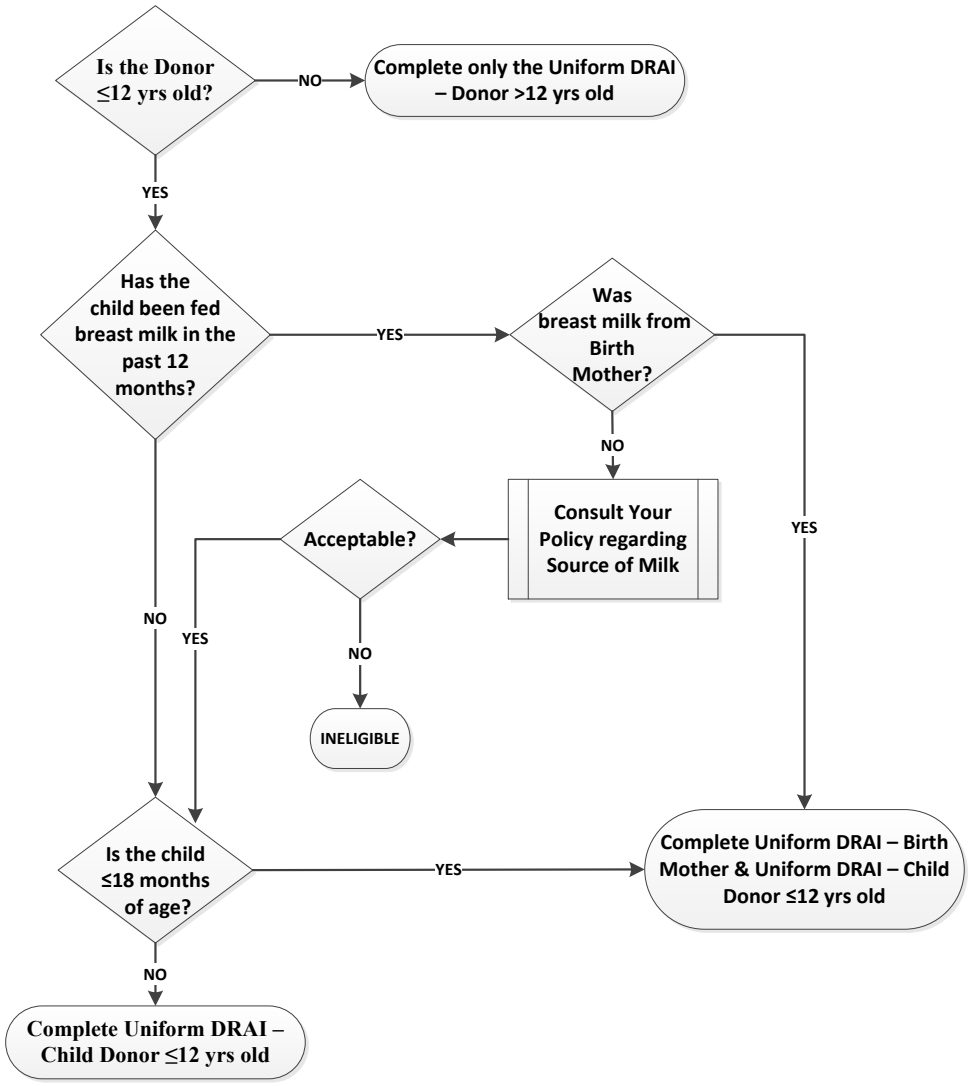
VI. APPENDIX

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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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) A*vailability*.

(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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2. *Standards and Interpretive Guidelines*, AOPO, Vienna, VA, current edition

3. *Medical Standards*, EBAA, Washington, DC, current edition

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7. U.S. Department of Health and Human Services, Food and Drug Administration, Final Guidance for Industry, Current Good Tissue Practice (CGTP) and Additional

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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

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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 precut 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

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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 al[10] 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 μm/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 al[11] 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 Standards[8] 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

	No. Particles Per Cubic Meter by Micrometer Size					
Class	**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

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	—	—

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/m^3 value roughly corresponds to 25 CFU after 1-hour exposure on settle plates 90 mm in diameter.[24]

However, the National Health Service[22] recommends that ultraclean (laminar flow) operating room air sampled close to the wound during orthopedic implant surgery should contain $<$10 CFU/m^3 (196 CFU/m^2/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 al[14] have suggested a maximum value of 350 CFU/m^2/hr, which corresponds to approximately 2.5 CFU on settle plates 90 mm in diameter per 1-hour exposure. Pasquarella et al[13] have suggested a maximum value of 786 CFU/m^2/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 al[14] 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 surgery[25] 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

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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 Chapter, Section, Table, or Figure	Version 1.4.0 Chapter, Section, Table, or Figure	Change	Rationale
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

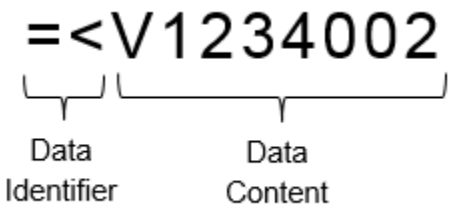
Data structures are the means by which information about ocular tissues is put into computer-friendly codes. Data structures define the technical characteristics necessary for the interpretation of the information. They specify the context and structure and provide the links to the appropriate reference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

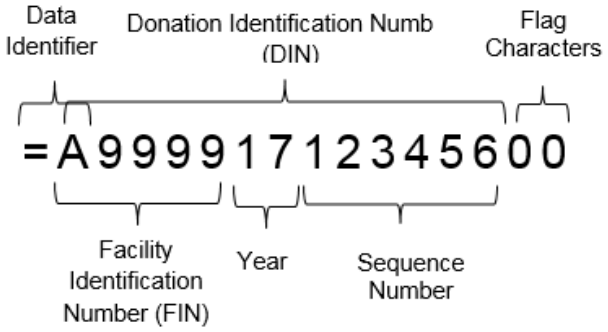
This chapter will include a high level description of the required data structures as well as other data structures that users may find useful in the labeling of ocular tissue. Specific details of coding are found in the *ISBT 128 Standard Technical Specification* (ST-001)] Guidance on how and when to 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

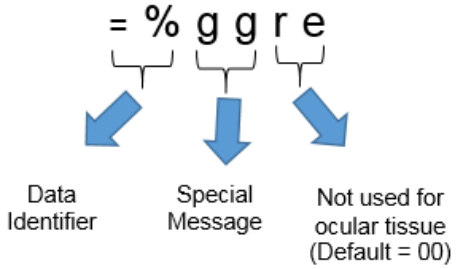


Table 1 Special Messages for Data Structure 002 (Excerpt of RT06)

gg	Interpretation
Mb	Biohazardous
Md	Discard (to be destroyed)
Mq	Quarantine/hold for further testing or processing
Mr	For research use only

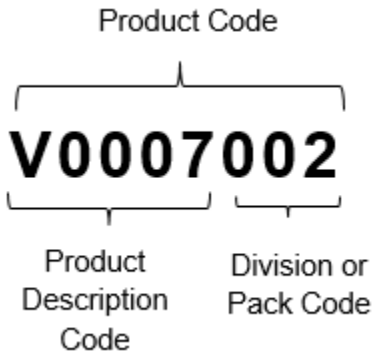
3.3 Product Code [Data Structure 003]

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]

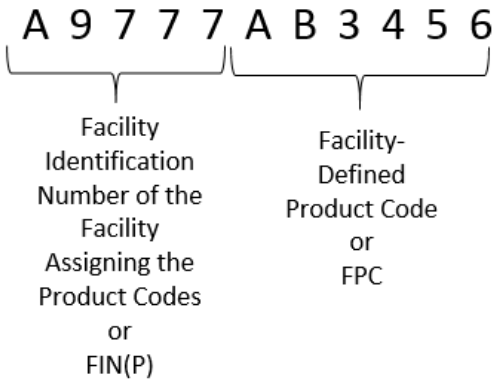
Data Structure 033 identifies the facility that assigned the Product Code (usually a processing facility). It is used when the facility that assigned the Product Code is not the same facility that assigned the DIN.

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.

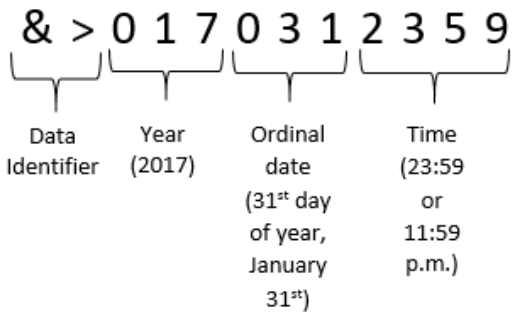
A full list of specified sequence compound messages is found in Table W2, [RT017] ICCBBA-Specified Compound Messages on the ICCBBA Website. Requests for additional entries should be submitted to the ICCBBA office (tech.manager@iccbba.org).

3.6 Date and Time Data Structures

3.6.1 Expiration, Recovery, and Production Dates and Times

There are a number of data structures designed to encode specific types of time (expiration, recovery, and production). All use the last three numbers of the year (e.g., 2017 becomes 017 in the code); the ordinal number within the calendar year (or Julian date), where the days of the year are numbered sequentially beginning with 001 on January 1; and, for some, the time based on a 24-hour clock. If the product expires at midnight, 2359 (23:59 or 11:59 p.m.) is encoded. See Figure 6.

Figure 6 Expiration Date and Time Data Structure



The types of time data structures are differentiated using the data identifier (see beginning of Section 3) as shown in Table 2. Some of the data structures include only the date while others include both date and time. Where options exist, facilities may select whatever data structure works best for them.

Table 2 Data Identifiers for Date and Time Data Structures.

Type of Time	Data Identifier
Expiration Date and Time [Data Structure 005]	& >
Collection/Recovery Date [Data Structure 006]	= *
Collection/Recovery Date and Time [Data Structure 007]	& *
Production/Processing Date and Time [Data Structure 009] (may be used for Date and Time of Preservation)	& }

3.6.2 Flexible Date and Time

As the use of ISBT 128 spread from blood to other MPHO, 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).

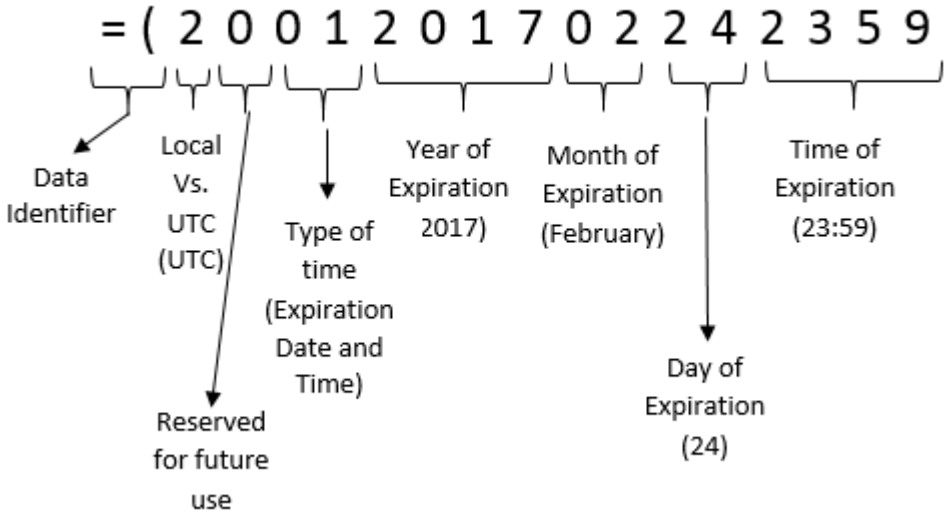
The first character of the data content indicates if the time is local (encoded as a 1) or UTC (encoded as a 2). The second character is reserved for future use. The third and fourth characters indicate the type of date and time (Expiration is 01, Collection/Recovery is 02, Production/Processing is 03, 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.

<u>All tissues:</u>

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.

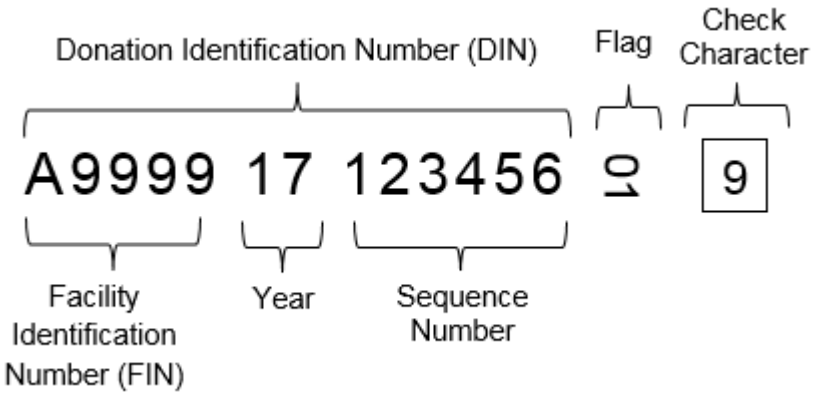
4.3.1 Donation Identification Number [001]

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	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. Note: The word “Ethanol” does not have to be printed twice if the concentration is printed on the label,	CORNEA in Ethanol Example text: 100% Ethanol
	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
Ocular Tissue, Non-Clinical	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

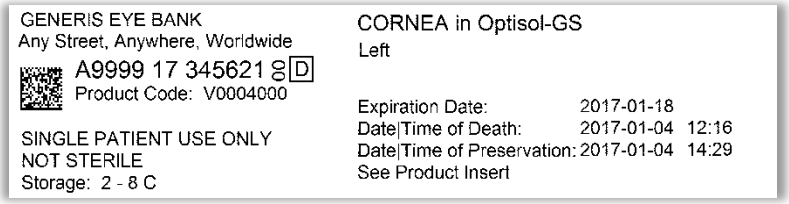


Figure 10 Cornea, Anterior and Posterior Layers

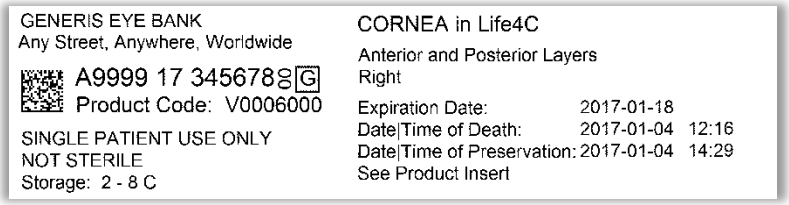


Figure 11 Partial Sclera

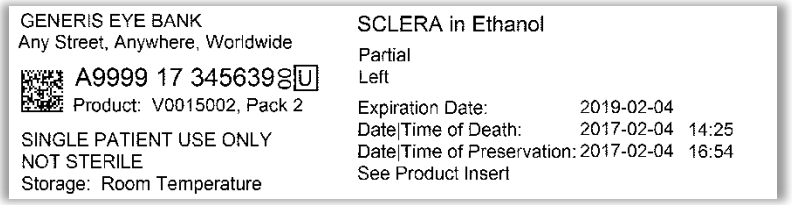
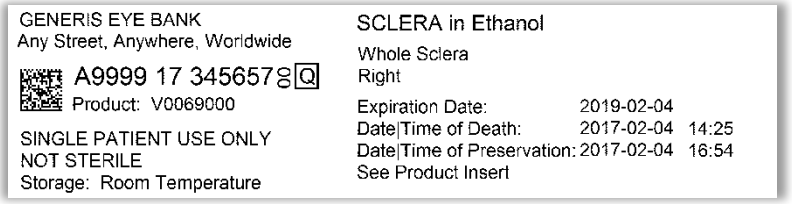


Figure 12 Whole Sclera



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)

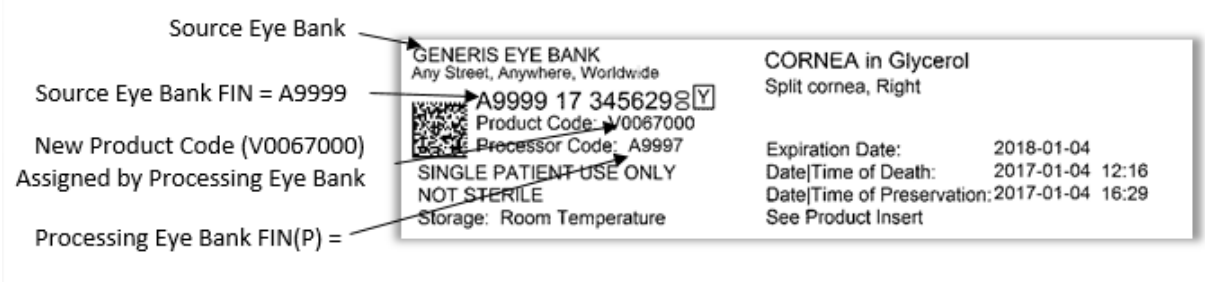
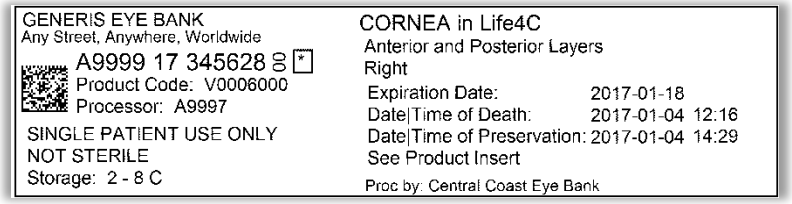
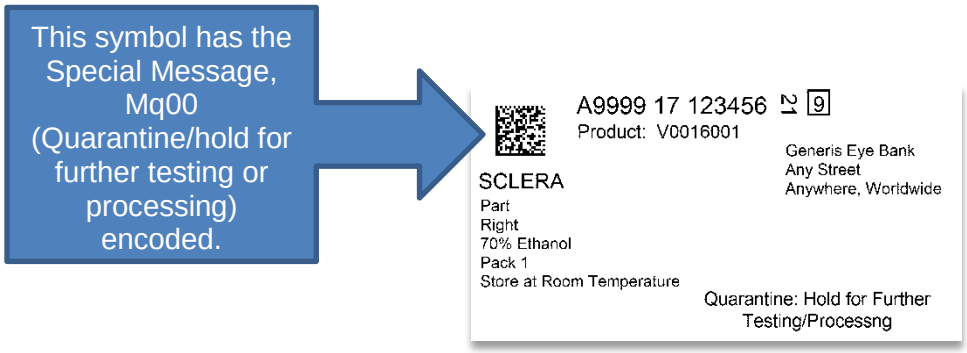


Figure 14 Cornea, Anterior and Posterior Layers with FIN(P)



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.

