Medical Advisory Board Agenda

Saturday, June 20, 2020
4:00PM – 6:00PM

A. Call To Order

B. Approval of Minutes

C. Committee Reports
   I. Medical Review Subcommittee (Macsai)
   II. Policy & Position Research Subcommittee (Aldave)
   III. Accreditation Board (Stoeger)
   IV. Certification Board (Galloway)
   V. Technician Education (Galloway)
   VI. Technical Procedures Manual (Titus)

D. Old Business
   I. Donor Prep Subcommittee (Meinecke)

E. New Business
   I. Recommended changes to M1.500 and G1.000 (Mathes)
   II. QA Committee Recommendations to Technical Procedures Manual (Arnett)
   III. Recommended change to M1.600 (Stoeger)
   IV. Corrections and addition to definitions (Philippy)
   V. COVID-19 (Li)
   VI. E-StatIS – EBAA Statistical Information System (DeMatteo)

F. Late Additions

G. For Information and Review

H. Adjournment

Medical Advisory Board Meeting Minutes
Thursday, October 10, 2019
Palace Hotel – San Francisco, CA

I. Call to Order

Dr. Jennifer Li called the meeting to order at 1:00pm.

The following members were present:

Jennifer Li, MD	Medical Advisory Board Chair
Winston Chamberlain, MD, PhD	Medical Advisory Board Vice Chair
Woodford Van Meter, MD	EBAA Chair
Kevin Corcoran, CAE	EBAA President & CEO
Jennifer DeMatteo	EBAA Director of Regulations & Standards
Eric Meinecke, CEBT	Medical Advisory Board Secretary
Tony Aldave, MD	Policy & Position Research Subcommittee
Tony Bavuso, CEBT	
Beth Binnion, CEBT	
Jason Brosious, CEBT	
Patricia Dahl, CEBT	
Donna Drury, CEBT	
Sander Dubovy, MD	
Sean Edelstein, MD	
Josh Galloway, CEBT	Tech Ed & Certification Board Chair
David Glasser, MD	
Sandeer Hannush, MD	
Holly Hindman, MD	
Bennie Jeng, MD	
Christopher Ketcherside, MD	Accreditation Board Co-Chair
David Korroch, CEBT	
Anup Kubal, MD	
Marian Macsai, MD	Medical Review Subcommittee
Kyle Mavin, CEBT	Accreditation Board Co-Vice Chair
Shahzad Mian, MD	
Brian Philippy, CEBT	

Jim Quirk, CEBT	
Michelle Rhee, MD	Accreditation Board Co-Vice Chair
George Rosenwasser, MD, CEBT	
Christopher Stoeger, CEBT	Accreditation Board Co-Chair
Alan Sugar, MD	
Joel Sugar, MD	
Michael Titus, CEBT	Tech Procedures Manual Subcommittee
David Verdier, MD	
Jim Wagner, CEBT	

II. Approval of Minutes

Dr. Li called for a motion to accept the minutes from the June 7, 2019 meeting held in Scottsdale, Arizona.

A motion was made and seconded to approve the minutes without change. Motion Passed.

III. Committee Reports

A. Medical Review Subcommittee

Dr. Marian Macsai reviewed the Online Adverse Reaction Reporting System (OARRS) summary data and graphs. Dr. Macsai informed the MAB that the EBAA has reached out to the Centers for Disease Control and Prevention (CDC) to determine if the OARRS data could be validated. A Keratoplasty Infections Surveillance Survey (KISS), in cooperation with the CDC, was proposed and Dr. Macsai requested four to five surgeons to volunteer to evaluate the survey prior to the launch of the study. The following individuals offered to work on this project with Dr. Macsai: Winston Chamberlain, Sean Edelstein, Holly Hindman, Bennie Jeng, Anup Kubal, Jennifer Li, Michelle Rhee, George Rosenwasser, and Michael Straiko.

There was significant discussion about eye banks obtaining post-operative outcomes from surgeons and the associated challenges. Dr. Li asked that Dr. Macsai and the Medical Review Subcommittee discuss this and come back to the next MAB meeting with recommendations (if any) on how to improve the process of collecting data from the surgeons. Dr. Macsai invited anyone interested in this topic to email her (mmacsai@northshore.org).

