MEDICAL ADVISORY

October 30, 2019

The following changes were made at the October 10, 2019 meeting of the Medical Advisory Board and will become effective on January 1, 2020.

E1.100 Recovery

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

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

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

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

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

F1.300 Determination of Surgical Suitability

The eye bank responsible for evaluation of ocular tissue shall specify whether the tissue meets the criteria for penetrating keratoplasty (PK), anterior lamellar keratoplasty (ALK/DALK), Descemet's stripping endothelial keratoplasty (DSEK/DSAEK), Descemet's membrane endothelial keratoplasty (DMEK), keratolimbal allograft, and "other" surgical use (e.g. keratoprosthesis, long-term preservation for later shunt patch/ALK/tectonic use, experimental surgical use, etc.).

Corneoscleral Disc Minimum Suitability Standards

Minimum suitability for penetrating keratoplasty (PK):
- No ~~stromal~~ infiltrates
- No pterygia, neovascularization, foreign bodies, or visually significant stromal scars within intended graft area
- No Descemet's membrane detachment or tears within intended graft area
- No evidence of endothelial dystrophy
- Minimum endothelial cell density (as defined in eye bank's policy)
- No Down syndrome or evidence of ectatic dystrophy (e.g. keratoconus, keratoglobus, etc.,
- No prior laser or incisional refractive surgery (e.g. radial keratotomy, lamellar inserts, photoablation, etc.)

Minimum suitability for anterior lamellar keratoplasty (ALK/DALK):
- No ~~stromal~~ infiltrates
- No pterygia, neovascularization, foreign bodies, or visually significant stromal scars within intended graft area
- No Down syndrome or evidence of ectatic dystrophy (e.g. keratoconus, keratoglobus, etc.)
- No prior laser or incisional refractive surgery (e.g. radial keratotomy, lamellar inserts, photoablation, etc.)

Minimum suitability for Descemet's stripping endothelial keratoplasty (DSEK/DSAEK):
- No ~~stromal~~ infiltrates
- No foreign bodies or visually significant scars affecting posterior stroma within intended graft area
- No Descemet's membrane detachment or tears within intended graft area
- Minimum endothelial cell density as defined in eye bank's policy
- Sufficient rim size and corneoscleral disc size to facilitate mounting on artificial anterior chamber

Minimum suitability for Descemet's membrane endothelial keratoplasty (DMEK):
- No ~~stromal~~ infiltrates
- No foreign bodies
- No Descemet's membrane tears within intended graft area
- Minimum endothelial cell density as defined in eye bank's policy)

Minimum suitability for keratolimbal allograft (KLA):

- No ~~stromal~~ infiltrates
- Sufficient scleral rim (minimum must be defined in eye bank's policy)
- Conjunctiva must be intact over sufficient portion of rim to facilitate allograft (rim portions may be considered from mated pairs)
- No history of melanoma or metastatic cancer of a solid organ

Minimum suitability for Keratoprosthesis (K-Pro):

- No infiltrates
- No pterygia, neovascularization, foreign bodies, or significant corneal thinning
- No prior refractive surgery (e.g. radial keratotomy, lamellar inserts, photoablation, etc.)
- No Down syndrome or evidence of ectatic dystrophy (e.g. keratoconus, keratoglobus, etc.)

Minimum suitability for Long-Term Cornea Preservation/Other:

- No ~~stromal~~ infiltrates
- No pterygia on graft segments

Sclera Minimum Suitability Standards

Minimum suitability for sclera for any surgical use:

- No ~~stromal~~ infiltrates on cornea from the eye that produced scleral grafts
- No history of melanoma or metastatic cancer of a solid organ

L1.100 Tissue Report Form

In special circumstances, like approved research programs, the Medical Advisory Board may waive certain label and tissue report form requirements. Approval for omissions must be obtained in advance from the MAB and surgeons receiving study tissues must consent in advance to any masking of standard required data.

Tissue distributed for transplant use shall be accompanied by a tissue report form. The tissue report shall contain the following:

All Tissues:

1. Name of (Source) eye bank
2. Location of eye bank
3. Telephone number of eye bank
4. ISBT 128 tissue identifier.
5. Type of storage solution
6. All dates shall be written as YYYY-MM-DD HH:MM to harmonize with the ISO 8601 requirements.

7. If cornea is processed, clearly indicate the type of processing performed or the indicated use (e.g. endothelial keratoplasty, posterior lamellar keratoplasty, anterior lamellar keratoplasty, laser assisted keratoplasty, etc.).
8. Tissue evaluation reporting requirements according to Matrix II.
9. Name and EBAA Accreditation Status of each establishment that performs any of the following steps in the preparation of tissue: recovery, processing, storage, evaluation, donor eligibility determination and distribution.
10. A summary of records reviewed regarding the eligibility of tissue for transplant.