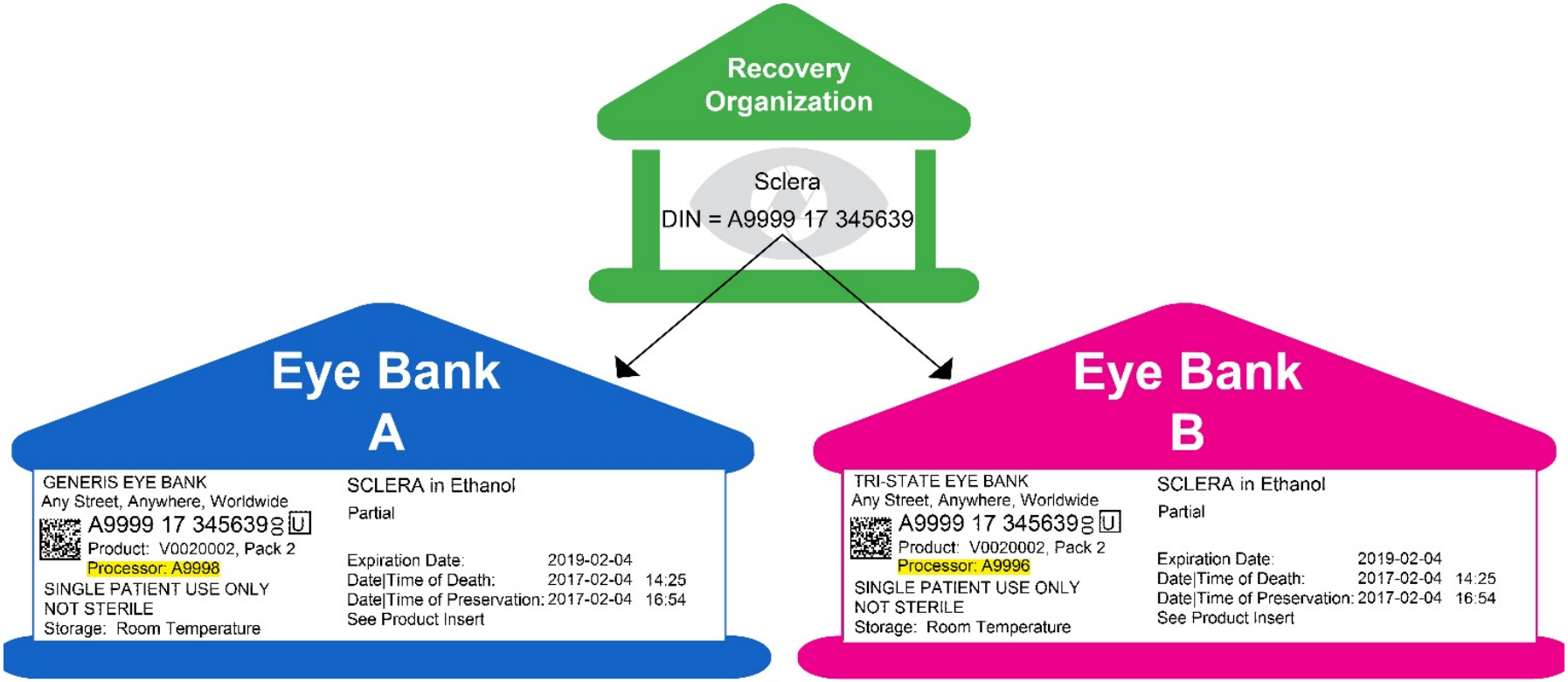
Bank A created:
DIN: A9997 17 345639
Product Code: V0020002 (SCLERA|Ambient storage|Ethanol|Part, NS)
Processing Facility Information Code: A9998000000

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: • 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

Contents

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

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.

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,

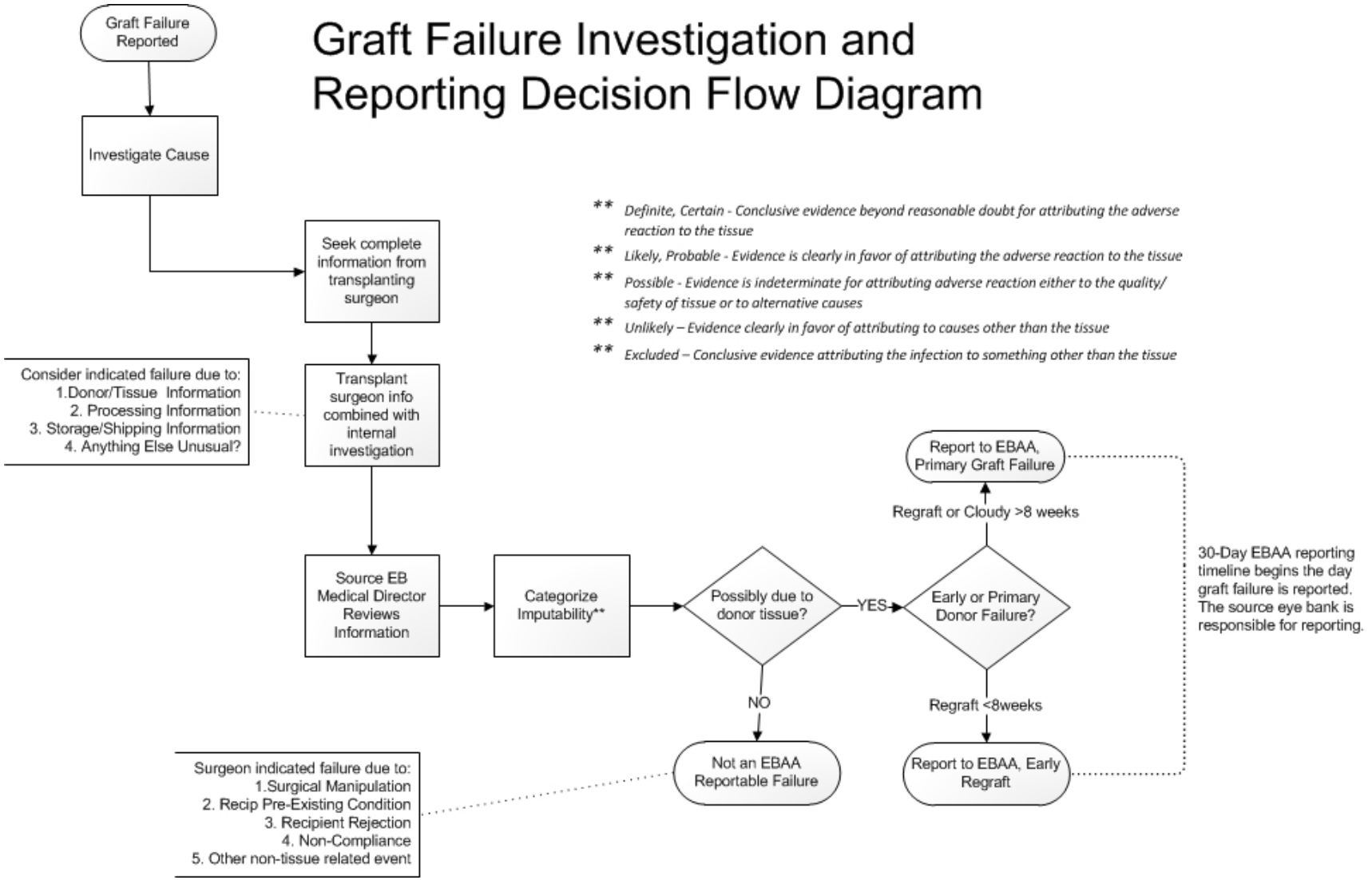
  For endothelial keratoplasty: tissue manipulation intraoperatively (e.g. upside down), re-bubbling, surgeon experience is less than ten cases, poor surgeon cut, presence of anterior chamber IOL, incision size, number of folds, insertion/folding technique, use of forceps, dislocation.

- 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

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 for investigating reports of ocular infection:

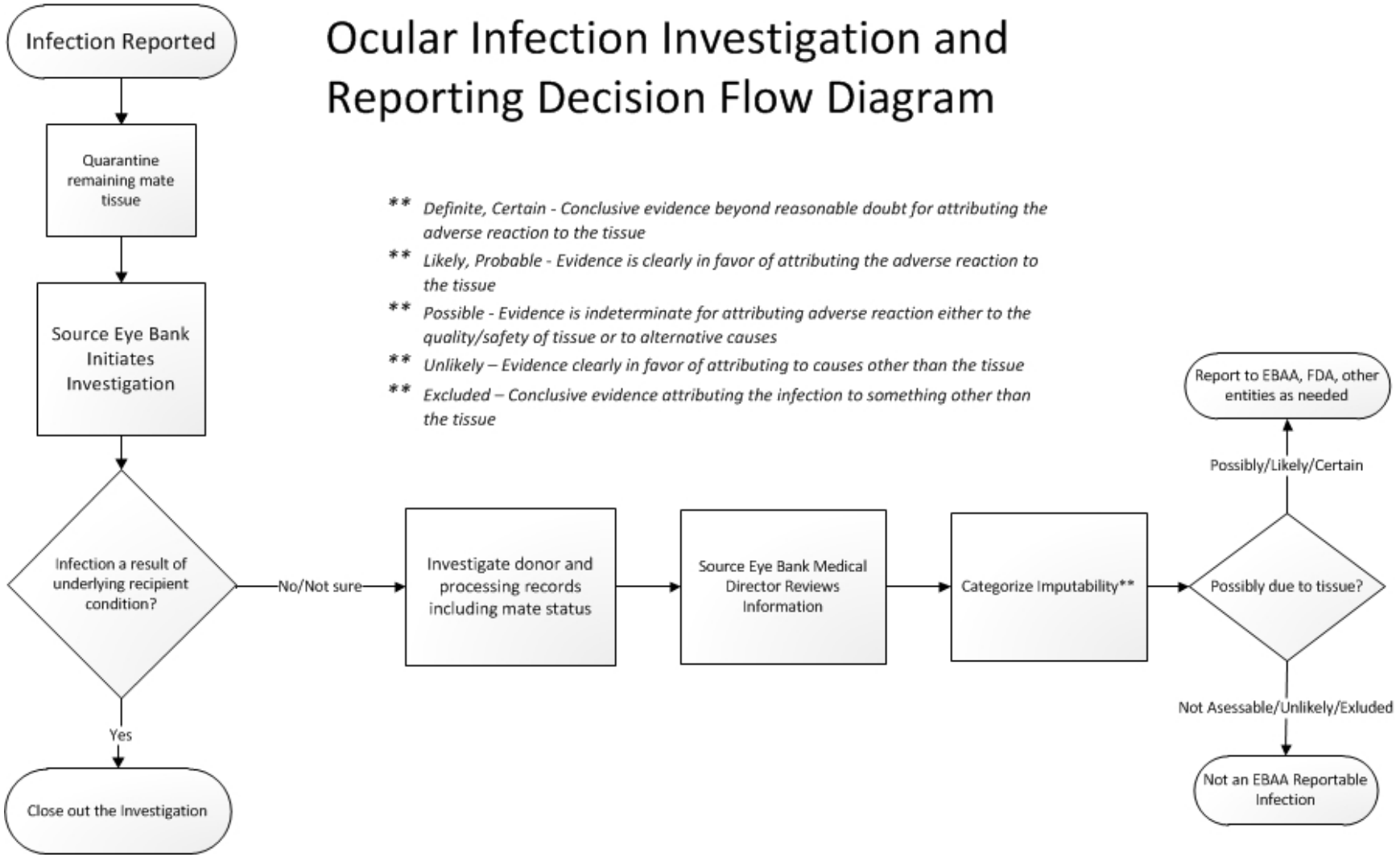
As part of the investigation, review records for possible sources of contamination

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



** *Definite, Certain - Conclusive evidence beyond reasonable doubt for attributing the adverse reaction to the tissue*

** *Likely, Probable - Evidence is clearly in favor of attributing the adverse reaction to the tissue*

** *Possible - Evidence is indeterminate for attributing adverse reaction either to the quality/safety of tissue or to alternative causes*

** *Unlikely – Evidence clearly in favor of attributing to causes other than the tissue*

** *Excluded – Conclusive evidence attributing the infection to something other than the tissue*

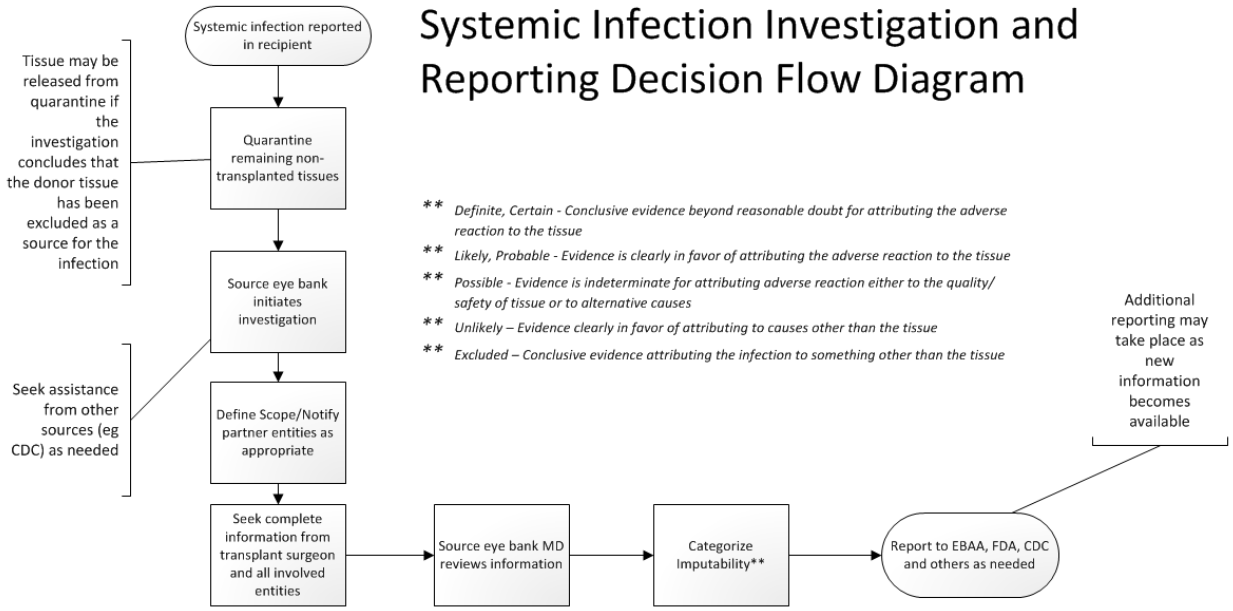
3. Systemic Infection in a Recipient

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)

- 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

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.

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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.
Penicillum spp.
Yeast – non-specified

Virus

Herpes simplex
Cytomegalovirus

Parasites

Acanthamoeba spp. (if known, add the species to the comments)

Other

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Guide to Medical Examiner and Coroner Cases

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American Association of Tissue Banks®

EYE BANK ASSOCIATION OF AMERICA®

ASSOCIATION OF ORGAN PROCUREMENT ORGANIZATIONS

International Association of Coroners & Medical Examiners

A training and educational tool collaboratively developed by the American Association of Tissue Banks, the Eye Bank Association of America, the Association of Organ Procurement Organizations, and the International Association of Coroners & Medical Examiners.

Background and Objective

Many potential donors of organs, tissues, and eyes are under medicolegal jurisdiction and require release before donation can occur. Although many death investigators support donation, much is at stake when evaluating a medicolegal case for release. Victims, their families, alleged perpetrators, prosecution and defense attorneys, and law enforcement agencies are all seeking the truth in the assessment of cause and manner of death. Death investigators are committed to performing the very best investigation possible to find the cause and manner of death. If the death investigators do not have a positive relationship with those in the donation community, it can affect their willingness to allow donation on medicolegal cases. If the opportunity to donate organs, tissues, or eyes are lost, this can affect the lives of many of those waiting for life-enhancing or life-saving donations and deny a potential donor family the opportunity to heal through donation. Education, communication, and consistency are necessary to ensure the best possible outcome for all involved. Information and education are powerful; however, if they cannot be properly communicated, then the knowledge is lost.

