MEDICAL ADVISORY

July 8, 2019

The following changes were made at the June 7, 2019 meeting of the Medical Advisory Board and will become effective on October 1, 2019.

B1.200 Inspections by Official Agencies

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

D1.110 EBAA Contraindications to Transplant

Determination of donor eligibility is an eye banking function including considerations listed in multiple sources (e.g. US Food and Drug Administration, Health Canada, various state departments, Medical Director input, etc.). In addition to these sources, the EBAA Medical Advisory Board has determined that t~~T~~issues from persons with the following are potentially health threatening for the recipient(s) or pose a risk to the success of the surgery and shall not be offered for surgical purposes:

A. All Ocular Donors

1. death of unknown cause and there is likelihood of other exclusionary criteria;
2. congenital rubella;
3. Reye syndrome within the past three months;
4. Active viral encephalitis of unknown origin or progressive encephalopathy (e.g., subacute sclerosing panencephalitis, progressive multifocal leukoencephalopathy, etc.);

5. active bacterial or viral meningitis;
6. active bacterial or fungal endocarditis;
7. suspected rabies and persons who, within the past six months, were bitten by an animal suspected to be infected with rabies;
~~8. Down Syndrome - exclusively for penetrating keratoplasty or anterior lamellar keratoplasty;~~
~~9.~~8. intrinsic eye disease;
    a. retinoblastoma;
    b. malignant tumors of the anterior ocular segment or known adenocarcinoma in the eye of primary or metastatic origin;
    c. active ocular or intraocular inflammation: conjunctivitis, keratitis, scleritis, iritis, uveitis, vitreitis, choroiditis, retinitis; or
    ~~d. congenital or acquired disorders of the eye that would preclude a successful outcome for the intended use, e.g., a central donor corneal scar for an intended penetrating keratoplasty, keratoconus, and keratoglobus;~~
~~10.~~9. active leukemias;
~~11.~~10. active disseminated lymphomas;
~~12.~~11. Parkinson, amyotrophic lateral sclerosis, multiple sclerosis, and Alzheimer disease;
~~13.~~12. Creutzfeldt-Jakob disease (CJD), variant Creutzfeldt-Jakob Disease (vCJD), or family member with CJD;
~~14.~~13. history of Ebola Virus Disease (EVD);
~~15.~~14. history of melanoma with known metastatic disease*

~~B. Donors for Penetrating Keratoplasty Procedures~~

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

~~C. Donors for Anterior Lamellar Keratoplasty Procedures, Tectonic Grafts, and Patch Grafts such as for glaucoma drainage devices (non-vascular ocular tissue excluding sclera).~~

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

~~D. Donors for Epikeratoplasty Procedures~~

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

~~E. Donors for Endothelial Keratoplasty Procedures~~

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

~~F. Scleral Tissue Donors~~

~~Criteria are the same as listed for penetrating keratoplasty, except that tissue with non-infectious local eye disease or refractive surgery affecting the cornea is acceptable for use. Death to preservation time may be extended. Donors with history of melanoma (with or without metastasis) or solid, cancerous, non-melanoma tumor with metastasis are contraindicated (unless the donated tissue is irradiated).~~

~~G. Donors for Keratolimbal Allograft Procedures (vascular ocular tissue)~~

~~Conjunctival and limbal area must be intact and free of evidence of disease (e.g. pterygium, neovascularization). Structural condition of central stroma and endothelium is inconsequential. Limbal tissue and peripheral corneal tissue are vascular tissue. Donors with a history of melanoma (with or without metastasis) or a solid cancerous, non-melanoma tumor with metastasis are contraindicated.~~

* Excluded from this contraindication are tissues subjected to terminal sterilization methods that deactivate neoplastic cells (e.g. gamma irradiation of corneas preserved in albumin)~~irradiated tissue is excluded from these contraindications~~

F1.100 Slit Lamp Examination

The corneoscleral disc shall be examined for epithelial and stromal pathology and in particular endothelial disease using slit lamp biomicroscopy. Whole eyes to be distributed for lamellar processing must have the same examination. Corneoscleral discs that have been processed for lamellar keratoplasty procedures shall be re-evaluated by slit lamp biomicroscopy to ensure that there was no damage to the relevant transplantable tissue.

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

The eye bank should delineate a "clear zone" on each cornea as a measurement of diameter (in millimeters) of the clear central cornea, free of neovascularization, pterygia, arcus, or other stromal anomalies. Anterior stromal scars may be omitted from clear zone measurement, as long as details of scar location, size, and relative depth are made available to the transplanting surgeon. Clear zone measurements are acknowledged to impact surgical suitability determination more significantly for surgery types utilizing the anterior corneal segment (e.g. PK, ALK, K-Pro). Eye banks are encouraged to provide a measurement of an arcus clear zone (a measurement of clear central cornea free of arcus only), if that measurement may responsibly improve or otherwise clarify surgical suitability determination.

F1.300 Determination of Surgical Suitability ~~Eligibility for Surgical Use~~

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~~/or tectonic use~~ "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 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
- 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
- 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 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

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

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

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

1. "For Non-clinical Use Only"
2. "Bio-hazardous" or bio-hazard legend
3. "Not for Transplant"

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

EBAA Guidance

I. Risk Factors

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

a. Men who have had sex with another man in the preceding 5 years (risk factor for HIV and Hepatitis B).
b. Persons who have injected drugs for a non-medical reason in the preceding 5 years, including intravenous, intramuscular, or subcutaneous injections (risk factor HIV, Hepatitis B and Hepatitis C).
c. Persons 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, Netherlands, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, United Kingdom, and Yugoslavia)*** from 1980 until the present (note this criterion includes time spent in the U.K. from 1980 through 1996).

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.***

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

G1.000

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

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

The quality assurance program shall address applicable requirements relating to the following eye bank functions:

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

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

The Quality Assurance Program shall establish a system for reporting, documenting, and investigation of deviations (read as "errors or accidents," as defined by Health Canada). Deviations for distributed tissue relating to eye bank functions must be reported to the federal regulators and EBAA.

The eye bank's quality assurance program shall include a method for the receiving surgeon to report adverse reactions from the transplantation of corneal, scleral, or other ocular tissue to the distributing eye bank. The distributing eye bank must forward the adverse reaction information to the source eye bank, which made the donor eligibility determination. The source bank must perform an investigation and must report the adverse reaction information within 30 days to the EBAA office for review by the Medical

Advisory Board. In accordance with Health Canada, adverse reactions involving a relevant communicable disease must be reported to Health Canada within 24 hours~~15 calendar days~~ of receipt of the information if the adverse reaction is fatal, life-threatening, results in permanent impairment or damage or requires medical or surgical intervention.

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

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

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

The following change was approved by the Medical Advisory Board but is contingent on cost analysis and EBAA Board approval. Medical Standard M1.600 will not be updated until the Board approves this change.

Pending Board approval, this change will become effective on January 1, 2020.

M1.600 Statistical Reporting

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

Each source eye bank shall report information on surgery date for domestic tissue placements, in addition to surgical technique, indications for surgery, and destination country for all tissue.