B. Policy & Position Research Subcommittee

No report.

C. Accreditation Board

Chris Stoeger reported that the Accreditation Board met that morning. Before reporting on the accreditation results, Chris wanted to inform the MAB that in 2019, three separate targeted off-cycle inspection committees were mobilized to address concerns provided to the EBAA in writing. One resulted in the denial of accreditation to a bank previously accredited, one resulted in the change of accreditation status from three years to one year, and one resulted in no change to the accreditation status.

In the current cycle, seventeen banks were inspected. Five banks had no findings, fifteen banks received a three-year accreditation, one bank received a one-year accreditation, and one bank was denied accreditation.

Kevin Corcoran informed the AB that the EBAA is beginning to formulate plans for accreditation of non-member banks. Chris said the EBAA Board of Directors would be discussing this later in the day. The AB also heard a report on the use of video in accreditation inspections and a pilot group was working on this topic.

The AB did request that the Matrix II in Medical Standard L1.100 be updated to include both the date and time that cooling of ocular tissues or body refrigeration began. The current matrix only as time.

A motion was made and seconded to change L1.100 Matrix II to read, “Date and time that cooling of ocular tissues or body refrigeration began.” Motion Passed.

D. Certification Board

Josh Galloway reported that the Fall 2019 CEBT exam will take place October 12-26. Candidates from the US, Canada and Saudi Arabia have registered for the exam. The Spring CEBT Exam will take place April 11-25, 2020. Starting spring 2020, Professional Testing Corporation will be partnering with Prometric and will be using their testing center network. This change will increase the number of location options candidates have to take the exam. Application information will be sent out in November.

E. Technician Education

Josh Galloway reported that the committee planned the webinar “Ocular Research Tissue: From the Eye Bank to the Researcher” which took place in August. The speakers for this session were Kristen McCoy (Eversight), Sung Lee (Lions Gift of Sight), David Ammar (Lions Eye Institute for Transplant and Research), and Dan Stamer (ARVO). Josh said the session was available on EBAA’s eyeLEARN. The Technician Education Committee is currently planning additional webinars and will have more information soon. The 2019 Slit Lamp Microscopy Seminar will take place October 24-25 at Lions Gift of Sight in St. Paul, Minnesota. Josh reported that registration is open but would be closing on Monday. Finally, the Technician Education

Seminar (TES) will take place February 20-22, 2020 in Philadelphia at the Lions Eye Bank of Delaware Valley.

F. Technician Procedure Manual

Michael Titus reported that the Technical Procedures Manual Subcommittee had been tasked with including the tissue evaluation recommendations of the Tissue Suitability Subcommittee during the last MAB meeting in June. The subcommittee met several times via conference call and email and proposed changes to F1.200 and F1.300 of the EBAA Technical Procedures Manual. In addition, the subcommittee proposed adding the "Recommended Minimum Standards for Surgical Suitability by Surgical Type" to F1.200. Procedure F1.400 Pachymetry Measurement was also added.

During the subcommittee's work, they identified that K-Pro was omitted from F1.300 – Determination of Surgical Suitability in the Medical Standards.

Brian Philippy commented that while measurement of arcus clear zone had been appropriately added to F1.200, clear zone was not. Michael Titus said his subcommittee would look at that. Dr. Jennifer Li also asked that pleomorphism be added back into the definition of terms for F1.300.

A motion was made and seconded to make the updates (including adding definitions of clear zone and pleomorphism) to the Procedures Manual. Motion Passed.

The discussion then turned to F1.300. After a lengthy discussion, the following friendly amendments were made:

- The word "stromal" was removed from all sections (will read No infiltrates).
- Down syndrome or evidence of ectatic dystrophy was added to K-pro section.
- The DMEK section was changed to read "No Descemet's membrane tears within intended graft area.

The section on K-Pro was modified to read as follows:

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.).

A motion was made and seconded to update F1.300 as discussed. Motion Passed.