Despite the essential role death investigator relationships have on donation, national guidance or training material has not been developed for the donation community. While much emphasis has been placed on death investigators' support of donation, there has been little focus given to how the donation community may support the death investigation process. A lack of standard procedures, training, or practices promoting the preservation of evidence can all be contributing factors to the death investigator declining donation.

The American Association of Tissue Banks (AATB), the Eye Bank Association of America (EBAA), the Association of Organ Procurement Organizations (AOPO), and the International Association of Coroners & Medical Examiners (IACME) recognize the critical role that death investigators play in donation. This document has been developed to provide examples of beneficial practices and case studies that illustrate how such practices have been successfully utilized in tissue and eye donation cases under death investigator jurisdiction.

These practices are not requirements or standards but were developed to inform the donation community about practices that may beneficially serve the donor, donor family, and recipient by establishing measures to improve interactions on cases shared by death investigators and recovery organizations. Practices, policies, and procedures should be developed by each individual recovery organization in collaboration with the death investigation offices in their service area.

Defining Donation Stakeholders

Throughout this document organ, tissue, and eye organizations will be referred to generally as **recovery organization(s)**. These organizations may handle all areas of organ, tissue, and eye recovery and donation or may handle specific roles in their designated areas of donation.

What is Death Investigation?

A death investigation is a formal inquiry into the circumstances surrounding the death of a human being where investigative information is considered with autopsy findings and adjunctive studies (if performed) to determine the cause and manner of death (OSAC). The four primary sources of information used during a death investigation include information from: the body, any associated scene(s), a review of medical history, and information provided by family members and/or other witnesses. Death investigators may obtain information about the death directly, through verbal or written reports, or through review of photographs/ videos.

US Death Investigation Systems

US death investigation system structures and practices are highly variable. Titles, qualifications, authority, and responsibilities vary by state and county. State laws/statutes determine the roles of death investigators in your service area. Throughout this document we will describe common participants in the death investigation process (e.g., coroners, medical examiners, forensic pathologists, medicolegal death investigators, justices of the peace) will be referred to uniformly as **Death Investigators**.

A **coroner** (C) is generally an elected or appointed official whose duty is to oversee medicolegal death investigations, usually for a single county, and ensure certification of cause and manner of death. Coroner training and experience varies widely by jurisdiction and duties can vary based on local enabling statutes.

A **forensic pathologist** (FP) is a physician who is certified in forensic pathology by the American Board of Pathology (ABP) or who, prior to 2006, has completed a training program in forensic pathology that is accredited by the Accreditation Council on Graduate Medical Education or its international equivalent or has been officially "qualified for examination" in forensic pathology by the ABP. May be employed as a medical examiner or as a consultant to a coroner or Justice of the Peace.

A **medical examiner** (ME) is most often an appointed forensic pathologist whose duty is to oversee medicolegal death investigations, perform postmortem examinations, and certify cause and manner of death.

A **medicolegal death investigator** (MDI) is an individual who performs medicolegal death investigations. In practice, this title is often used to distinguish death investigators who gather information from outside of the autopsy suite from the forensic pathologist conducting the autopsy.

Some jurisdictions, particularly those which include outlying or remote populations, manage the death investigations locally, but transport the body to a regional center for autopsy.

There is currently no minimum national requirement for MDI training or experience, but a voluntary national certification process has been in place since 2005. Whether certified as a Diplomate (D-ABMDI) or a Fellow (F-ABMDI), certification demonstrates that a death investigator meets minimum competence in the investigation of deaths according to commonly accepted standards.

State and Regional Death Investigation Systems

Attempts to broadly categorize the US death investigation systems fail to adequately describe death investigation on a local level. For this reason, it is critical that recovery organizations establish policies, practices, and procedures within and include guidance from their local death investigation authorities. Though useful, efforts to define US death investigation, refer to **Figure 1**, tend to oversimplify the systems, when there are a variety of combinations. In some medical examiner systems, county-level investigation of death is administered by the county prosecutor/District Attorney while in other systems a Sheriff Coroner or Justice of the Peace may oversee death investigation. The map shows that while this model seems simple at first glance, there are a variety of combinations of the medical examiner/coroner system throughout the country which can make certain jurisdictions appear more complicated. For example, it is possible that in a jurisdiction with an elected coroner or justice of the peace, a board-certified forensic pathologist may be hired to conduct autopsies under the supervision of the coroner. It is also possible that a forensic pathologist may choose to run for elected coroner in another jurisdiction, thereby ensuring that the coroner position is staffed by an individual with extensive training in forensic pathology and death investigation.

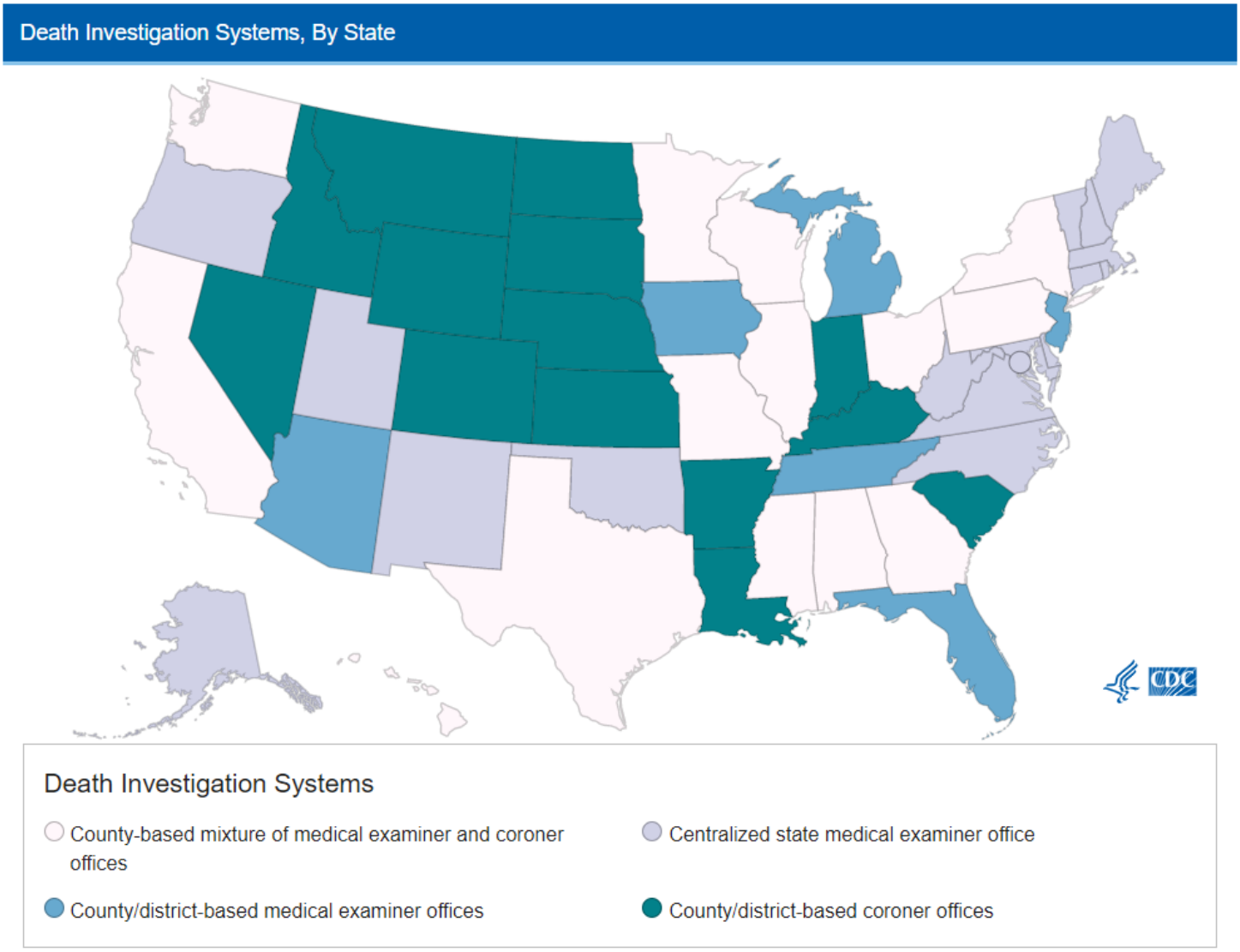


Figure 1. Death investigation systems, by state. Image: Centers for Disease Control and Prevention.

Communication and Relationship Management

Clear communication and proactive relationship management is at the heart of effective coordination of donation cases. This section describes best practices implemented in many different areas in the United States where the death investigators and local recovery organization work together successfully. Communication, as described in this section, encompasses both case-by-case communication as well as structured communication pathways developed to support timely and efficient problem-solving in complicated situations.

Relationship management cannot be discussed without mentioning the topic of trust. Death investigation offices and recovery organizations both have critical responsibilities with implications for public health, criminal justice, public policy, medical research, and community caretaking. Each office needs to be able to trust the other office to perform their role responsibly. The following guidelines outline ways in which roles and responsibilities can be proactively created, thus building trust through the establishment of clear and concise performance practices.

Contracts and Agreements

Business relationships that require timely and effective communication between offices are often best managed by establishing a shared written process for collaboration and communication. Although the

♦♦♦ Case Study ♦♦♦

A 37-year-old male with a history of alcohol dependency was found dead at the bottom of the stairs leading to his garden level apartment. The weather was cold, snow was on the ground, and there was some question as to the cause and manner of death. At the time of screening, it was unclear whether the decedent fell and died as a result of a head injury, foul-play, or hypothermia. Given the circumstances, the chief medical examiner was consulted. The death investigators agreed to release the body for the recovery of skin grafts and other specific tissue prior to autopsy (also called a *post* or *post-mortem*), but after an external examination was conducted and photographs obtained. As agreed upon in the interoffice MOU, the death investigator completed the release form and sent it to the established fax line at the recovery organization. The release form documented which tissues were released and, more importantly, which tissues could not be recovered prior to autopsy (e.g., heart for valves, lower leg blood vessels). The form also documented the number and color of blood vacutainers requested by the death investigator to be left with the decedent for toxicological analysis. The next day, the death investigator called their point of contact at the recovery organization and asked why only grey-top vacutainers were left with the decedent. The recovery organization manager opened the case and reviewed the release document faxed over by the death investigator and saw that red-top vacutainers were also requested.

It was determined that the recovery organization staff on the case assumed that this office only wanted grey-top vacutainers and did not reference the agreed upon release document. Corrective action and recovery organization staff training was conducted. The death investigator was informed of these corrective measures in an effort to rebuild trust in the donation process.

methods for documenting such agreements vary greatly on a national level, there are some typical best practices that have been employed successfully. These include interoffice *memoranda of understanding* (MOU), *letters of agreement* (LOA), or contracts that support the statutory requirements of the local city and/or county for both death investigation and donation.

A *memorandum of understanding* may be the simplest and most effective way to generate a document that meets the needs of both offices. While not an official contract, an MOU can succinctly outline mutually agreed upon practices. In addition, an MOU is easier to update when needed improvements come to light during the management of cases and decedent-related situations over time.

Letters of agreement are similar to MOU documents, but they are formatted to be closer to the structure of a contract and are commonplace in business agreements. They can be structured in a way to outline agreed upon practices.

Official contracts are sometimes used to manage interoffice business relationships and are the most formal way to capture agreed upon guidelines. A contract is advantageous since it will capture the signatures of key leadership professionals in each office to ensure that guidelines outlined in the document are mutually beneficial. Contracts are also typically used in situations where there is fiduciary responsibility of one or both of the parties in the contract. For example, the local statutes for coroner may require that the office have a contract with local recovery organizations and require that a recovery organization pay a specified fee for the case-by-case or monthly use of a dedicated recovery room within the ME/C autopsy facility. Since the

environmental requirements for successful tissue recovery are key to an aseptic recovery, a contract can also specify which party in the contract is responsible for the repair and upkeep of the recovery room used by the recovery organization. The contract may specify when and how often payment is rendered to the county and under what conditions. While all three examples given so far can include a *sunset clause*, thus allowing a document to get reviewed and reevaluated within a specified time period (e.g., every 1–3 years), a contract is most likely to contain such a clause.

Donation Related Expenses

It is the responsibility of the donation organization to ensure every avenue to preserve the opportunity for donation is exhausted. Additional evidence, such as tests and diagnostics, may enable the death investigator to make an informed decision concerning the release of organs and tissues for donation.

Expenses associated with the donation process are the responsibility of the donation organization. Such expenses include but are not limited to donor transportation, tests, and diagnostics such as radiography, and clinical consultations. The donation organization may establish protocol with individual death investigation offices determining the need for such practices or may elect to handle specific requests on a case-by-case basis.

Standard Operating Procedures

The use of standard operating procedures (SOPs) is not new to the functioning of a successful recovery organization and the use of such resources should not be overlooked when working with a death investigation office. As you will see in this guide, there are many details that must be attended to on each donor case and having procedures to outline these requirements is key. While there will be similar content that could apply to procedures written by different recovery organizations (e.g., handling of decedent personal belongings, handling of potential evidence, when to contact the death investigator on call), each death investigation office and recovery organization may prefer to handle these situations in a customized manner according to business needs as well as local and national statutes and regulations.

Effective Collaboration

One of the most important and effective best practices that your recovery organization can implement is one that Dr. Charles V. Wetli used during his tenure at the Suffolk County Medical Examiner's Office in New York. In a mutual agreement between the recovery organizations and death investigation office, a single point of contact at each organization was established for situations where problems were identified. A single point of contact may effectively remove any confusion on the part of the death investigation office regarding whom to contact and how to communicate the issue.

Unusual and/or suspicious findings are often identified during the physical assessment performed by the recovery organization. This is especially problematic if there is any possibility the finding may be related to the cause and/or manner of death. The commonly accepted protocol is to stop the donation process and contact the death investigator.

Blood sample acquisition provides an excellent opportunity to communicate and cooperate with a death investigator on a shared case. Routine cases are typically not an issue, as blood can be drawn either intravascularly by the recovery organization prior to autopsy or by the pathologist if the autopsy precedes the recovery. Problems arise in situations where a potential donor is plasma diluted and a pre-mortem hospital sample must be acquired for testing. As the death investigator has jurisdiction, the recovery organization will need to collaborate with them to potentially share or split pre-mortem samples to proceed

with donation. This is ideal as it allows both agencies to meet their separate needs, the death investigator to run toxicological testing and the recovery organization to run serological testing.

Interoffice communication can take place at any point during the management of a case and should not be limited to the time of the referral. The death investigation office can provide information that may be critical in determining donor eligibility, which can ultimately lead to the discard or release of the recovered tissues. While it may seem as though recovery organizations are more likely to consume information provided by the death investigation office, recovery organizations can also share critical information that can assist a death investigator.

Routine Communication

Once agreements, protocols, and customer service tools have been implemented, there are still opportunities to engage in communication. Regularly scheduled meetings may be mutually beneficial. In these scheduled meetings, outcomes, statistics, and overarching feedback can be provided and discussed by the recovery organization and death investigation office. Routine communication can also be related to the request and receipt of completed or preliminary autopsy reports, which are needed to finalize donor eligibility determination and release for tissue processing and distribution.

Donor Referral Systems

Many deaths take place outside of the hospital setting and may not be referred to the recovery organizations through standard channels. Developing a death referral agreement between the recovery organization and death investigation office may promote the opportunity for donation in the case of deaths which otherwise may have not been reported to the recovery organization.

Several recovery organizations and death investigation offices have established automated electronic referral programs to streamline this process and reduce the risk of human error. Automated referral systems may reduce staff time from both the donation organization and death investigator and enable expeditors information sharing through real-time case updates and the distribution of relevant records. Exploration of these referral programs may be beneficial.

Educational Opportunities

Educational opportunities for both death investigators and recovery organization staff can be placed in two categories: initial training and ongoing training. Initial training can involve the onboarding of both death

♦♦♦ Case Study ♦♦♦

A 54-year-old woman was found dead in bed by family members in the morning. The death investigator arrived onsite to conduct the investigation and the family members left the residence shortly after being interviewed by the death investigator. The death investigator contacted the recovery organization to refer the case. Due to training conducted in his office, he followed the checklist in his investigative folder and remembered to document the whereabouts of the family after they left the residence. The recovery organization called the telephone number provided by the death investigator and the recovery organization was able to successfully complete a donor authorization and Donor Risk Assessment Interview (DRAI). The recovery was successfully completed on the same day, between the external examination and post-mortem examination of the decedent.

investigators and recovery organization staff by their respective offices about procedures, forms, and guidelines. Ongoing training can take place in many different situations. Monthly or quarterly meetings and office sponsored skills days provide opportunities for learning. It may be helpful to give the death investigation office the opportunity to interface with critical recovery organization staff on a regular basis. Examples of orientation and training may include but are not limited to the items listed below.

Donation Organization Training Opportunities

- Recovery organization staff observing post-mortem examinations.
- Recovery organization staff learning how to take photos of the donor for investigative purposes from death investigators.
- Recovery organization staff obtaining continuing education credits by participating in local or regional death investigation courses, a practice supported by AATB, EBAA, and AOPO.
- Recovery organization staff participating in *ride along* investigations with death investigators for that office.
- Recovery organization staff to attending a local or regional death investigator's association meeting to network and learn about common issues associated with donation.
- Recovery organization hiring a full-time employee to work as a liaison in the death investigation office.
- Recovery organization taking a tour of the death investigation office in order to understand the different aspects of death investigation including; toxicology, autopsy document release, family viewing areas, and decedent arrival/departure storage protocols.