Matrix II: Reporting Requirements			
Content on Tissue Report Form	**Unprocessed Tissue**	**Processed Tissue**	
	Short or Intermediate-Term Storage	**Intermediate-Term Storage***	**Long-Term Storage****
Donor age	Required	Required	Not Required
Donor cause of death	Required	Required	Not Required
Donor death date and time	Required	Required	Not Required
Preservation date and time	Required	Required	Not Required
Additional processing date and time		Required	Not Required
Date and time that cooling of ocular tissues or body refrigeration began	Required	Required	Not Required
Name/identifier of technician who recovered tissue	Required	Required	Not Required
Name/identifier of technician who initially preserved (stored) tissue	Required	Required	Not Required
Name/identifier of technician(s) who evaluated tissue	Required	Required	Not Required
Name/identifier of technician who processed tissue		Required	Not Required
Morphology and dimensions of processed tissue		Required	Required
Diameter of processed graft		Required	Not Required
Pachymetry (graft thickness)	Not Required	Required	Not Required
Slit lamp observations	Required	Required	Required (other visual exam acceptable)
Specular microscope observations (including endothelial cell density)	Required (unless whole eye, anterior or tectonic use only)	Required (unless anterior or tectonic use only)	Not Required
Suitability for indicated surgical uses	Required	Required	Required

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

Introduction

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

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

Although EBAA Medical Standard D1.800 permits recovery of ocular tissue from living donors, this appendix outlines the contraindications for tissue recovered from non-heart-beating (cadaveric) donors. Additional screening and testing may be required for living donors.

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

I. Risk Factors

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

a. Men who have had sex with another man in the preceding 5 years (risk factor for HIV and Hepatitis B).
b. Persons who have injected drugs for a non-medical reason in the preceding 5 years, including intravenous, intramuscular, or subcutaneous injections (risk factor HIV, Hepatitis B and Hepatitis C).
c. Persons who have engaged in sex in exchange for money or drugs in the preceding 5 years (risk factor for HIV, Hepatitis B and Hepatitis C).
d. Persons who have had sex in the preceding 12 months with any person described ***(as above in I.a-c)*** or with any person who has HIV infection, including a positive or reactive test for HIV virus, hepatitis B infection, or clinically active (symptomatic) hepatitis C infection.
e. Persons who have been exposed in the preceding 12 months to known or suspected HIV, HBV, and/or HCV-infected blood through percutaneous inoculation (e.g., needle stick) or through contact with an open wound, non-intact skin, or mucous membrane.

f. Children born to mothers with or at risk for HIV infection, ***if the child is 18 months of age or younger, or if the child was breast-fed within the preceding12 months.***
g. Persons who have been in juvenile detention, lock up, jail or prison for more than 72 consecutive hours in the preceding 12 months (risk factor for HIV, Hepatitis B and Hepatitis C).
h. Persons who have lived with (resided in the same dwelling) another person who has hepatitis B or clinically active (symptomatic) hepatitis C infection in the preceding 12 months.
i. Persons who have undergone tattooing, ear piercing or body piercing in the preceding 12 months, in which sterile procedures were not used, e.g., contaminated instruments and/or ink were used, or shared instruments that had not been sterilized between uses were used.
j. Persons who have had a past diagnosis of clinical, symptomatic viral hepatitis after their 11th birthday, unless evidence from the time of illness documents that the hepatitis was identified as being caused by hepatitis A virus, Epstein-Barr Virus (EBV), or cytomegalovirus (CMV).
k. Persons who are deceased and have a documented medical diagnosis of sepsis or have documented clinical evidence consistent with a diagnosis of sepsis that is not explained by other clinical conditions at the time of death. ***An eye bank should make a determination on how to routinely handle situations of clinical history proximal to death in which sepsis was suspected at the time of admission or part of a differential diagnosis during admission in which the patient may have been shown through clinical data not to be septic prior to death.***
l. Persons who have had smallpox vaccination (vaccinia virus) in the preceding 8 weeks should be evaluated as follows:

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

1. You should defer the donor until after the vaccination scab has separated spontaneously, or for 21 days post-vaccination, whichever is the later date, and until the physical examination or physical assessment includes a confirmation that there is no scab at the vaccination site.

2. In cases where a scab was removed before separating spontaneously, you should defer the donor for two months after vaccination.

3. ***In cases where the eye bank cannot determine how the scab separated, you should defer if the vaccination was less than 21 days ago. Deferral is not necessary if the scab is not visible upon external examination and the vaccination was greater than 21 days ago.***

4. For persons who have experienced vaccinia complications, you should defer the donor until 14 days after all vaccinia complications have completely resolved. ***Deferral is not necessary if the date of vaccinia complication resolution is indeterminate and there are no visible signs of vaccinia complications.***

5. Persons who acquired a clinically recognizable vaccinia virus infection by contact with someone who received the smallpox vaccine (i.e., touching the vaccination area or the scab, including the covering bandages, or touching clothing, towels, or bedding that might have come

into contact with an unbandaged vaccination area or scab).