IV. Old Business

A. Standardized Data Collection for Surgeons

Dr. Holly Hindman reported that her subcommittee discussed this topic at length and the recommendation was to request surgeons/surgery schedulers to be clearer about the indication for use when requesting tissue and for eye banks to provide a list of indications on request forms or in their on-line tissue request portals.

B. EBAA BOD's decision regarding Transplant Connect's proposal to include additional 9 fields to the stat report

Kevin Corcoran reported that the additional fields would not be added to the stat report at this time. The EBAA Board of Directors discussed the situation with not having a proposal from Transplant Connect and the decision was made to evaluate other vendors for the EBAA statistical report data collection next year. EBAA will be requesting proposals from other vendors in addition to Transplant Connect for future statistical report data collection.

V. New Business

A. Proposed change to E1.100

With the goal of reducing fungal infections, Dr. Straiko presented a change to EBAA Medical Standard E.100. That change was as follows:

"Povidone-iodine solution shall contact the surface of any ocular tissue intended for transplant at least ~~once~~ twice 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 exposures to the solution shall be specified in the eye bank's operating procedures."

The proposed change was based on Georgia Eye Bank's procedural change and the data collected by a large surgery center in its service area demonstrating that the change significantly reduced positive rim cultures and infections. There was significant discussion on this topic (both for and against making a change to the medical standards). Dr. Li asked that the word "entire" be added in front of the word surface in the first sentence.

A motion was made and seconded to modify E1.100 as presented by Dr. Straiko with the friendly amendment by Dr. Li. Motion Passed. *The change to the medical standard will be effective January 1, 2020.*

More investigation into this topic was recommended by the MAB. Dr. Li suggested a subcommittee be formed to dive deeper into this topic and report back at the next meeting with potential further recommendations on donor prep procedures. Subcommittee members include: Eric Meinecke (Chair), Dr. Michael Straiko, Dr. Sadeer Hannush, Ingrid Schunder, Brian Philippy, Kyle Mavin, William Buras, Dr. Sean Edelstein, Edwin Roberts, Dr. Shahzad Mian, Michael Titus, and Darrell Fisher.

B. Recommendation to create Subcommittee/Strikeforce to address critical and time-sensitive issues impacting EBAA members

Eye banking is becoming increasingly complex and the need to respond rapidly to emerging diseases and critical issues that could potentially impact the quality and safety of corneal tissue distributed for transplant is becoming increasingly important. Brian Philippy proposed that the MAB create a standing subcommittee or strike force charged with convening and addressing issues in a rapid manner, consistent with either our inherent need to react fast to protect recipients (e.g. Zika, Ebola, etc.) or multi-eye bank "ticking clock" items (e.g. possible reporting deadlines like 24 hours for CTO or 15 days for FDA).

Dr. Li asked how this proposal is different than how the current MAB operates. Dr. Li explained that the MAB has been able to respond quickly to issues and provide guidance and support to eye banks. Dr. Tony Aldave also commented that his subcommittee (Policy & Position Research Subcommittee) plays a role in assisting the EBAA and MAB with handling emerging diseases and critical issues. The recommendation to form a standing subcommittee/strike force was not approved but the topic did generate a lot of good discussion.

C. EBAA Statistical Report Ledger CY 2019

Jennifer DeMatteo briefly reviewed 6 months of statistical data (Jan-Jun 2019).

VI. Late Additions

A. David Korroch announced Donna Drury as the next EBAA Heise Awardee recipient.

B. Jennifer DeMatteo proposed the following revisions to EBAA Medical Standards Appendix II: FDA-defined Contraindications to Transplant:

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.

A motion was made and seconded to revise EBAA Medical Standards Appendix II: FDA-defined Contraindications to Transplant as presented by Jennifer DeMatteo. Motion Passed.

VII. For Information and Review

A. Informational Alert: Altaire Pharmaceuticals Recalls Multiple Ophthalmic Products (July 17, 2019)
B. Informational Alert: Altaire Pharmaceuticals Recall Update (July 25, 2019)
C. The Focal Point: Advocacy & Legislative Update (September 10, 2019)
D. 2018 Povidone-Iodine Survey
E. Increasing Povidone-Iodine Exposure (Salisbury et al., 2019)
F. Increased Bactericidal Activity of Dilute Preparations of Povidone-Iodine Solutions (Berkelman et al., 1982)

VIII. Adjournment

A motion was made and seconded to adjourn the Medical Advisory Board meeting. Motion Passed.