Death Investigator Training Opportunities

- Death investigation staff witnessing the donor screening, authorization, and Donor Risk Assessment Interviews (DRAI).
- Death investigation staff being introduced to current clinical applications of organs, tissues, and eyes. Presentations may even be coordinated in cooperation with all local recovery organizations to cover all clinical applications in one presentation.
- Death investigation staff attending a recovery case with an experienced and knowledgeable team/ person. It is commonly recommended that anyone who views a recovery procedure be required to see the entire process, to ensure that the viewer sees the level of care and attention given to proper anatomical reconstruction/restoration.
- Death investigation staff receiving training on the impact of donation on the family of the decedent.
- Death investigation staff receiving training on how other recovery organization and partner agency collaboration efforts are resulting in mutually beneficial working relationships.

Requesting Approval for Donation

State and local statutes grant the death investigation office legal custody over a decedent as evidence. In many instances, the death investigator is the only party that may permit or deny authorized donation from moving forward. As a result, donation organizations often request permission from the death investigator to proceed with donation. In most states, if the death investigator feels that the removal of specific organs, tissues, or eyes would jeopardize the medical and legal determination of the cause and/or manner of death, they have the right to restrict donation either entirely or partially.

It is imperative that all relevant information and case details be shared so that accurate decisions can be made. Effective communication and information sharing helps ensure that the death investigator can make an accurate and informed decision concerning the approval of organ, tissue, or eye donation. The clear and direct communication of circumstances of death, medical and social history, and other relevant factors fosters a more trusting relationship and may increase the rate of approval of organs and tissues.

When the circumstances surrounding a death are unknown or puzzling, the death investigator may be hesitant to approve donation prior to the investigation. The death investigator may also have concern that physical evidence, such as trauma or abnormalities, may be lost or go unnoticed by the recovery organization. The potential of missing something vital to the determination of cause and manner of death may lead a death investigator to deny donation or to restrict specific organs or tissues.

The decision to approve organ, tissue, or eye donation can be based on their potential application. A death investigation office may be less likely to approve donation of organs, tissues, and eyes which are only acceptable for medical research or education, as they are not utilized directly in patient care or therapy. Donation organizations should establish practices ensuring the intended use for transplant or non-transplant of organs, tissues, or eyes is communicated to the death investigator.

Record Sharing with Death Investigators

Information obtained during or because of the donation process may be of value to the death investigation. Medical records may be considered evidence and should be provided to the death investigator for the sake of a comprehensive death investigation. Some state statutes require the sharing and documentation of all physical findings and medical records. Statutes, agreements, and practices for distributing records should be developed by the individual recovery organization and the death investigator. As the death investigation and surrounding information is time-sensitive, practices should be developed which promote an expeditious release of information.

What Information May Be Beneficial to the Death Investigator?

Examples of relevant beneficial information may include, hospital culture results, final diagnostic radiographic dictations, serology/NAT and other infectious disease testing results, funeral home information, tissue processing culture results, the Donor Risk Assessment Interview (DRAI), the donor chart and physical assessment forms, emergency services reports, and progress notes.

The physical assessment performed prior to recovery and autopsy may provide much needed information to the death investigation. The physical assessment can also aid in confirming the identification of the donor. Estimated or reported information about the donor's weight, height, sex, race, the hospital ID band with a medical record number (MRN), and reported tattoos or piercings, can be cross-referenced with the DRAI and other medical records. Accurate pre-recovery height and weight are of tremendous importance to the death investigation; in particular, an accurate assessment of heart weight by the examining death investigator depends heavily on body size.

Recovery notes documented before, during, and after the recovery may contain detailed information of physical findings and chain of custody of collected evidence. These may include blood samples, vitreous fluid, medication patches, IV medication, clothing, bagged hands for gunshot residue testing, subdermal or intramuscular bruising noted during recovery, and noted internal trauma within recovery sites (e.g., extremities, chest, abdomen).

Cardiac pathology reports and histology slides are essential for a death investigation. After valve recovery, the post-valve recovery heart remnant is usually examined by a pathologist and a cardiac pathology report is issued. Copies of slides and/or the heart remnant may be returned at the request of the agency investigating the death. These reports can provide information that may be helpful in determining manner or cause of death, such as valvular heart disease, cardiomyopathies, endocarditis, congenital heart malformations, ischemic heart diseases, or benign or malignant tumors. Procurement and processing notes are of great importance to the pathologists investigating the death and examining the heart.

Ocular images and documentation of ocular abnormalities can be useful in gathering information surrounding the death of an individual. Certain findings, such as conjunctival hemorrhage or petechiae, can indicate trauma that may not be apparent during the body inspection.

Donor Risk Assessment Interview (DRAI)

A donor risk assessment interview, or DRAI, is a documented dialogue conducted in person or by telephone with an individual or individuals knowledgeable of the donor's relevant medical history and social behavior. The relevant social history is elicited by asking questions regarding certain activities or behaviors that are considered to place such an individual at increased risk for a relevant communicable agent or disease.

Thorough risk assessment is performed by asking questions that are answered by the individual completing the DRAI, providing a vital tool to screen for eligibility. These answers are recorded as part of the donor chart and offer a detailed description of the donor's history. Information obtained from the interviewee on the DRAI by the recovery organization may be critical to the investigation and may include, but is not limited to alcohol use, prescription drug use, recreational drug use, over-the-counter drug use, mental illness, incarceration, chronic and acute medical history, surgical history, primary care physicians and specialists visited by the decedent, and travel history. This interview may provide critical information and details surrounding the donor's history that connect or contribute to the cause and manner of death. For example, the sudden, unexpected death of a middle-aged individual while walking on the street may be simply and easily explained if a chronic history of untreated cardiac disease is revealed in the DRAI. This information may even rule the case a natural death, therefore transitioning the death certification to the primary care physician or clinician instead of the death investigator.

Infectious Disease Screening Results: Reasonable Disclosure of Information

The Department of Health and Human Services 45 CFR 164.512(b)(1)(iv) permits the disclosure and sharing of protected health information by covered parties when there is the potential for contraction and/or spreading of communicable diseases. All relevant medical records are discoverable as physical evidence and relevant to the death investigation by death investigator.

Serological, nucleic acid testing (NAT) (AATB Standards for Tissue Banking D4.230), or infectious disease screening results (e.g., Ebola, Zika, SARS-CoV-2) may be provided in accordance with the established practices and procedures as agreed upon by the individual recovery organization and the death investigator. Agencies involved in donation and death investigation share responsibility regarding testing for infectious diseases. Death investigators and donation agencies need to establish procedures to notify each other of testing being performed. Agencies will share testing results to reduce incidence of discordant test results that render donors ineligible and confound outcomes.

Documentation

Documentation of relevant physical findings, medical record findings, case-related communication with the death investigator, a decedent's personal effects, and disposition may be considered evidence and be beneficial to the death investigator. Findings should be described, but not interpreted, as diagnosing injuries or findings may be inaccurate and/or contradict the diagnosis of the death investigator.

Documentation of critical communication between the death investigator and the recovery organization is not only required to maintain real-time donor record management but may be discoverable in a court of law or subpoenaed. Details that are documented surrounding death investigator's release for donation, such as restrictions and requests, should be uniform and standard practices should be developed for individual offices in collaboration with appropriate death investigators. Information documented should include the first and last names of the persons contacted, as well as their title. The dates and times of these conversations should also be captured. Documenting method of contact can also be helpful (e.g., phone, text, email).

Identification

Documentation of decedent identification is essential in retaining the integrity of the chain of custody. As the decedent is under death investigator jurisdiction, granting approval to recover prior to the viewing/external examination/autopsy places the responsibility of maintaining the chain of custody on the recovery organization. This includes ensuring the traceability and location of the decedent and all associated potential evidence.

Establishing the Chain of Custody

The Organization of Scientific Area Committees for Forensic Science (OSAC) defines chain of custody as, "The order in which a piece of evidence should be handled by persons investigating a case, specifically the unbroken trail of accountability that ensures the physical security of samples, data, and records in an investigation." Chain of custody should be established upon receipt of the donor, with the date and time recorded. Documentation of observations, physical evidence, belongings, witnesses, specimens for testing, and the location of recovery are a few examples of things that may be considered when documenting chain of custody.

When establishing custody, it may be beneficial to document any present parties. This includes recovery staff, transporters, mortuary service staff, hospital staff, death investigators, or funeral home staff. Documentation of witnesses is beneficial when itemizing belongings or specimens, establishing chain of custody, collecting specimens, and releasing custody. A detailed inventory of belongings and specimens, and their condition at the time of receipt, may aid in cases in which liability is in question or the viability of evidence is under scrutiny.

Documentation should be descriptive, but not definitive. For example, "yellow metal ring with clear stone" should be documented instead of "gold diamond ring". In the unfortunate event that belongings are lost or misplaced, documentation of decedent effects may be utilized in assessing property values.

Clothing or other items should not be physically altered, cut, or torn. These belongings may also hold value in the investigative process. Damage to clothing or belongings may be used to match decedent injuries and provide more detail concerning how the injury took place. For injuries such as blunt force or sharp force trauma (e.g., gunshot wounds or injuries from a pedestrian vs. car), preservation of belongings (e.g., clothing, damaged items found in pockets) is critical to identifying the point of impact or the trajectory of a projectile.

Documentation of transportation may also be beneficial and relevant in efforts to maintain a positive working relationship between the recovery organization and death investigation office to provide reference or arrival and departure times when the investigation, autopsy, or funeral services may be time sensitive or delayed due to the donation process.

Specimens collected for the death investigator are critical to the investigation and are considered physical evidence. Assuring the integrity and viability of this evidence is another critical element in maintaining the chain of custody. Just like patient belongings, transferred specimens should be documented when custody is obtained, at the time of collection, and when custody is relinquished.

The chain of custody of specimens is established when a representative of a recovery organization takes custody of a specimen or item. An example of this would be a recovery organization staff member picking up a pre-mortem blood sample from a hospital laboratory. Custody is then relinquished when custody is established by any other person(s). For example, after the recovery is completed, that same recovery staff member gives a portion of the pre-mortem sample to the death investigation office.

Establishing a chain of custody enables the ability to identify breaches in custody. For example, following recovery, a secure seal or lock placed on a body bag may provide confidence that the integrity of evidence enclosed within the bag is maintained. A seal or lock may be single-use or reusable, (e.g., tag, wire lock, zip tie) which must be actively removed or damaged to open the body bag. Documenting when locks and seals are applied to evidence helps to provide a timeline of when a breach in the chain of custody may have taken place and can help identify the location of lost evidence or decedent belongings.

Cooling

Documentation of cooling times is not only essential for completing the donor record but may also be relevant to the death investigation. A lack of cooling can result in expedited decomposition and may impact findings. Therefore, detailed records of cooling timelines may be beneficial in diagnosing the onset of injury or identifying various post-mortem changes.

Eye and tissue banks also must document cooling times per AATB and EBAA Medical Standards. These cooling times help in determining the safety and eligibility of tissue. For eye donors, cooling time may be defined as the time the body is refrigerated or the time ice or cooling packs are placed on the closed eyes.

♦♦♦ Case Study ♦♦♦

An 18-year-old male died secondary to blunt force trauma from a motor vehicle collision. During treatment in the field, medics cut the decedent's clothing and inadvertently also cut through a metal necklace that was noted to be silver in color. Death was pronounced at the scene and all belongings, including the necklace, were enclosed in the body bag and transported to the local hospital morgue. The legal next-of-kin authorized donation and upon receipt of the decedent, the recovery technician noted a "broken silver-colored metal necklace and a cut black shirt" in the decedent's belongings. The family called, seemingly distraught, on the following day stating the recovery technician had destroyed the decedent's belongings. Documentation upon establishing custody permitted concise, positive follow-up to the grieving family members, as the damage occurred during life-saving efforts by paramedics.

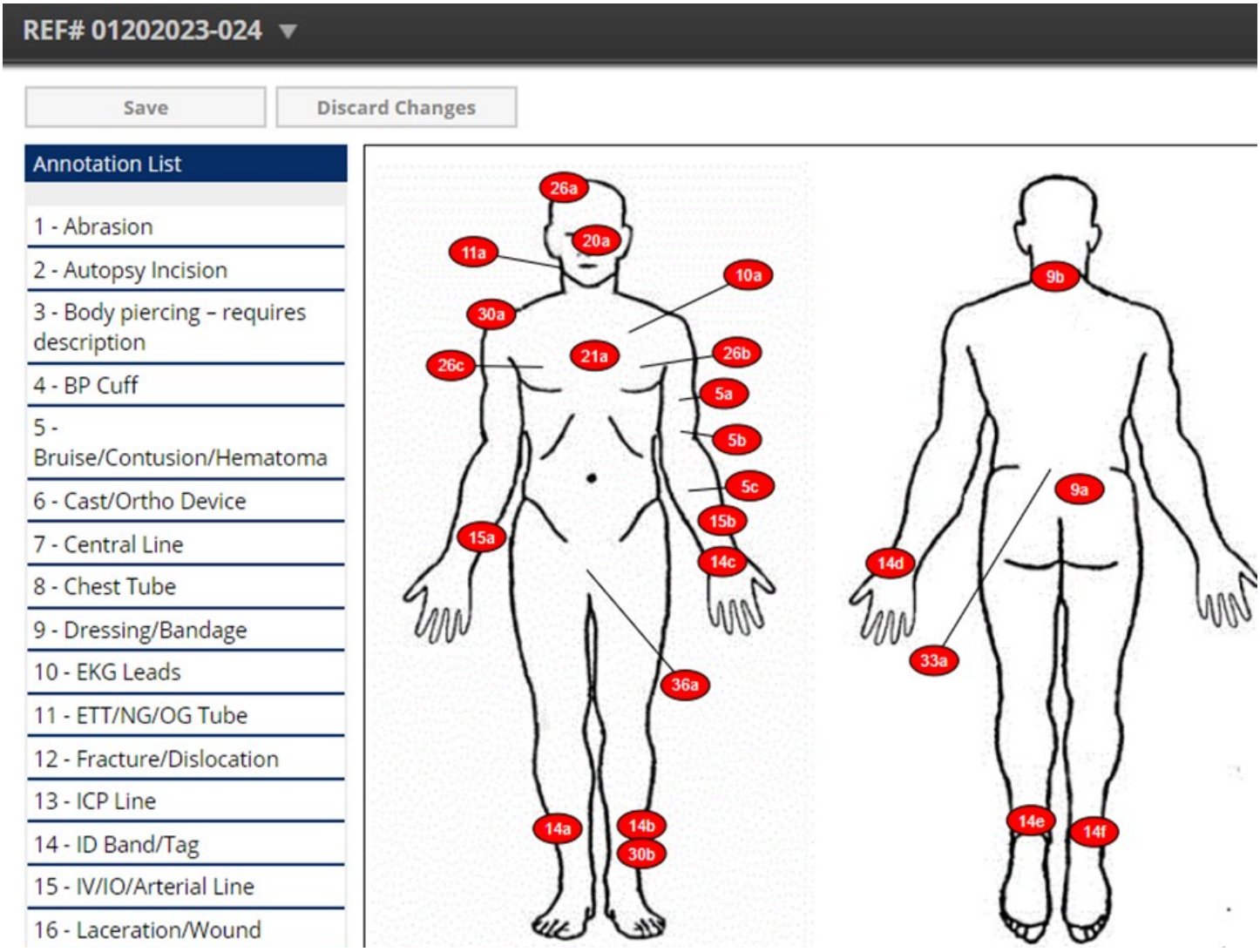
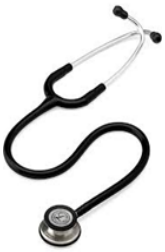


Figure 2. The image above illustrates how physical assessment findings may be documented in a donor record.



Medical Findings

Any new medical findings or potential diagnoses should be treated as though they are equally as important as the physical findings. Abnormal findings, diagnostic outcomes, and suspicion of active viral infections or communicable diseases should be relayed to the death investigator expeditiously. Signs of chronic comorbidities or diagnosis by a clinician directly related to the cause of death, or contributing to the cause of death, should also be relayed in an urgent manner.

Physical Assessment Findings

All physical assessment findings should be documented in detail to ensure that there is a record of relevant or discoverable findings, refer to **Figure 2**. This may include the identification of injuries, abnormalities, or *pertinent negatives* (the absence of outstanding or expected findings). This practice is essential to the proper completion of donor records and may also impact the death investigation. Detailed record keeping also provides historical reference points if an inquiry is made later.

Documentation should remain descriptive, with no interpretation offered. Identification of injuries and/or lesions (e.g., abrasions, contusions, lacerations, blood clots) should include the location of the finding and the estimated size.

♦♦♦ Case Study ♦♦♦

A 36-year-old male was admitted to the emergency room after suffering an apparent cardiac event with no prior medical history and no visible injuries or other concerning scene findings. He died in the cardiac intensive care unit (ICU) several days after admission. Due to the sudden nature of the death in combination with the decedent's young age, the case was under death investigator jurisdiction. Although the family gave authorization for donation and completed a DRAI, the death investigator was hesitant to release for donation. Upon further evaluation of the medical records, diagnoses of cardiomegaly, hypertension, and severe cardiopulmonary insufficiency were noted. This information was relayed to the death investigator, who then declined further death investigation, as the case was now considered a natural death. This case serves as an example of how recovery may confirm medical suspicions and strengthen relationships between donation organizations and death investigators.