6. ***For cadaveric donors who have received a smallpox vaccination or had close contact with the smallpox vaccination site of someone else, you should examine the skin and defer if a scab or other signs of vaccinia are present.***

7. You should defer persons who developed other complications of vaccinia infection acquired through contact with a vaccine recipient until 14 days after all vaccinia complications have completely resolved. ***Deferral is not necessary if the date of vaccinia complication resolution is indeterminate and there are no visible signs of vaccinia complications. Deferral is not necessary for anyone who did not develop vaccinia complications.***

m. Persons who have had a medical diagnosis or suspicion of WNV infection (based on symptoms and/or laboratory results or confirmed WNV viremia) you should defer for 120 days following diagnosis or onset of illness, whichever is later.

n. Persons who have tested positive or reactive for WNV infection, using an FDA-licensed or investigational WNV NAT donor screening test in the preceding 120 days.

o. Persons who have been treated for or had syphilis within the preceding 12 months. We do not recommend deferral of donors if evidence is presented that the treatment occurred more than 12 months ago and was successful.

p. Persons who have been diagnosed with vCJD or any other form of CJD. Note: If the individual knowledgeable about the donor's medical and travel history is not familiar with the term "Creutzfeldt-Jakob Disease" or "variant Creutzfeldt-Jakob Disease," you may try to describe those in layman's terms. If the person being interviewed is still not familiar with those terms, you may consider the lack of familiarity with those terms as a negative response to questions using those terms.

q. Persons who have been diagnosed with dementia or any degenerative or demyelinating disease of the central nervous system or other neurological disease of unknown etiology. ***Examples include Parkinson, amyotrophic lateral sclerosis, multiple sclerosis, Alzheimer disease, Guillain-Barre, and Chronic Inflammatory Demyelinating Polyneuropathy (CIPD).*** Potential donors who have a diagnosis of delirium (e.g., delirium caused by toxic/metabolic diseases or recent head trauma) would not necessarily be considered to have a diagnosis of dementia and should be evaluated by the Medical Director. ***(Ocular tissue*** from donors with dementia confirmed by gross and microscopic examination of the brain to be caused by cerebrovascular accident or brain tumor and who are confirmed not to have evidence of TSE on microscopic examination of the brain may be acceptable based on an evaluation by the Medical Director).

r. Persons who are at increased risk for CJD. Donors are considered to have an increased risk for CJD if they have received a non-synthetic dura mater transplant, human pituitary-derived growth hormone, or have one or more blood relatives diagnosed with CJD.

s. Persons who have a history of CJD in a blood relative unless the diagnosis of CJD was subsequently found to be an incorrect diagnosis, the CJD was iatrogenic, or the laboratory testing (gene sequencing) shows that the donor does not have a

mutation associated with familial CJD.

t. Persons who spent three months or more cumulatively in the United Kingdom ***(England, Northern Ireland, Scotland, Wales, the Isle of Man, the Channel Islands, Gibraltar, and the Falkland Islands)*** from the beginning of 1980 through the end of 1996.

u. Persons who are current or former U.S. military members, civilian military employees, or dependents of a military member or civilian employee who resided at U.S. military bases in Northern Europe (Germany, Belgium, and the Netherlands) for 6 months or more cumulatively from 1980 through 1990, or elsewhere in Europe (Greece, Turkey, Spain, Portugal, and Italy) for 6 months or more cumulatively from 1980 through 1996.

v. Persons who spent 5 years or more cumulatively in Europe ***(Albania, Austria, Belgium, Bosnia-Herzegovina, Bulgaria, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Liechtenstein, Luxembourg, ~~Macedonia~~Montenegro, Netherlands, North Macedonia, Norway, Poland, Portugal, Romania, Serbia, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, United Kingdom, or former~~and~~ Yugoslavia, Republic of Macedonia, and Czechoslovakia)*** from 1980 until the present (note this criterion includes time spent in the U.K. from 1980 through 1996).

w. Persons who received any transfusion of blood or blood components in the U.K. or France between 1980 and the present.

x. ***If the eye bank is not testing for HIV I/II using a test kit specifically labeled as sensitive for detection of HIV group O antibodies, then deferral includes*** persons or their sexual partners who were born or lived in certain countries in Africa (Cameroon, Central African Republic, Chad, Congo, Equatorial Guinea, Gabon, Niger, or Nigeria) after 1977 (risk factor for HIV group O).

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 African Republic, Chad, Congo, Equatorial Guinea, Gabon, Niger, or Nigeria***, after 1977 (risk factor for HIV group O).

z. Persons who are xenotransplantation product recipients or intimate contacts of a xenotransplantation product recipient. *Xenotransplantation* is any procedure that involves the transplantation, implantation, or infusion into a human recipient of either: (1) live cells, tissues, or organs from a nonhuman animal source; or (2) human body fluids, cells, tissues, or organs that have had ex vivo contact with live nonhuman animal cells, tissues, or organs. *Xenotransplantation products* include live cells, tissues, or organs used in xenotransplantation. Biological products, drugs, or medical devices sourced from nonliving cells, tissues or organs from nonhuman animals, including but not limited to porcine insulin and porcine heart valves, are not considered xenotransplantation products. *Xenotransplantation product* recipient means a person who undergoes xenotransplantation. *Intimate contact of a xenotransplantation product* recipient means a person who has engaged in activities that could result in intimate exchange of body fluids, including blood or saliva, with a xenotransplantation product recipient. ***Intimate***

partners of recipients of the xenotransplantation product Epicel™ need not be deferred.