COMMITTEE REPORTS

MEDICAL REVIEW SUBCOMMITTEE

OARRS

The Online Adverse Reaction Reporting System

Adverse Reactions Reasonably Likely/ Proven to be Due to Donor Tissue

Report generated 20 May 2020 5:10pm EDT

	2014	2015	2016	2017	2018	2019	2020	Mean
Primary Graft Failure	**50**	**48**	**45**	**55**	**87**	**84**	**6**	**43.27**
Recipient's Age (mean)	64.59	64.25	64.59	64.62	69.46	68.66	72.33	66.52
Donor's Age (mean)	54.48	54.48	56.89	56.65	57.14	59.44	47.67	55.99
Donor Cause of Death								
Heart disease	14 (28%)	16 (33%)	15 (33%)	13 (24%)	28 (32%)	23 (27%)	1 (17%)	13.4 (31%)
Cancer	12 (24%)	12 (25%)	8 (18%)	17 (31%)	14 (16%)	22 (26%)	1 (17%)	10.13 (23%)
Cerebrovascular accident	4 (8%)	4 (8%)	5 (11%)	3 (5%)	9 (10%)	5 (6%)	2 (33%)	3.6 (8%)
Respiratory disease	3 (6%)	2 (4%)	2 (4%)	6 (11%)	6 (7%)	5 (6%)	0 (0%)	3.13 (7%)
Trauma	10 (20%)	1 (2%)	4 (9%)	5 (9%)	5 (6%)	7 (8%)	1 (17%)	4.13 (10%)
Toxic / Accident	2 (4%)	2 (4%)	0 (0%)	2 (4%)	0 (0%)	1 (1%)	0 (0%)	0.8 (2%)
Other	5 (10%)	11 (23%)	11 (24%)	9 (16%)	25 (29%)	21 (25%)	1 (17%)	8.07 (19%)
Mated Cases	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Procedure Type								
Penetrating keratoplasty (includes LAK/IEK)	20 (40%)	22 (46%)	17 (38%)	12 (22%)	9 (10%)	11 (13%)	0 (0%)	13.93 (32%)
Anterior lamellar keratoplasty (includes ALK, DALK)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.2 (0%)
Endothelial keratoplasty: DSEK, DSAEK, DLEK	26 (52%)	20 (42%)	21 (47%)	33 (60%)	57 (66%)	41 (49%)	4 (67%)	23.53 (54%)
Endothelial keratoplasty: DMEK or DMAEK	3 (6%)	6 (13%)	7 (16%)	10 (18%)	21 (24%)	32 (38%)	2 (33%)	5.53 (13%)
Scleral graft	1 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (0%)
Source of Lamellar Cut								
N/A	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	9 (11%)	0 (0%)	0.6 (2%)
Surgeon	2 (7%)	2 (8%)	1 (4%)	2 (5%)	5 (6%)	12 (14%)	0 (0%)	3.33 (11%)
Processing establishment - source eye bank	18 (62%)	19 (73%)	21 (75%)	31 (72%)	44 (56%)	43 (52%)	6 (100%)	20.27 (68%)
Other processing establishment	9 (31%)	5 (19%)	6 (21%)	10 (23%)	29 (37%)	19 (23%)	0 (0%)	5.67 (19%)
Type of Lamellar Cut								
N/A	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	16 (19%)	0 (0%)	1.07 (4%)
Microkeratome	28 (97%)	23 (92%)	23 (82%)	34 (79%)	61 (78%)	41 (49%)	2 (33%)	24.33 (82%)
Manual Dissection	1 (3%)	2 (8%)	5 (18%)	9 (21%)	17 (22%)	26 (31%)	4 (67%)	4.27 (14%)
Tissue Preloaded								
Yes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	6 (7%)	20 (24%)	2 (33%)	1.87 (12%)
No	0 (0%)	0 (0%)	1 (100%)	47 (100%)	81 (93%)	64 (76%)	4 (67%)	13.13 (88%)