It should be noted that there are differing perspectives on whether a recovery organization should document exact measurements of physical findings. While it is considered more accurate to measure a wound, scar, or other finding, there is a possibility that the death investigator will also measure the same findings, refer to **Figure 3**. If the physical assessment and autopsy measurements contradict one another, it may call into question which measurement is correct. It is most likely the measurement on the autopsy report will stand as a death investigator has more experience and training in the proper measurement of physical findings. This can be avoided by providing approximate measurements of physical findings, such as comparing the size to another well-known object (e.g., round lesion approximately the size of a quarter). Such documentation should also be maintained throughout the tissue recovery**.** The location, description, and size of abnormal intraoperative findings should be detailed in the same manner.

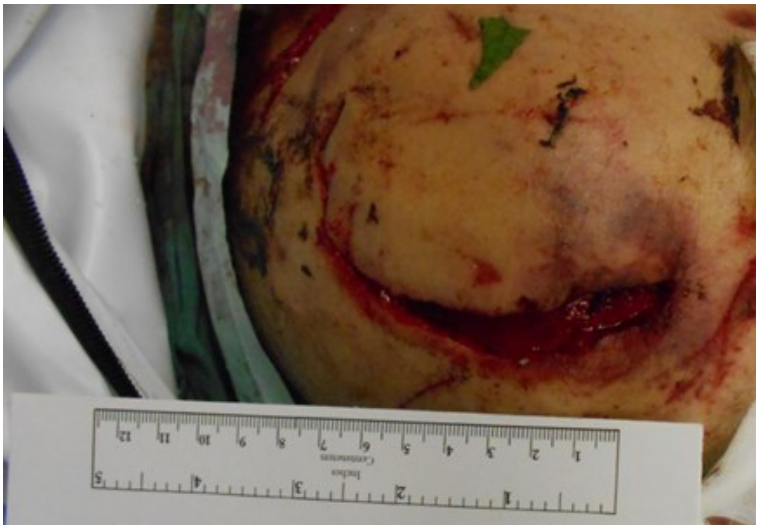


Figure 3. Apparent small laceration, roughly 2" superolateral to the right tibial tuberosity. Photo: Craig Nelson, MD.

Significant Ocular Exam Findings

Ocular examination, refer to **Figure 4**, performed by the eye bank may yield information pertinent to the examination and/or eye donor eligibility. Once the eye bank performs a procedure (e.g., in situ excision or enucleation), the condition of the eyes will change. Observations noted during the pre-recovery ocular examination may include systemic (e.g., jaundice, sarcoidosis), local (e.g., petechial hemorrhages, pterygium, infiltrates, melanoma), surgical (e.g., previous cornea transplant, LASIK or other cornea re-shaping procedures, glaucoma tube shunt, iridectomy), traumatic (e.g., laceration, abrasion), or circumstantial (e.g., dirt, glass, debris) findings. The significance of observations to each involved party varies by case. For instance, an observation of a corneal transplant or prosthetic eye has relatively obvious implications for the

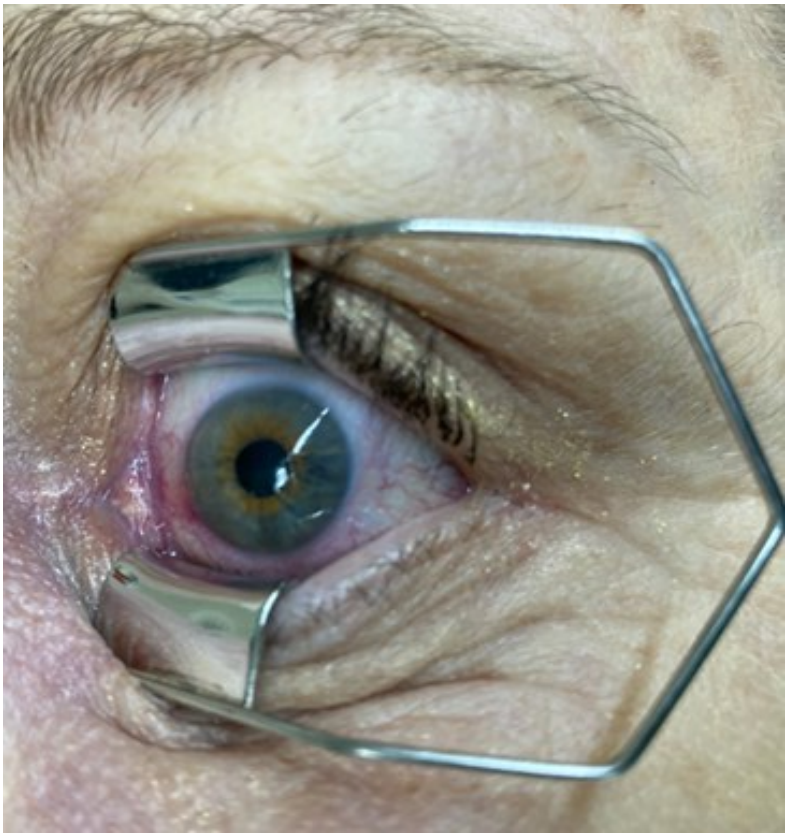


Figure 4. An ocular speculum placed to perform an ocular examination.

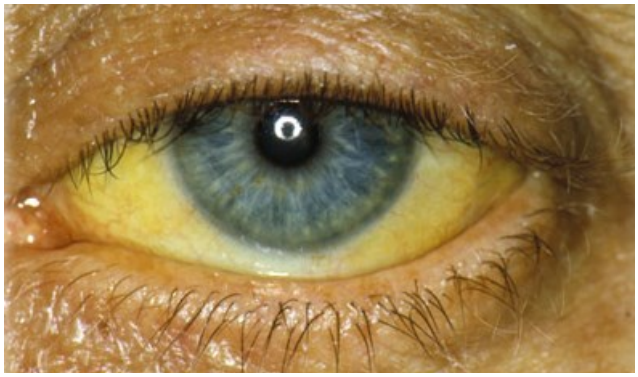


Figure 5. Icterus, also known as scleral jaundice.

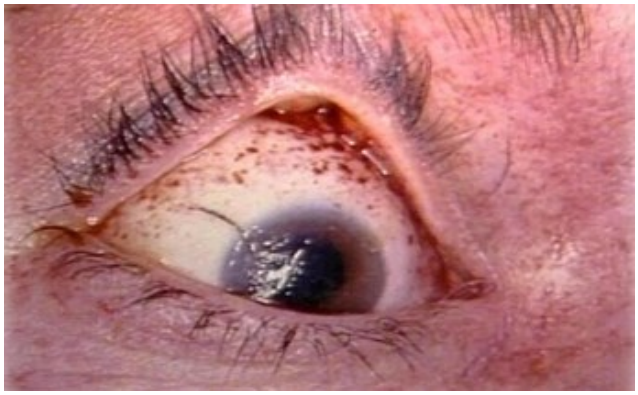


Figure 6. Petechiae due to strangulation.

eye bank, but may also be useful to the death investigator to assist in the identification process or in the investigation of case circumstances (e.g. the deceased is identified as having poor vision which may be relevant in the investigation). It is important for the eye bank recovery technician to note if contact lenses were present in the donor's eyes from an investigative, identification, and chain of custody perspective.

Jaundice, refer to **Figure 5**, is usually an indicator that there is an issue with a person's liver, gallbladder, or pancreas. This can be attributed to a variety of factors, which include cirrhosis, heart failure, hepatitis, sickle-cell anemia, acute pancreatitis, and carcinomas. Because it is possible to see jaundice in the ocular tissue only, it is important to document as a finding for the death investigator.

Petechial hemorrhages, refer to **Figure 6**, are small red or purple pinprick size dots of blood that appear under the skin or mucous membranes. Two of the main causes are trauma and excessive pressure (e.g., vomiting, strangulation, violent coughing). Asphyxiation, accidental or intentional, may result in the presence of petechial hemorrhaging of the face or conjunctiva, which is significant to the death investigation.

Preservation of Evidence

In cases where recovery takes place prior to the death investigation, critical pieces of physical evidence may be obtained or moved from their original location due to the nature of the recovery process. Removal of clothing, belongings, therapeutic medical devices/portals of entry (e.g., central lines, endotracheal tubes [ET], intravenous lines [IV], intraosseous catheters, gunpowder residue on the hands, and/or dirt or debris surrounding an area of injury or wound prior to evaluation and documentation by the death investigator would be considered an alteration of evidence. Removal or alteration of any items or evidence should not occur without the expressed permission of the death investigator.

♦♦♦ Case Study ♦♦♦

A 35-year-old woman was found dead as a result of head and neck injuries. The death investigator suspected that the injuries and cause of death were due to a fall taken by the decedent. The death investigator released for eye donation prior to autopsy. During the recovery, the technician noted petechiae on both eyes that were overlooked by hospital staff. The technician notified the death investigator of this finding and additional medicolegal investigation was performed. The death was determined to be a domestic violence homicide resulting from strangulation. Physical exam findings can be difficult to detect even in fatal strangulation cases. This technician's attention to detail allowed for identification of a dangerous criminal and protection of potential future victims. As the death investigator collected information surrounding the case, there was suspicion of domestic abuse. The petechiae that was noted by the technician led the death investigator to look at the injuries more closely. Because of this information, it was discovered that the fall was secondary to strangulation. NOTE: Based on the agreed upon protocol with the death investigation office, photographic evidence may be sufficient, or it may require an additional phone call prior to recovery.

The establishment of defined practices and procedures to ensure the integrity of findings and chain of custody, such as decedent belongings and physical evidence, will strengthen the relationship between a death investigation office and a recovery organization. Clear and specific documentation (chain of custody) regarding movement of the body (e.g., hospitals, death investigation offices, funeral homes) may locate items or evidence that may go missing when and if the chain of custody has been broken.

Recovery and Evidence Preservation

Efforts should be made to limit manipulation or alteration of anatomical findings during recovery, as the body may contain clues that can help confirm or clarify the circumstances around the manner and/or cause of death. For example, the recovery of pelvic tissue may cause disruption of abdominal findings or breach the peritoneum. The rupture of the bladder during recovery eliminates the option for post-mortem urine collection, which may be essential for toxicological testing by the death investigator.

♦♦♦ Case Study ♦♦♦

A family of four and delivery truck driver for a furniture company were involved in a motor vehicle accident. A member of the family of four and the delivery truck driver were killed in the accident, and both became eye and tissue donors. During the recovery process, the eye bank removed contact lenses from the delivery truck driver. The presence of the contact lenses was noted on the physical assessment under the ocular findings. The contact lenses were placed into a red top vacutainer with saline and logged in as decedent belongings. Subsequently, the surviving family members attempted to bring a wrongful death lawsuit against the furniture company. The family claimed that the driver was at fault because he was not wearing his glasses at the time of the accident. However, due to the eye bank documentation of the contact lenses found in the decedent's eyes upon recovery, this claim was accurately disputed.

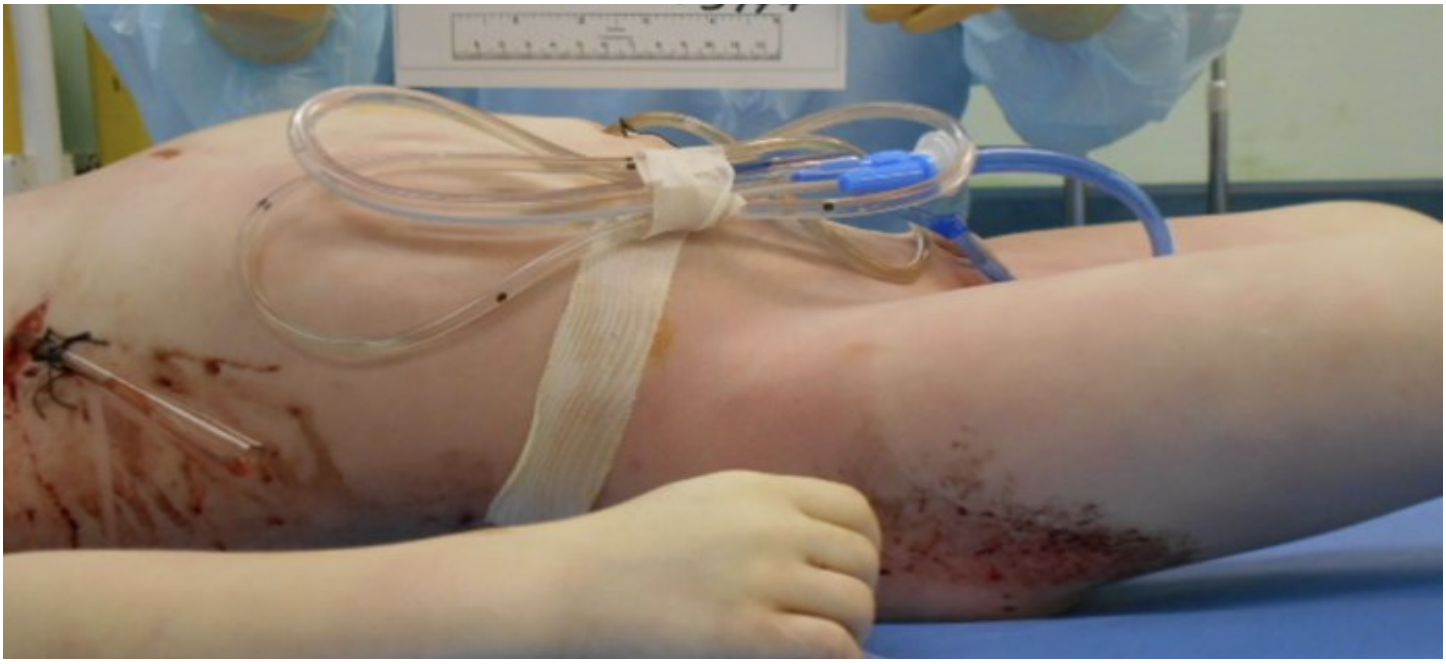


Figure 7. Debris and medical artifact. Photo: Craig Nelson, MD.

Photography

Recovery may cause alteration to the donor's physical appearance. The death investigator may request images to preserve evidence or the chain of custody. Images should be captured in a manner which enables the death investigator to clearly identify the anatomical or physical location of the photographed area. Photography should follow protocol established by the death investigation office and the individual recovery organization.

Photographs should provide a clear reference with respect to specific points in time in the recovery process including 1) the receipt of the donor body, 2) prior to the removal of any medical/therapeutic artifacts and belongings/clothing, 3) after the removal of these items but before donor preparation, and 4) after the donor preparation, but before recovery.

Figure 7 demonstrates capturing images after the removal of clothing but prior to the removal of medical artifacts such as IV lines and chest tubes. This image also demonstrates the critical role photographs may play in capturing artifact, such as debris or blood, prior to the completion of donor preparation.

Items (e.g., chest tubes, central lines) in an area of injury that do not prevent a proper donor preparation or recovery should remain in place and not disturbed whenever possible. For example, an endotracheal tube will not prevent the proper preparation or recovery of tissue from the lower extremities and may be relevant to the death investigation. This would be considered a medical/therapeutic artifact which should be left in place. The death investigator should be consulted if artifacts or belongings overlaying an area of injury may preclude a proper donor preparation or surgical recovery.

Editing Images

Images taken for the purpose of evaluation by a death investigator should not be altered or manipulated in any way prior to delivery to the death investigator.

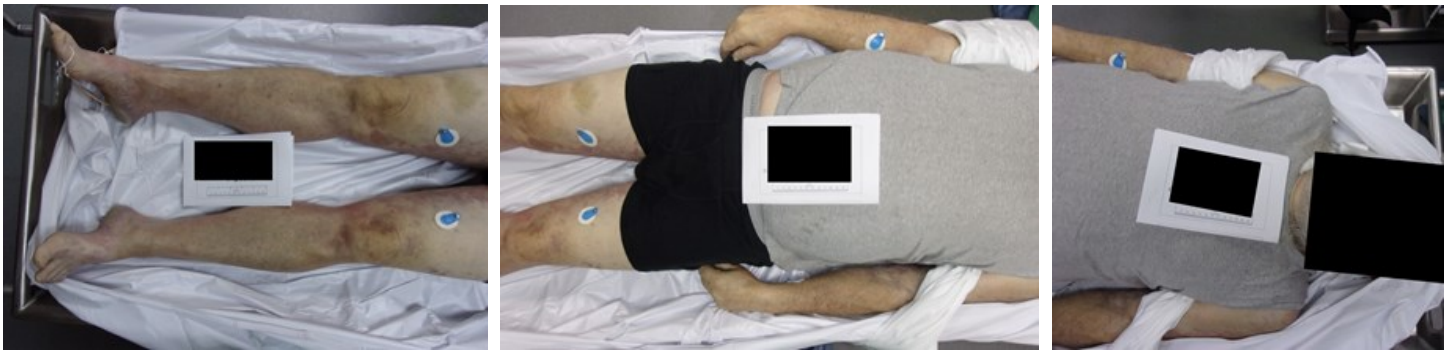


Figure 8. Full body photographs. Photo: Craig Nelson, MD.

Full Body Images

Images for investigative purposes should not exclude any detail. This is contrary to most recovery photography protocol, which seeks to exclude identifying traits or characteristics of a decedent. Full body or overall images should include all aspects of the body, utilizing a technique which provides an accurate perspective and a range which provides sufficient detail for review and identification of all findings for investigative purposes. For example, capturing images of each plane of the body (anterior, posterior, left, and right) and in thirds (head to mid-torso, mid-torso to mid-thigh, and mid-thigh to foot). **Figure 8** provides examples of images captured within a single plane, the anterior view, in thirds, with a photo scale prior to the removal or alteration of any effects.