Location of Tissue Transplant								
United States	33 (66%)	25 (52%)	28 (62%)	37 (67%)	69 (79%)	52 (62%)	4 (67%)	34.07 (79%)
International	17 (34%)	23 (48%)	17 (38%)	18 (33%)	18 (21%)	32 (38%)	2 (33%)	9.2 (21%)
Preoperative Diagnosis								
A. Post-cataract surgery edema	7 (14%)	11 (23%)	13 (29%)	6 (11%)	13 (15%)	9 (11%)	1 (17%)	7.53 (17%)
B. Keratoconus	6 (12%)	5 (10%)	5 (11%)	8 (15%)	1 (1%)	2 (2%)	0 (0%)	3.73 (9%)
C. Fuchs' dystrophy	11 (22%)	15 (31%)	14 (31%)	26 (47%)	43 (49%)	39 (46%)	3 (50%)	16.2 (37%)
D. Repeat corneal transplant	7 (14%)	0 (0%)	3 (7%)	5 (9%)	6 (7%)	7 (8%)	2 (33%)	4.47 (10%)
E. Other degenerations or dystrophies	4 (8%)	4 (8%)	1 (2%)	4 (7%)	9 (10%)	5 (6%)	0 (0%)	2.27 (5%)
F. Post-refractive surgery	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (0%)
G. Microbial changes	2 (4%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)	0 (0%)	0.47 (1%)
H. Mechanical or chemical trauma	0 (0%)	2 (4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.33 (1%)
I. Congenital opacities	1 (2%)	0 (0%)	1 (2%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	0.33 (1%)
K. Non- infectious ulcerative keratitis or perforation	0 (0%)	1 (2%)	3 (7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.27 (1%)
L. Other causes of corneal dysfunction or distortion (non-endothelial)	5 (10%)	3 (6%)	2 (4%)	1 (2%)	3 (3%)	0 (0%)	0 (0%)	3.67 (8%)
M. Other causes of endothelial dysfunction	5 (10%)	2 (4%)	3 (7%)	2 (4%)	9 (10%)	15 (18%)	0 (0%)	2.8 (6%)
Z. Unknown, unreported, or unspecified	2 (4%)	4 (8%)	0 (0%)	2 (4%)	3 (3%)	6 (7%)	0 (0%)	1.13 (3%)
Endothelial Density (mean)	2759.38	2779.3	2809.76	2852.31	2905.37	2842.58	2771.83	2817.9
Death to Cooling (mean hrs)	4.43	4.41	4.66	4.53	4.98	5.12	3.17	4.26
Range	1–11	0–16.17	0.3–21.6	0–20.62	0–21	0–20.6	1.5–4	0–21.6
Death to Preservation (mean hrs)	12.47	13.94	11.86	11.27	12.25	30.58	9.13	13.79
Range	3.45–25	5.25–23.38	4–23.83	2–24	3–24	3.8–1515	4–14	1–1515
Death to Surgery (mean days)	11.66	7.19	7.04	7.29	6.38	6.43	6.33	6.87
Range	1–243	2–13	3–14	3–14	2–14	2–15	6–8	1–243
Preservation Method								
Optisol-GS	47 (94%)	42 (88%)	39 (87%)	53 (96%)	75 (86%)	71 (85%)	6 (100%)	40.33 (93%)
Life4C	2 (4%)	5 (10%)	6 (13%)	1 (2%)	9 (10%)	13 (15%)	0 (0%)	2.47 (6%)
Eusol-C	0 (0%)	0 (0%)	0 (0%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	0.13 (0%)
Cornea Cold®	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)	0 (0%)	0 (0%)	0.07 (0%)
Other	1 (2%)	1 (2%)	0 (0%)	0 (0%)	2 (2%)	0 (0%)	0 (0%)	0.27 (1%)
Was storage solution changed after processing?								