The camera should always be held perpendicular to the subject being photographed. Some death investigation offices require that images of the decedent show the entire body, from head to toe, in a single photograph. Anatomical orientation should be provided to reduce or eliminate confusion or assumptions. While this may be possible in an autopsy suite, as most are equipped with platforms for photographers to stand on above the patient, this may not be possible for a recovery staff in a standard operating room or other recovery environment. This should be discussed with the death investigation office in advance.

Photo Scale and Donor Identifier

A scale, a measuring tool (e.g., ruler, placard), and a patient identifier (e.g., donor number), should be used when images are captured for screening/eligibility and forensic or investigative purposes. Death investigators typically use an American Board of Forensic Odontology (ABFO) No. 2 Photomacrographic scale, refer to **Figure 9**. This scale provides an accurate source of reference for visualization and the ability to scale measure the size of elements in the image in a scientific manner. The scale should be placed near the area being captured to provide an accurate point of reference and at 90 degrees of the area being photographed. Pre-printed Avery labels with scales can be used, as these are cheap, disposable, and can be attached to other items.

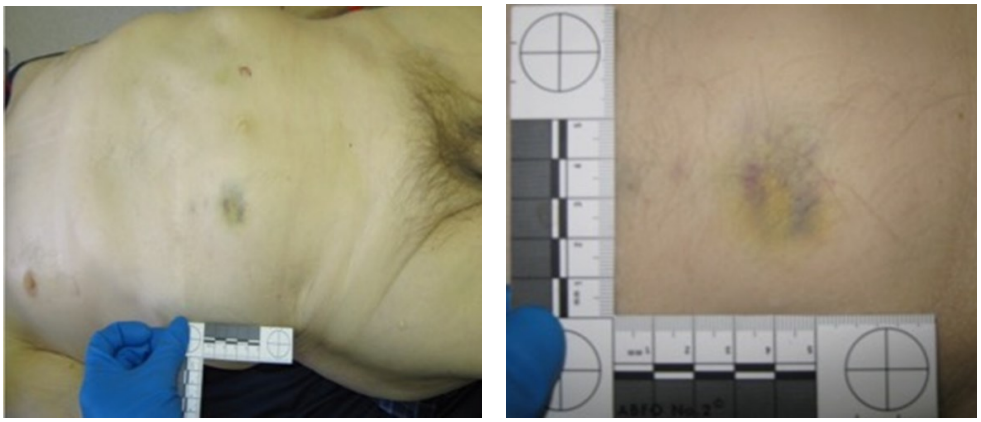


Figure 9. These images demonstrate scaling and capturing the location of a physical finding.

Belongings and Chain of Custody

Photographs may be used to document the chain of custody of donor personal belongings, the condition of belongings, and specimens being moved or transported with the body. Images of belongings or specimens received with the body should be captured at receipt of the donor, prior to the alteration or removal of any items from the initial state of the body. Images of belongings or samples to be transported or moved with the body following recovery should be captured in the manner in which they are left by recovery staff. These images may be used to establish the organization's appropriate handling and transfer of the belongings and specimens.

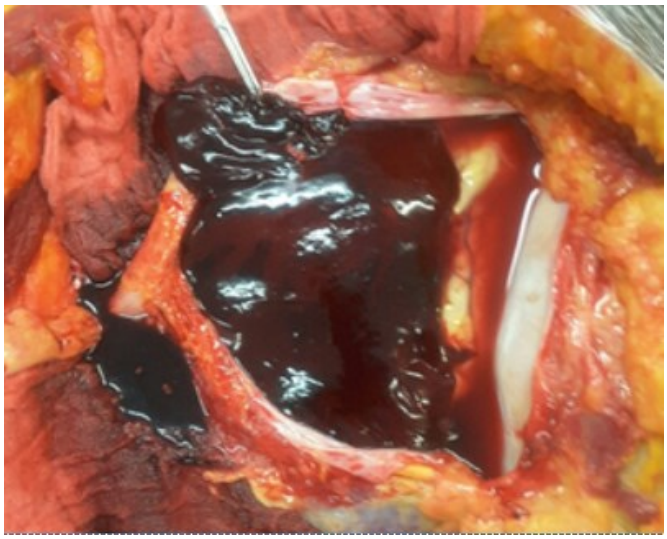


Figure 10. Coagulated blood noted after pericardial excision and prior to cardiectomy. Photo: Craig Nelson, MD.

Internal/Intraoperative Photography

Findings may be discovered during the recovery that require images of an area that are within a sterile field, refer to **Figure 10**. Care must be taken to avoid contamination of the surgical field. If a close-range image is essential, photography equipment should be utilized in a manner which maintains the integrity of the sterile field and sterile recovery staff. If available, a sterile ruler or sterile scalpel handle with a ruler may be included in the field to provide scale. Actions and movements should be in accordance with the Association of periOperative Registered Nurses' Standards and follow the guidelines set forth in the AATB Aseptic Technique Guide.

Ocular Images

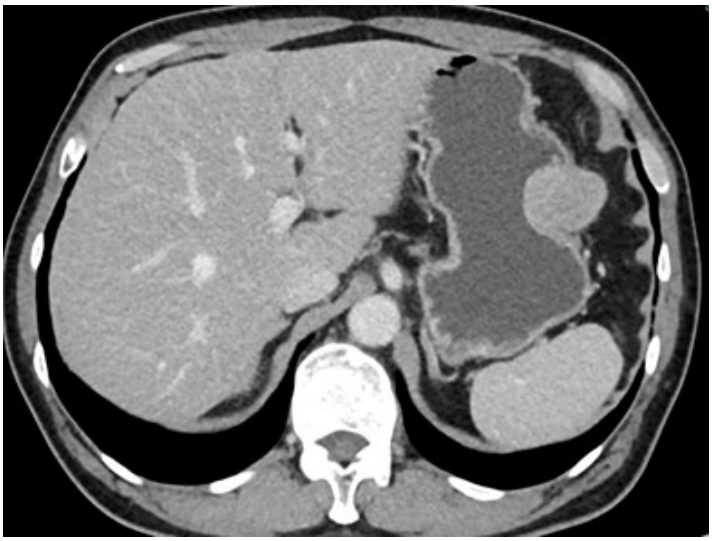
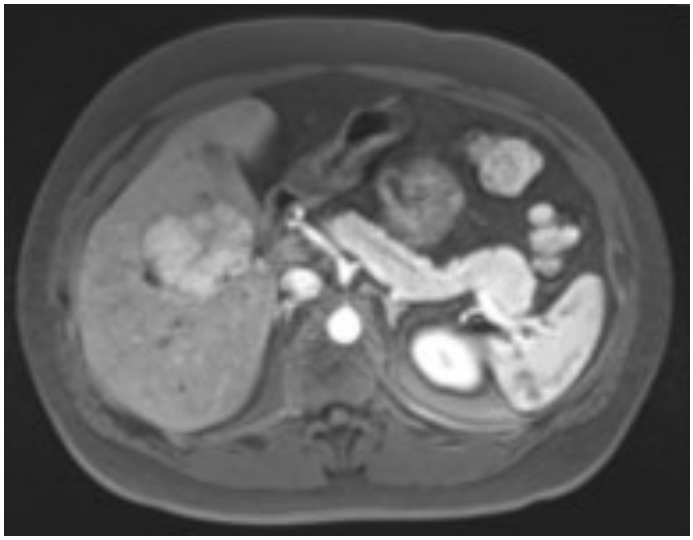
If required, ocular photographs should be taken prior to and after the recovery process. The intended purpose is to identify eye color, trauma (e.g., petechiae, subconjunctival hemorrhage), and the presence of contact lenses. Each of these can contribute to the determination of the cause of death. Care should be taken to follow the death investigation office's processes for taking photographs. Please refer to the individual eye bank's protocol with the death investigation office for exact imaging and file transmission preferences.

Reconstruction/Restoration

Organizational practices may require the capture of images for documentation of the donor prior to and/or following recovery. This may be done to provide a point of reference in circumstances in which the impact of the donation process or the integrity of restoration efforts is in question. If these efforts are in question, these images may help provide evidence that actions of the recovery organization did not cause any liability on their part. Images should include the entire surgical site prior to and following recovery.

Shared Organ Cases

In some circumstances images may be required on shared organ, tissue, and eye cases. This may include the capture of images of the patient on a hospital unit prior to organ recovery. In such situations, the patient may be unstable and altering the position of the body may have adverse effects, such as shifting medical devices critical to patient stability. Under such circumstances, it may be acceptable to complete partial image capture (e.g., anterior, left, right) to avoid excessive manipulation. In-situ images of organs prior to removal from the body during organ recovery may be requested as a condition for release from the death investigation office.

Figures 11 and 12. Examples of CT (left) and MRI (right) images. Photos: Angela Levy, MD.

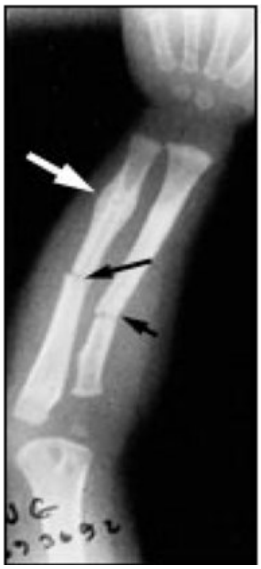
Radiography

In many cases the existence, extent, location, or severity of injuries and/or trauma may not be apparent during an external examination. The concern of the death investigator may be the oversight of internal injuries with limited or no external trauma. Furthermore, there may be concern of alteration, loss, or misdiagnoses of internal injuries such a soft tissue trauma or bone fractures due to the recovery process. Pre-recovery radiography may enable the death investigator to differentiate trauma or resuscitative efforts from artifacts of the recovery process. For example, during resuscitative efforts ribs may be fractured. If a heart for valves is recovered it may be difficult for the death investigator to clearly confirm if the origin of fractures is trauma, resuscitative efforts, or transection of ribs during the heart recovery process.

Radiography – A technique of viewing structures of the body using electromagnetic radiation. Usually, radiographs are performed to view internal structures in situ but can also be used to analyze bones, tissues, and organs ex situ. X-rays, skeletal survey, CT, and MRI are commonly used radiography techniques.

♦♦♦ Case Study ♦♦♦

An 18-year-old male was involved in a hit-and-run motor vehicle collision. 911 was called. Upon their arrival, he was in respiratory distress and had to be emergently intubated. He was taken to the nearest emergency department where he became unconscious. A large bruise was noted on his forehead, but no other traumatic external findings. The CT scan showed marked cerebral edema, subarachnoid hemorrhage, and a right subdural hematoma. His condition deteriorated and he was pronounced brain dead 12 hours later. His mother consented to organ, tissue, and eye donation, but the death investigator was hesitant to release for donation because the investigation pointed toward a homicide. The death investigator needed to be confident that no other trauma was missed, or artifact created by recovery procedure. Therefore, a full body CT was ordered by the recovery organization. The study was negative for visceral and bony trauma. Due to these findings, the death investigator consented to organ, eye, and tissue recovery.



Skeletal Survey – A series of x-rays of all the bones in the body. A standard survey includes skull, spine, pelvis, ribs, and extremities. Skeletal surveys are used to assess entities such as bony trauma, non-accidental injuries in children, injury patterns, abnormal bone development, malnutrition, abnormal collections of air, and bone damage due to tumors. It is also used to detect foreign bodies such as bullets or medical devices.

Computed Tomography (CT) – An imaging scan that uses ionizing radiation to view both hard and soft tissues in slices as if the body were sliced like a loaf of bread. The word *tomo* means slice. CT scans are often used to view bony fractures, bone pathology, organ injury or disease, and fluid collections such as blood, refer to **Figure 11**. Three dimensional CT can also be performed.

Magnetic Resonance Imaging (MRI) – Body imaging that uses magnetic fields, radio waves, and field gradients to generate images of the body, refer to **Figure 12**. MRI is used to analyze soft tissues such as the brain, heart, liver, fat, cartilage, and tumors. It can also detect small hemorrhages. MRI has superior contrast resolution compared to CT.

Sudden Unexpected Infant Death

Sudden unexpected infant death (SUID) is the death of a seemingly healthy infant with no clear indication of trauma or acute onset of injury or illness. Investigations into SUID cases may be inconclusive due to the lack of physical findings or known contributing health issues. Some sudden unexpected infant deaths may be attributed to genetic disorders or mechanical asphyxiation, such as wedged between pillows or co-sleeping.

Infants may not exhibit many physical indicators of assault, abuse, or other trauma, such as defensive injuries, and cannot move themselves out of harmful or dangerous positions. Death investigators may complete additional investigative measures, such as doll reenactments, to understand the scene and circumstances surrounding SUID cases. Due to the potential to overlook physical findings at autopsy after donation, death investigators are often hesitant to permit the recovery of the heart for valves or ocular tissue.

Donation organizations must build relationships and discuss responses to these sensitive cases with death investigators. Every effort should be made to accommodate and support infant and child death investigation research by providing records and specimens when able.

♦♦♦ Case Study ♦♦♦

A six-month-old infant was found dead in her crib with no noted medical issues. The parents were approached for donation and authorized heart for valve donation. The death investigator was not going to permit recovery because the cause of death was unknown, and underlying trauma may have been present. The tissue recovery organization provided a skeletal survey and a full-body CT scan. The death investigator agreed to release to recovery if the skeletal survey and full-body CT scan were normal. They also required a cardiology report from the cardiac pathologist, provision of heart histology slides, and return of the residual remains of the heart after resection of the valves. The heart valves were successfully recovered, and all requests were fulfilled.

Toxicology

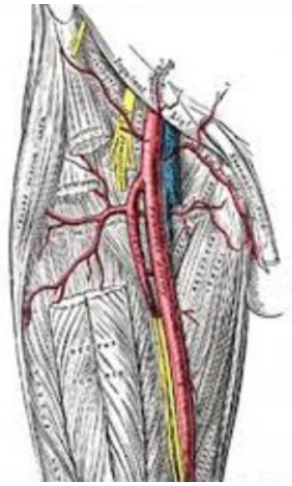
Toxicological testing, which oftentimes is performed in combination with an autopsy, looks for a variety of substances (analytes) present in the body. Examples of analytes include alcohols, illicit drugs, prescription drugs (taken as prescribed or abused), common poisons, and household and industrial chemicals. Toxicological screening may identify only one drug or substance, or it may highlight the presence of multiple substances.

Toxicological screening can provide qualitative information, such as identifying the presence of a substance or its metabolites. They can also provide quantitative information, which allows for the measuring of the quantity of the analyte present. It is important to note that chemicals, or analytes, can come to rest inside of a patient in a variety of ways. Absorption of a chemical or substance can occur through inhalation (e.g., lungs), ingestion (e.g., GI tract), injection (e.g., veins), or direct contact with the skin or mucous membranes (e.g., mouth, nose, dermal patches). This is why the DRAI (medical/social interview) specifically asks if the method of drug use is known, as the same substance can be snorted/smoked or injected.

When toxicological screening is performed and how comprehensive or focused the tests are varies with jurisdiction and on a case-by-case basis depending on the circumstances of death.

One of the challenges with assessing toxicology against donor eligibility criteria is the fact that toxicological results may take weeks to months to be finalized. This is partly due to the fact that in some jurisdictions, it may be a requirement that all toxicological screening is run by a government laboratory rather than a private toxicology firm. Some recovery organizations have sought creative approaches to this issue by offering death investigation offices the option of running toxicological screening through a private laboratory at the recovery organization's cost. This is often seen as a win-win situation since toxicological results can be completed quickly and the death investigator does not have to pay for the tests.

It can be helpful, when evaluating toxicological results, to compare them to the documented physical assessment findings of the recovery organization staff and the physical assessment documented on the autopsy report. This is because the review of relevant medical records should yield facts and information that align with one another to create a uniform clinical picture of the decedent. For example, if questionable marks on the decedent's lips appear like burn marks, receiving a toxicological result positive for methamphetamine is a confirmation that the patient was likely smoking the drug through a hot pipe during the time interval prior to death (days to weeks).



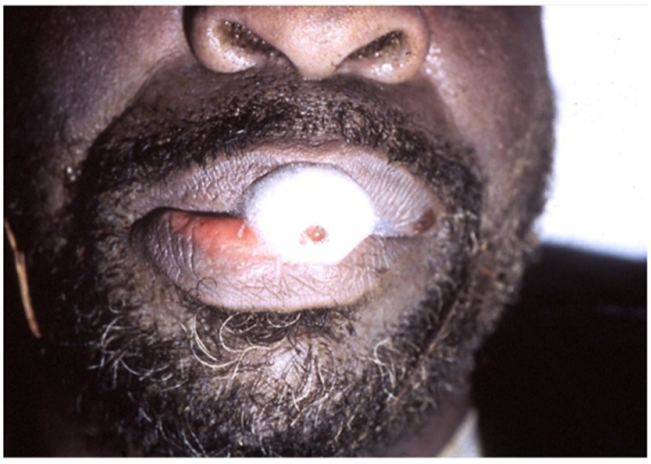
Specimens For Testing

The most common toxicological screens are performed on blood, but it is routine practice to analyze other specimens such as urine, gastric contents, liver, and vitreous humor. In some cases, toxicological evaluation of multiple body fluids is performed on the same patient.