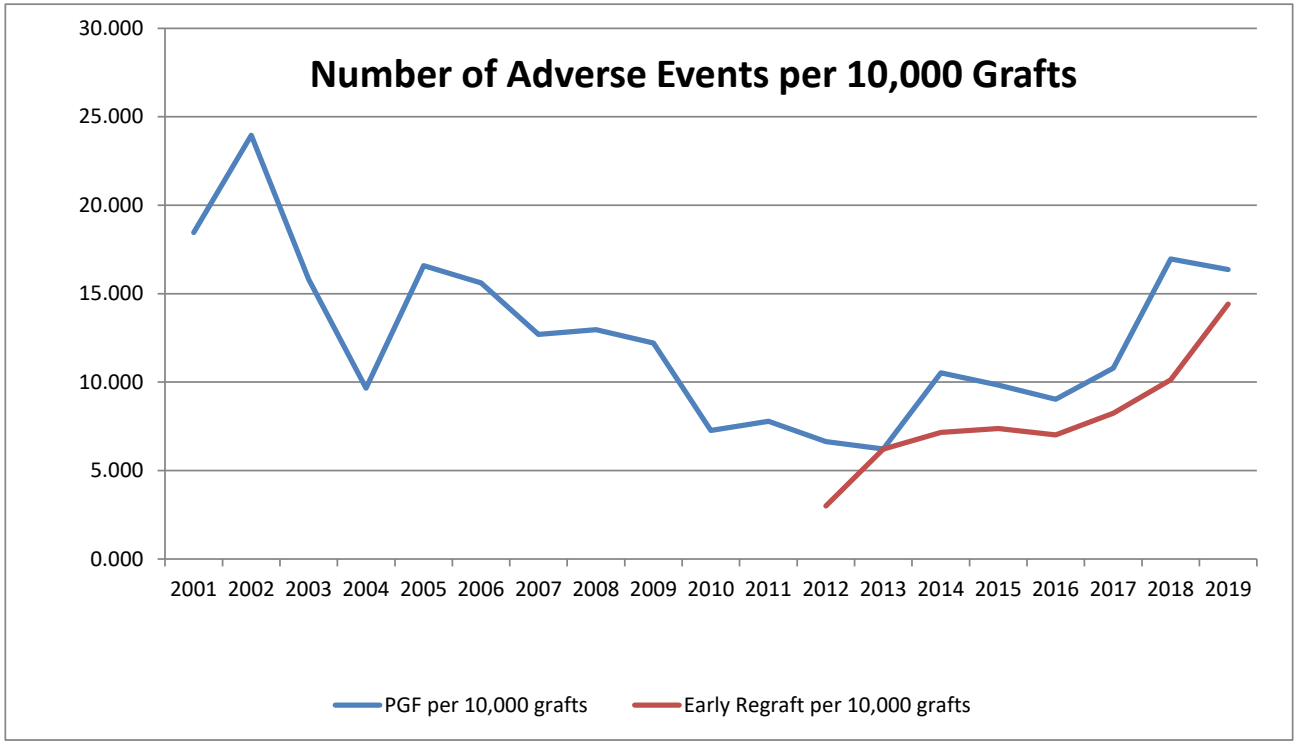
No	0 (0%)	0 (0%)	1 (100%)	19 (40%)	26 (30%)	26 (31%)	0 (0%)	4.8 (32%)
Yes	0 (0%)	0 (0%)	0 (0%)	28 (60%)	61 (70%)	58 (69%)	6 (100%)	10.2 (68%)
Post-Processing Preservation Method								
Optisol-GS	0 (0%)	0 (0%)	0 (0%)	24 (80%)	36 (58%)	52 (90%)	6 (100%)	7.87 (76%)
Life4C	0 (0%)	0 (0%)	0 (0%)	6 (20%)	7 (11%)	4 (7%)	0 (0%)	1.13 (11%)
Cornea Cold®	0 (0%)	0 (0%)	0 (0%)	0 (0%)	9 (15%)	0 (0%)	0 (0%)	0.6 (6%)
Other	0 (0%)	0 (0%)	0 (0%)	0 (0%)	10 (16%)	2 (3%)	0 (0%)	0.8 (8%)
Antifungal Supplementation?								
No	0 (0%)	0 (0%)	0 (0%)	28 (100%)	59 (97%)	65 (87%)	5 (83%)	10.47 (92%)
Yes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (3%)	10 (13%)	1 (17%)	0.87 (8%)
Recovery Procedure								
In-situ corneal excision	48 (96%)	48 (100%)	44 (98%)	55 (100%)	86 (99%)	81 (96%)	6 (100%)	42.47 (98%)
In-laboratory corneal and/or scleral excision after enucleation	2 (4%)	0 (0%)	1 (2%)	0 (0%)	1 (1%)	3 (4%)	0 (0%)	0.8 (2%)
Donor Site Facility								
Hospital	33 (66%)	21 (44%)	31 (69%)	35 (64%)	43 (49%)	53 (63%)	4 (67%)	27.73 (64%)
Medical examiner	9 (18%)	4 (8%)	5 (11%)	3 (5%)	7 (8%)	6 (7%)	0 (0%)	4.47 (10%)
Funeral home or mortuary	2 (4%)	12 (25%)	1 (2%)	5 (9%)	12 (14%)	9 (11%)	0 (0%)	4 (9%)
Other	6 (12%)	11 (23%)	8 (18%)	12 (22%)	25 (29%)	16 (19%)	2 (33%)	7.07 (16%)
	2014	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**Mean**
Early Regraft	**34**	**36**	**35**	**42**	**52**	**74**	**13**	**36.78**
Recipient's Age (mean)	67.76	67.53	65.09	68.33	66.63	67.26	75.15	67
Donor's Age (mean)	54.47	56.42	53.74	59.52	58.85	61.99	54	58.42
Donor Cause of Death								
Heart disease	11 (32%)	11 (31%)	11 (31%)	17 (40%)	13 (25%)	19 (26%)	6 (46%)	11.11 (30%)
Cancer	10 (29%)	7 (19%)	3 (9%)	4 (10%)	8 (15%)	30 (41%)	1 (8%)	8.89 (24%)
Cerebrovascular accident	3 (9%)	8 (22%)	5 (14%)	6 (14%)	10 (19%)	5 (7%)	0 (0%)	4.56 (12%)