Drawing blood from a peripheral blood vessel (e.g., the femoral vein or artery) may result in a more accurate toxicological assessment than blood drawn from the thorax (e.g., subclavian blood vessels, inferior vena cava, heart). This is due the fact that different tissue types *take up*, or absorb, different levels of substances. Blood located in the chest, following cardiac cessation, can yield inaccurate toxicological results due to the redistribution of substances as they diffuse between the blood

♦♦♦ Case Study ♦♦♦

An obese male was discovered by his roommate laying supine on the floor between the sofa and living room table. He was last seen alive 3 hours ago. Upon discovery, his skin was cool to the touch and there was no pulse. He was cyanotic (blue skin) and had bubbly foam emanating from his mouth and nose. The death investigator was contacted and upon investigation, he was pronounced at the scene. On the coffee table was a closed metal box, a spilled bottle of soda, and several burn marks. The decedent was a smoker. On the floor was a leather belt laying next to a pile of dirty laundry. A small gauge insulin needle was found on the table, but this was associated with his 10-year history of insulin-dependent diabetes mellitus (IDDM). Although distraught, his family authorized donation and there was nothing in his medical history that contraindicated donation. His musculoskeletal tissue, skin, and eyes was recovered for donation. Six weeks later, the autopsy report with toxicological profile was released and the main abnormality was that the donor was positive for heroin and 6MAM-morphine. The manner of death was filed as *accident*. The cause of death was an acute overdose of heroin.



Foam cap present in some cases including drug overdose. Photo: Kim A. Collins, MD.

You may have already noticed certain details in the scene investigation that were relevant but overlooked by (or not communicated to) the recovery organization before donation. Although the patient was diabetic, this did not fully explain the presence of the needle on the table. It is known that heroin abusers often keep their *kit*, or drug paraphernalia, in containers that they store and bring out when they are ready to take another dose. Insulin-sized needles are often used for intravenous drug abuse since they are small and are less likely to cause track marks or show needle marks after injection. The presence of the belt on the floor could have indicated that the patient did not keep a tidy home, or it may have been used to put pressure on his upper arm during the injection of drugs (it can be noted that a trained death investigator would inspect the belt for teeth marks, since this is how the belt is held tight during injection). The presence of a foam cone or foam cap over the mouth and nose can indicate an acute overdose of opiates due to acute pulmonary edema. Unfortunately, unless this is observed and documented immediately, this foam is transient and can be wiped away or vanish later when the decedent is placed in the body bag and moved to another location. A foam cone is rarely, if ever, noticed during a recovery organization's physical assessment at the time of recovery.

and surrounding organs (e.g., the heart and stomach). If a death investigator has requested that a recovery organization draw blood to conduct toxicological screening, extracting blood from the decedent's peripheral vessels is better than obtaining the blood from the heart or a more central vessel. The preferred sample site should be discussed with the partnering death investigation professionals and documented, along with the date and time of draw.

On the other hand, blood used for serological testing often has the best quality when drawn from the blood vessels of the thorax (e.g., subclavian vessels). This is due to the fact that blood in the legs may begin to form thromboemboli (clots) earlier than blood found in larger vessels near the heart. Blood that has begun to clot is difficult to draw and difficult to centrifuge when being prepared for antigen, antibody, and NAT (nucleic acid testing) to determine donor eligibility. Hemolysis (the rupturing of red blood cells) represents degraded specimen quality and may contribute to false positive serologic test results. Sometimes toxicological results are obtained from bile, gastric contents, solid organ samples, and even hair. The toxicological results from an inpatient hospital chart more frequently involve identification assays performed on urine and are not always reflective of the same substances found at time of death in the blood.

Vacutainers Used for Testing

Blood can be placed in various types of blood vacutainers depending on the type of testing to be performed. While blood for serological testing by the recovery agency is most often placed into red, tiger (black and red marble), or purple (lavender) top vacutainers, blood for toxicology may be placed into a grey top vacutainer which contains a preservative (sodium fluoride) and an anticoagulant (potassium oxalate). Once a grey or purple top tube is filled, it should be inverted several times in order to ensure that the additives in the vacutainer thoroughly mixes with the blood. Blood in a grey top tube is not acceptable for infectious disease testing.

Figure 13. Clean vitreous sample.

Vitreous Humor and Toxicological Screening

Vitreous humor is the transparent, colorless, gelatinous mass that fills the space between the lens of the eye and the retina lining the back of the eye, refer to **Figure 13**. It is produced by cells in the non-pigmented portion of the ciliary body. Unlike the fluid in the frontal parts of the eye (aqueous humor), which is continuously replenished, the gel in the vitreous chamber is stagnant. The metabolic exchange and equilibration between systemic circulation and vitreous is so slow that vitreous is sometimes the preferred choice as an “alternate bio-specimen” for post-mortem analysis. Additionally, vitreous is generally less susceptible to contamination due to the closed structure of the eye and is better preserved than blood after death.

Procurement of Vitreous

For eye donors it is preferred that the vitreous fluid be drawn post-corneal recovery. For many eye banks, vitreous draw prior to recovery precludes the tissue’s viability for transplant. Technicians are trained on proper vitreous sample collection, labeling, and chain of custody according to the death investigation office’s standards. Vitreous can be drawn after corneal recovery using a needle and syringe inserted into the globe of the eye, far from the clear cornea. The insertion is best at the lateral canthus, introducing the end of the needle to the center of the globe. The vitreous should be withdrawn slowly. A vacuum collection system should not be used thus rendering the specimen inadequate due to retinal contamination. The following things should be considered when drawing vitreous:

- The gauge of the vitreous needle. The larger the gauge, the increased likelihood for the introduction of contaminants.
- The size of the syringe. The larger the syringe, the greater increase in the pressure of the draw and likelihood for the introduction of contaminants.

- Consider including supplies to draw a vitreous sample from each eye. If a contaminated sample is recovered from the first eye, there is an opportunity to draw a clean sample from the second eye.
- Death investigators should be discouraged from using unsterile or reusable supplies to recover vitreous samples. Unsterile or reusable supplies may introduce artifacts from previous investigations into the current one, contaminating medicolegal specimens.
- Determine during penlight exam if vitreous has been drawn prior to ocular recovery. Vitreous that has been drawn prior to cornea recovery may compromise the cornea and render donor tissue ineligible for transplant. Before proceeding, ensure the cornea is uncompromised, sterile equipment was used, and the lot/ manufacturer/expiry information for the sterile equipment is available to the eye bank.
- As required, the eye bank will draw vitreous specimens. Eye banks should be encouraged to draw vitreous through the iris after removal of a cornea (to prevent contamination).
- Cases in which the death investigation office is holding off on vitreous draw while recovery is pending could result in the death investigation office missing their opportunity to draw vitreous. Eye banks and death investigation offices should coordinate carefully together to ensure this opportunity is not missed.
- The eye bank's standard operating procedure (SOP) should be followed if vitreous has been drawn prior to ocular recovery. Depending on the how the vitreous was drawn (e.g., aseptically or not, through the clear cornea) and the resulting shape of the cornea, some eye banks will continue with the recovery. Others will choose not to recover the tissue regardless of how vitreous was drawn.

Approximately 2 mL of fluid can be aspirated from each eye. The vitreous should be placed in a sterile tube. Unless otherwise specified by the death investigator, the specimen should be collected in a red top with no additives. The specimen should be clear and colorless. If small flecks of black-brown retina appear in the sample, the sample may be deemed inadequate for evaluation.

Ensure that the proper protocol for handling and transporting samples is established and understood by all involved agencies. Once vitreous samples have been obtained it is important that they reach the designated destination for analysis. If the recovery of the sample takes place at the death investigator's office, there may be a designated location for storing the sample. Other circumstances may dictate that the sample be left with the decedent for transport to the death investigation office. Whatever protocol is implemented, it must be adhered to by all parties in order to facilitate the safe transport and chain of custody for the specimen.

Performable Post-Mortem Vitreous Analyses

Depending on the environment, vitreous fluid can be procured up to approximately 4 days after death. Vitreous is best stored in a refrigerated environment but can be frozen for the purpose of archiving. Testing of vitreous demonstrates chemical changes immediately or shortly after death and can be used to aid in determining the cause and or approximate time of death. Analyses that can be performed on vitreous fluid include chemistry for the following:

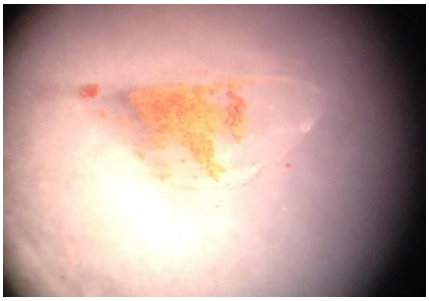
- Electrolytes: potassium, sodium, chloride, magnesium, calcium
- Physiological substances: glucose, ketones, urea, insulin, catecholamines, C-peptide
- Toxicology: drugs, ethanol
- Viral antibodies
- Acids
- Some trace metals

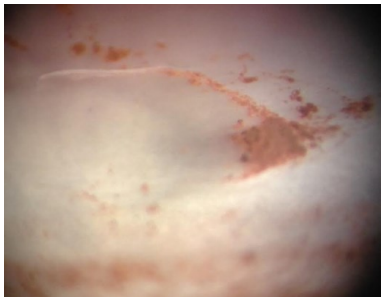
Contaminated Vitreous Samples

Care should be taken when vitreous samples are collected so as not to contaminate the sample with other substances. A contaminated vitreous specimen, refer to **Figure 14**, carries the risk of preventing proper identification of a potential cause and manner of death. Blood, povidone-iodine, uveal pigment, and bits of retinal material can all be considered contaminants to the sample that will affect the outcome of the testing or deem the sample unacceptable for analysis. The ramification for submitting a contaminated vitreous sample is, in part, a sample with particulates can physically clog the filtering mechanism. Secondly, if blood, povidone-iodine, ETOH, or some other non-vitreous component is in the tested sample, it can skew the results.

Figure 14. Contaminated vitreous sample.

Figures 15 and **16** demonstrate what a vitreous draw looks if the needle penetrates the cornea. Note the beveled shape, indicative of the shape of an aspiration needle. The deposition of red blood cells at the exit suggests the needle had been previously used on a blood draw. Following the rationale that different tissues within the body absorb analytes at different rates, a death investigator may compare the vitreous toxicological results to the blood toxicological results in order to correlate the post-mortem findings with the given history.





Figures 15 and 16. Slit lamp image of a cornea (endothelial side) after penetrated by a needle. Photos: Samantha Wetzler, MD.

Clots: Thrombus, Thromboembolus, and Post-Mortem Clot

There are many circumstances which may lead to sudden unexpected death which do not have any warning or contributory history. One such instance is pulmonary thromboembolism. Identifying clots during tissue recovery may be helpful in the death investigation process and establishing these practices in collaboration with the death investigator may preserve the opportunity for donation on sudden unexpected deaths.

A thrombus or pre-mortem clot that forms within an artery, vein, or heart chamber, is composed of blood elements (blood cells, platelets, and fibrin). A thrombus forms due to vessel injury, heart chamber injury, or blood stasis. There are several risk factors for thrombus formation including obesity, pregnancy, smoking, injury, recent surgery, and sedentary lifestyle. The blood components attach to the vessel wall as thin layers creating a striped appearance both grossly and microscopically (lines of Zahn). The layers are dark red (blood cells) and gray (fibrin and platelets). Usually, these form in the deep leg veins or pelvic veins; however, they can form in other areas of vessel injury. Although such findings would not be the defining cause of death, finding a thrombus in the deep veins of the lower extremities may point to additional thrombi or thromboemboli, refer to **Figure 17**.

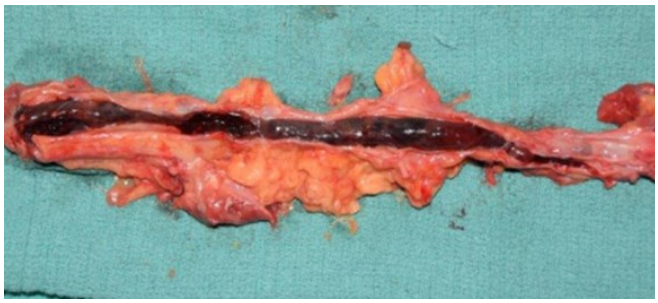


Figure 17. Deep vein thrombosis (femoral) found at autopsy. Photos: Daniel Schultz, MD.

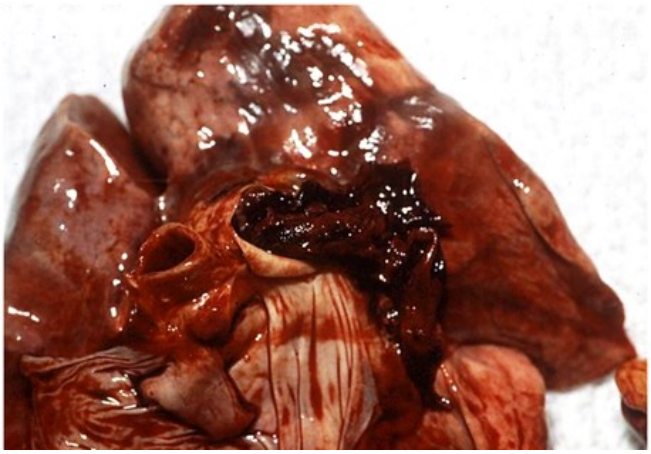


Figure 18. Pulmonary emboli. Photo: Kim A. Collins, MD

Blood Clots Discovered During Heart for Valve Recovery

The heart valve recovery is invasive and can potentially lead to the disruption, loss, or misdiagnosis of critical findings. The transection of the pulmonary veins and arteries during for valve recovery may preclude the death investigator from appropriately diagnosing these findings if effective practices are not in place.

Pulmonary thromboembolus, also called a pulmonary embolus (PE) — A thromboembolus within the pulmonary artery or the more distal vessels of the lungs which originally formed in a distant site (as a thrombus) and was dislodged to become an embolus, or thromboembolus, and traveled to the lung. The pulmonary thromboembolus is often the diameter of the deep leg vein, such as the popliteal vein, and is coiled upon itself, obstructing the left, right, or both pulmonary arteries, refer to **Figure 18**.

Thromboembolus — A thrombus that has become dislodged and travels to a different location in the body. The word *embolus* means *to throw.* A thromboembolus is often coiled upon itself and has the diameter of the vessel in which it originally formed. The cut surface can have a striped appearance due to the layering of the blood elements when it originally formed. It is slightly firm and friable and is usually in a right heart chamber, pulmonary artery, and/or vessel(s) of the lung. Much like thrombi found in the legs, these findings of thromboemboli are essential to the death investigation. Thromboemboli within the heart, lungs, or associated vasculature will likely either be or directly contribute to the cause of death.

Blood Clots Discovered During Lower Musculoskeletal or Vascular Recovery

Deep leg veins — The legs have superficial veins (near the body surface) and deep veins (deep within the leg). They are the iliac, femoral, popliteal, and tibial veins.

♦♦♦ Case Study ♦♦♦

A 65-year-old accountant was working overtime during tax season. She drove an hour to her condominium late one evening. Upon walking to the elevator, she became short of breath and collapsed. The doorman called 911. She was pronounced dead on the scene. Her past medical history included diabetes mellitus and obesity. The death investigator felt the cause of death was heart-related and allowed pre-autopsy tissue recovery. During recovery of the heart, the technician saw the finding depicted in **Figure 18.** The technician immediately halted the recovery procedure and photographed the pulmonary thromboembolus. She then called the death investigator to relay the finding. The death investigator was pleased with her detection and quick notification. The death investigator requested that the pulmonary thromboembolus be placed in a container of formalin if it became dislodged during recovery. This way the thromboembolus could be processed in the histology laboratory for microscopic examination if needed. The cause of death was certified as pulmonary thromboembolus, a finding that may have gone unnoticed if not for the technician's careful attention.