Respiratory disease	1 (3%)	4 (11%)	6 (17%)	3 (7%)	4 (8%)	6 (8%)	1 (8%)	3.33 (9%)
Trauma	5 (15%)	3 (8%)	4 (11%)	0 (0%)	6 (12%)	4 (5%)	1 (8%)	2.78 (8%)
Toxic / Accident	0 (0%)	1 (3%)	1 (3%)	0 (0%)	1 (2%)	0 (0%)	0 (0%)	0.33 (1%)
Other	4 (12%)	2 (6%)	5 (14%)	12 (29%)	10 (19%)	10 (14%)	4 (31%)	5.78 (16%)
Mated Cases	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Procedure Type								
Penetrating keratoplasty (includes LAK/IEK)	4 (12%)	6 (17%)	6 (17%)	2 (5%)	5 (10%)	2 (3%)	1 (8%)	3.89 (11%)
Endothelial keratoplasty: DSEK, DSAEK, DLEK	25 (74%)	19 (53%)	18 (51%)	21 (50%)	25 (48%)	19 (26%)	7 (54%)	18.56 (50%)
Endothelial keratoplasty: DMEK or DMAEK	5 (15%)	11 (31%)	11 (31%)	19 (45%)	22 (42%)	53 (72%)	5 (38%)	14.33 (39%)
Source of Lamellar Cut								
N/A	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (3%)	1 (8%)	0.33 (1%)
Surgeon	1 (3%)	1 (3%)	0 (0%)	4 (10%)	2 (4%)	3 (4%)	0 (0%)	1.89 (6%)
Processing establishment - source eye bank	24 (80%)	28 (93%)	23 (79%)	20 (50%)	28 (60%)	46 (62%)	12 (92%)	22.89 (69%)
Other processing establishment	5 (17%)	1 (3%)	6 (21%)	16 (40%)	17 (36%)	23 (31%)	0 (0%)	8.11 (24%)
Type of Lamellar Cut								
N/A	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (3%)	1 (8%)	0.33 (1%)
Microkeratome	25 (83%)	21 (70%)	19 (68%)	21 (55%)	26 (55%)	20 (27%)	7 (54%)	19.44 (59%)
Manual Dissection	5 (17%)	9 (30%)	9 (32%)	17 (45%)	21 (45%)	52 (70%)	5 (38%)	13.11 (40%)
Tissue Preloaded								
Yes	0 (0%)	0 (0%)	0 (0%)	2 (7%)	14 (27%)	41 (55%)	2 (15%)	6.56 (35%)
No	0 (0%)	0 (0%)	1 (100%)	26 (93%)	38 (73%)	33 (45%)	11 (85%)	12.22 (65%)
Location of Tissue Transplant								
United States	29 (85%)	32 (89%)	34 (97%)	38 (90%)	51 (98%)	67 (91%)	10 (77%)	33 (90%)
International	5 (15%)	4 (11%)	1 (3%)	4 (10%)	1 (2%)	7 (9%)	3 (23%)	3.78 (10%)
Preoperative Diagnosis								