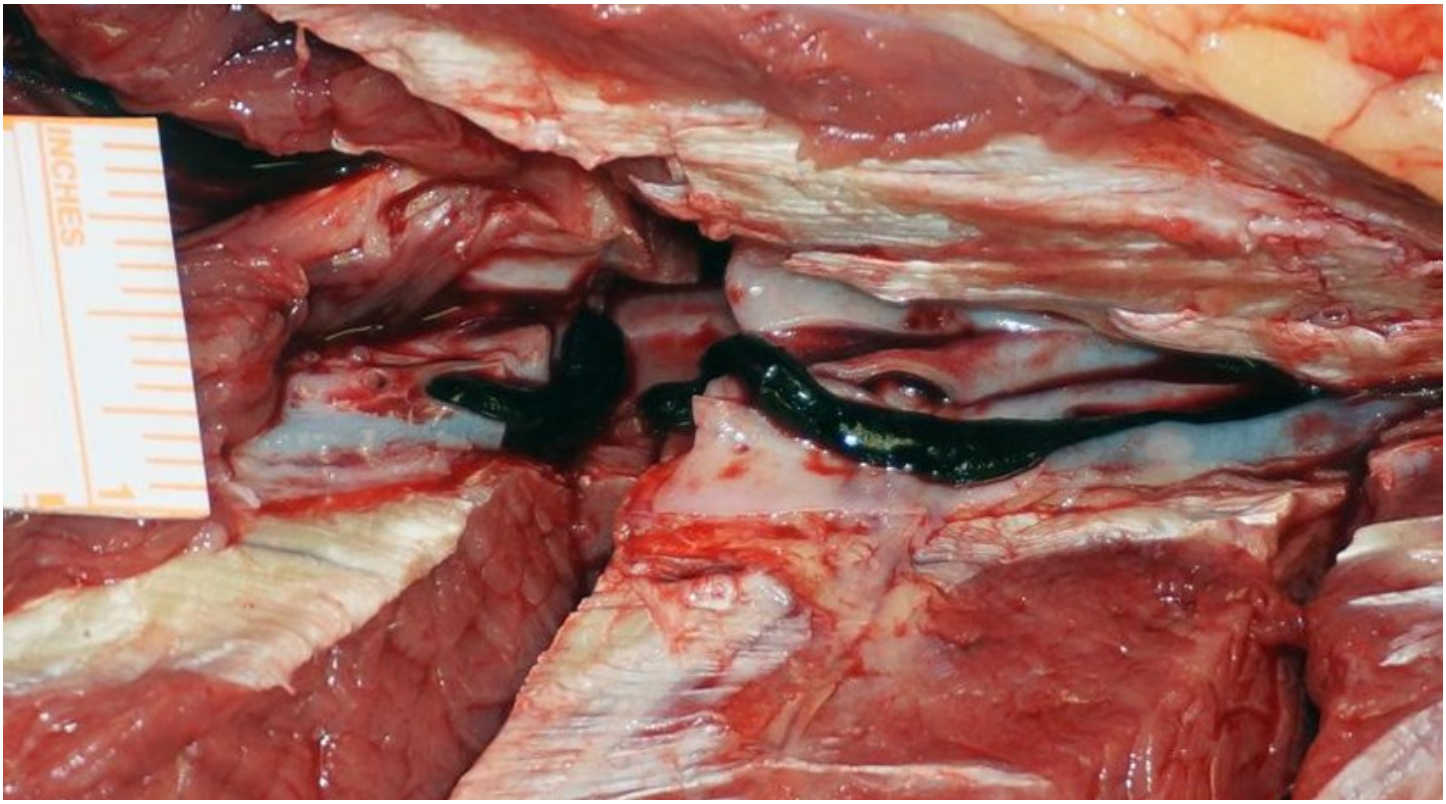


Figure 19. In situ deep vein thrombosis, lower extremity. Photo: Joseph Prahlow, MD.

Thrombus — As described above, a thrombus may be discovered in a deep leg vein, refer to **Figure 19**. A thrombus may be attached to the vein wall or unattached within the vein.

Post-mortem blood clot — A clot that forms within a blood vessel after death due to the settling and separation of blood components. The separation of the blood components leaves a two layer, dark red and yellow-tan, appearance but not the multiple striped lines of Zahn as in a thrombus. Many describe it as looking like chicken fat. The consistency is soft and slightly rubbery. This type of clot assumes the shape and diameter of the blood vessel in which it is found post-mortem.

Documentation and Preservation of Thrombi, Thromboemboli, and Post-Mortem Blood Clots

Documentation of the location and size of the clots may prove beneficial to the death investigator. Practices may be established by the recovery organization and the death investigator to document, photograph and collect such findings for further evaluation in the death investigation.

The death investigator should be consulted if any such findings are unexpectedly discovered during recovery. Documentation, photography, and collection practices of such clots should be established by each recovery organization and practices may be specific to individual death investigators depending on the circumstance and jurisdictions.

1. Photograph the clot in situ.
2. Gently place the specimen into a container and send with the decedent to the death investigator for evaluation.
3. Document on paperwork the location, size, appearance, and disposition of the clot specimen.

Conclusion

The American Association of Tissue Banks, the Eye Bank Association of America, the Association of Organ Procurement Organizations, and the International Association of Coroners & Medical Examiners recognize the essential role that death investigators play in the donation process and acknowledge the concerns of death investigation professionals with respect to potential loss of information and evidence during the donation process. We recognize that jurisdictions, roles, and expectations will differ greatly between regions, states, and counties. As such, we recommended that individual recovery organizations establish standard procedures and practices in collaboration with death investigators in their service areas.

To ensure the best possible outcome for individuals, families, recovery organizations, and our death investigation colleagues, it is imperative to proactively establish positive relationships and information sharing.

The practices illustrated throughout this guide may assist in the preservation of evidence and in some instances enable donation to take place in cases which would have not otherwise been possible. These practices are not requirements or standards but are intended to serve as a point of reference, education, and summary of possible solutions in order to further educate the donation community about the death investigation process.

♦♦♦ OSAC Glossary ♦♦♦

All definitions in this section and in **green** in the text can be found at
https://www.nist.gov/topics/organization-scientific-area-committees-forensic-science/osac-lexicon

Accidental Death — An unexpected or unforeseen death due to injury.

Algor Mortis — The change of body temperature to ambient temperature. A body will not cool if it is located in an environment greater than 98.6 degrees F.

Analyte — A chemical substance to be identified and/or measured.

Analysis — Analytical activity carried out during the forensic process to determine characteristics, specifications, or relevance of potential exhibits or conditions. The measurement of analyte and/or evaluation of data.

Analyze — To examine, measure, or test the properties of a material for evaluation purposes.

Antemortem — Before death.

Artifact — A by-product, artificial feature, or change resulting from human activity or a technical process.

Autopsy — A diagnostic medical procedure consisting of postmortem external and internal examination of a human body; conducted by a pathologist. It may be supplemented by ancillary tests and examination such as toxicology, histologic evaluation, and specialty consultation.

Best Practice — A system of processes, checks and testing that will deliver an outcome that has fewer problems and fewer unforeseen complications, and that combines the attributes of the most efficient and most effective ways of accomplishing a task based on proven and provable methods.

Blood — Blood is a body fluid in humans and other animals that delivers necessary substances such as nutrients and oxygen to the cells and transports metabolic waste products away from those same cells.

Blood Clot — A gelatinous mass formed by a complex mechanism involving red blood cells, fibrinogen, platelets, and other clotting factors.

Blunt Force Trauma — An alteration to the skeleton produced by low-velocity impact from a blunt object (e.g., being struck by an object or concussive wave) or the low-velocity impact of a body with a blunt surface (e.g., motor vehicle accident or fall).

Capture — To record data, such as an image, video sequence, audio stream, or biometric sample to digital storage, often by means of a sensor.

Cause of Death (COD) — Medical opinion of the disease or injury that resulted in a person's death.

Chain of Custody — The process used to maintain and document the chronological history of an item of evidence. Documents the individual who collected the evidence and each person or agency that subsequently takes custody of it. This chain of custody verifies evidence integrity meaning that the evidence being analyzed is the same evidence that was found at the scene and that there was no opportunity for the evidence to be tampered or compromised. A chain of custody should be maintained for an item until it is released, disposed of or destroyed.

Confirmatory Test — A test that is specific for a biological material or substance of interest and that is used for the conclusive identification of a biological fluid; this usually refers to a serological or microscopic test for detection of a particular biological fluid (e.g., blood or semen).

Contamination — Unintended presence, or introduction, of particles, chemicals, and other substances.

Continuing Education — An educational activity (such as a class, lecture series, conference, seminar, or short course) that is offered by a recognized organization or individual that updates participants in their relevant area of knowledge.

Coroner — Generally an elected (sometimes appointed) official whose duty is to oversee medicolegal death investigations, usually for a single county, and certify cause and manner of death. An officer of a county of municipality whose chief function is to investigate by inquest as before a jury any death not clearly resulting from natural causes (see medical examiner).

Database — An authoritative repository of information used for storage, search and analysis.

Death Certificate — A formal vital statistics document certifying the identification, cause and manner of death of a particular individual.

Death Scene — The site where a person has died; the term may also refer to the location where the decedent was found.

Decedent — A deceased individual.

Documentation — Written notes, audio/videotapes, printed forms, sketches and/or photographs that form a detailed record of the scene, evidence recovered, and actions taken during the search of the crime scene.

Evidence — Objects or information which should be identified and collected for appropriate documentation and analysis to support conclusions in forensic scene investigations.

Forensic — The use or application of scientific knowledge to a point of law, especially as it applies to the investigation of crime.

Forensic Pathologist — A physician who is certified in forensic pathology by the American Board of Pathology (ABP) or who, prior to 2006, has completed a training program in forensic pathology that is accredited by the Accreditation Council on Graduate Medical Education or its international equivalent or has been officially "qualified for examination" in forensic pathology by the ABP. May be employed as a Medical Examiner or as a consultant to a coroner of Justice of the Peace.

Gross Examination — Assessment of materials with the naked eye.

Gunshot Residue — Sometimes defined as the total residues resulting from the discharge of a firearm. Constituted typically of nitrites and lead, as well as unburned and partially burned gunpowder particles, carbonaceous material plus metallic residues from projectiles, fouling, and any lubricant associated with the bullets. These are usually observed with the naked eye, or an optical microscope, and detected or visualized by the Griess test and sodium rhodizonate.

Homicide — Death as a result of a volitional act committed by another person (injury, poisoning, etc).

Image — Imitation or representation of a person or thing, drawn, painted, photographed, and so forth.

In situ — In the original place or position.

Ingestion — Taking of substances into the body by mouth.

Jurisdiction — A geographic area in which a medical examiner or coroner's authority applies. Legal authority to make legal decisions and judgments regarding a death, including performance of autopsy, as well as investigation and certification of cause and manner of death.

Manner of Death (MOD) — Classification system based on the circumstances under which death occurred; includes accident, homicide, natural, suicide, and undetermined. Death occurs in one of four manners: natural, if caused solely by disease; accidental, if it occurs without apparent intent; suicide, if caused by the deceased; homicide, if someone other than the deceased caused it.

Measurement Scale — An object showing standard units of length (e.g., ruler) used in documentation of an item of evidence.

Medical Examiner — An appointed medically qualified officer whose duty is to investigate deaths and bodily injuries that occur under unusual or suspicious circumstances, to perform post-mortem examinations.

Medicolegal — Pertaining to medicine and law.

Medicolegal Death Investigation — A formal inquiry into the circumstances surrounding the death of a human being; investigative information is considered with autopsy findings and adjunctive studies (if performed) to determine the cause and manner of death.

Medicolegal Death Investigation System — Medicolegal death investigation office(s) within a state or district (usually a medical examiner or coroner office) that is a jurisdictional unit with a single chief medicolegal death investigation officer.

Medicolegal Death Investigator — The medicolegal investigation includes the collection of data, photographs, evidence, witness interviews, external examination of the body at the scene, and other forensic information and analysis that will contribute to the determination of cause and manner of death, reconstruction of the accident or crime scene, and support the provision of survivability factors. The medicolegal investigation falls within the exclusive purview of the medicolegal authority operating at the scene of an incident. A formal inquiry into the circumstances surrounding the death of a human being; the conclusions of the investigation are taken in concert with the autopsy findings and adjunctive studies in determining the cause and manner of death.

Natural Death — Death due solely to natural disease.

Next of Kin — Legally determined hierarchy of interested parties who have authority over the body.

Notes — The written documentation of procedures, standards, control and instruments used, observations made, results of tests performed, charts, graphs, photographs, sketches and other documents generated that are used to support the analyst’s conclusions.

Nucleic Acid —An important class of macromolecules, which are polymers of nucleotides, found in all cells and viruses. DNA and RNA are the major types. The functions of nucleic acids have to do with the storage and expression of genetic information. Deoxyribonucleic acid (DNA) encodes the information the cell needs to make RNA and proteins. A related type of nucleic acid, called ribonucleic acid (RNA), comes in different molecular forms that participate in protein synthesis.

Pathology — The study and diagnosis of disease.

Personal Effects — This refers to property, including clothing, jewelry, wallets or other items found on a decedent’s body. Personal effects are categorized as associated or non-associated directly with the remain, with regard to proximity to the decedent (i.e. a wallet in a pocket of a decedent's pants would be considered associated PE; however, the same wallet found in the body bag of a visually unidentifiable decedent would be considered unassociated).

Personal Protective Equipment (PPE) — Equipment such as safety glasses, goggles, face shields, gloves, chemical-resistant suits, and so on that are worn or used to protect individuals from the dangerous effects of materials that they are handling or exposed to.

Physical Evidence — Anything that may be found or associated with criminal activity at a crime scene.

Policy — A guiding principle, operating practice, or plan of action governing decisions made on behalf of an organization.

Post-mortem — After death.

Postmortem Examination — An examination of a dead body to determine cause of death.

Pre-mortem — Before death.

Protocol — A set of instructions that explain the correct conduct and procedures to be followed in a specified situation.

Radiography — Technique for generating and recording an x-ray pattern for the purpose of providing the user with a static image(s) after termination of the exposure.

Residue — Remnants of a target substance that can be recovered and quantified.

Rigor Mortis — Stiffening of the body after death; a time dependent change that helps determine time of death.

Sample — A group of items, test results or portions of material, taken from a large collection of items, test results or portions of material, that serves to provide information that may be used as a basis for making a decision concerning the larger collection.

Scene — Any environment in which human remains and associated materials may be recovered.

Serology — The detection, characterization, identification, and/or typing of body tissues and fluids, either in native form or as stains or residues left at a crime scene using physical methods (normal and enhanced lighting), biochemical assays and/or microscopy; This definition applies to current crime biology laboratory practices which may be followed by DNA testing.

Sharp Force Trauma — Skeletal trauma produced by a tool that is edge pointed or beveled.

Specimen — Samples of tissues (including blood or hair), secretions (breast milk, saliva, or sweat), excretion products (bile, exhaled air, or urine), and other material such as stomach contents or vomit derived from a patient.

Standard — An established or widely recognized model of authority or excellence as a reference point against which other things can be evaluated or the ideal in terms of which something can be judged.

Standard Operating Procedure — Written procedure that describes how to perform certain organization activities.

Suicide — Death resulting from intentional self-inflicted act.

Trauma — A physical injury or wound caused by an external force of violence, which may cause death or permanent disability. Trauma is also used to describe severe emotional or psychological shock or distress.

Toxicology — A scientific discipline concerned with the analysis of biological materials for the presence of potentially harmful substances.

♦♦♦ Donation Glossary ♦♦♦

Anatomical Gift – a donation of all or part of a human body to take effect after the donor's death for the purpose of transplantation, therapy, research, or education.

Authorizing Person – Upon the death of the donor, the person, other than the donor, authorized by law to make an anatomical gift. 14th Edition AATB Standards for Tissue.

Consent for Donation – Consent for donation, also referred to as consent or first-person authorization (FPA), is the act of an individual electing to be a donor upon their death. Organs, tissue, and eye may be recovered from a FPA donor without receiving authorization from any other authorizing person at the time of death. Example recordings of first-person authorization or consent include state and federal donor registries or the donor designation on a driver's license.

Document of Gift – a donor card or other record used to make an anatomical gift. The term includes a statement or symbol on a driver's license, identification card, or donor registry.

Donor Risk Assessment Interview (DRAI) – 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). 14th Edition AATB Standards for Tissue Banking.

Donor Designation – the donor has made an autonomous decision via a document of gift to make an anatomical gift. This decision is to be honored and implemented and it not subject to change by others. Here is the exact language: *Section 8 of the UAGA is designed to state firmly the rule that a donor's autonomous decision regarding the making of an anatomical gift is to be honored and implemented and is not subject to change by others.*

Family History – An essential part of a patient's medical history in which he or she is asked about the health of members of the immediate family in a series of specific questions to discover any disorders to which the patient may be particularly vulnerable, such as "Has anyone in your family had tuberculosis? Diabetes mellitus? Breast cancer?" Hereditary and familial diseases are especially noted. The age and health of each person, age at death, and causes of death are charted. Often a genogram is developed for pictorial documentation. The family health history is obtained from the patient or family in the initial interview and becomes a part of the permanent record. Other questions, such as those concerning the age, sex, relationships of others in the household, and marital history of the patient, may also be asked if the information has not already been secured. Mosby's Medical Dictionary, 9th edition. © 2009, Elsevier.

Psychiatric History – A person's mental profile, which includes information about chief complaint, present illness, psychological adjustments made before onset of disease, individual and family history (Hx) of psychiatric or mental disorders, and an early developmental history (Hx). McGraw-Hill Concise Dictionary of Modern Medicine. © 2002, The McGraw-Hill Companies, Inc.

Physical Assessment (PA) – A recent ante-mortem or postmortem documented evaluation of a deceased donor's body that can identify evidence of: high-risk behavior and signs of HIV infection or hepatitis infection; other viral or bacterial infections; or, trauma to the potential recovery sites. 14th Edition AATB Standards for Tissue Banking.

Relevant Medical Records – A collection of documents including a current donor risk assessment interview, a physical assessment/physical examination, laboratory test results (in addition to results of testing for required relevant communicable disease agents), relevant donor records, existing coroner and autopsy reports, a certified copy or verified copy of the death certificate (when applicable), 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. 14th Edition AATB Standards for Tissue Banking.

Relevant Recovery Documentation – Records generated before, during, and/or after the Recovery of donated tissues which includes a Physical Assessment, a list of tissues recovered, as well as findings of internal trauma/injuries and/or surgical sites. 14th Edition AATB Standards for Tissue Banking.

Uniform Anatomical Gift Act – The Uniform Anatomical Gift Act (UAGA) allows a decedent or surviving relatives to donate certain parts of the decedent's organs for certain purposes, such as giving to those in need or for medical research. The act was revised in 1987 and again in 2006. The revisions made in 2006 aimed to address shortages and encourage donation.

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