A. Post-cataract surgery edema	5 (15%)	7 (19%)	3 (9%)	4 (10%)	6 (12%)	3 (4%)	1 (8%)	4 (11%)
B. Keratoconus	2 (6%)	3 (8%)	2 (6%)	1 (2%)	3 (6%)	0 (0%)	0 (0%)	1.78 (5%)
C. Fuchs' dystrophy	18 (53%)	13 (36%)	18 (51%)	23 (55%)	30 (58%)	53 (72%)	6 (46%)	20.33 (55%)
D. Repeat corneal transplant	4 (12%)	3 (8%)	2 (6%)	3 (7%)	4 (8%)	3 (4%)	2 (15%)	2.67 (7%)
E. Other degenerations or dystrophies	2 (6%)	4 (11%)	4 (11%)	5 (12%)	5 (10%)	8 (11%)	1 (8%)	3.44 (9%)
F. Post-refractive surgery	0 (0%)	0 (0%)	1 (3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.11 (0%)
G. Microbial changes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.11 (0%)
I. Congenital opacities	0 (0%)	0 (0%)	1 (3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.11 (0%)
L. Other causes of corneal dysfunction or distortion (non- endothelial)	0 (0%)	2 (6%)	1 (3%)	0 (0%)	1 (2%)	1 (1%)	0 (0%)	0.89 (2%)
M. Other causes of endothelial dysfunction	1 (3%)	4 (11%)	3 (9%)	6 (14%)	3 (6%)	4 (5%)	2 (15%)	2.78 (8%)
Z. Unknown, unreported, or unspecified	2 (6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (3%)	1 (8%)	0.56 (2%)
Endothelial Density (mean)	2902.06	2813.31	2815.51	2925.14	2857.19	2794.72	2769.85	2829.01
Death to Cooling (mean hrs)	3.46	3.19	3.87	4.33	3.86	4.05	3.95	3.95
Range	1–9	0–11	0.78–18	0.58–17	0–13.4	0–13.6	2–9	0–18
Death to Preservation (mean hrs)	11.77	11.81	11.43	10.98	56.91	11.99	14.82	22.96
Range	4.5–23.58	3–23.5	2.85–23.5	2.18–24	1–2356	1–23	7–23	1–2356
Death to Surgery (mean days)	6.26	6.61	5.51	5.79	5.79	5.96	5.92	6.04
Range	2–20	3–14	2–9	1–9	2–13	2–13	3–9	1–20
Preservation Method								

Optisol-GS	32 (94%)	35 (97%)	33 (94%)	42 (100%)	45 (87%)	65 (88%)	11 (85%)	33.89 (92%)
Life4C	2 (6%)	1 (3%)	2 (6%)	0 (0%)	7 (13%)	9 (12%)	2 (15%)	2.89 (8%)
Was storage solution changed after processing?								
No	0 (0%)	0 (0%)	0 (0%)	6 (21%)	14 (27%)	12 (16%)	0 (0%)	3.56 (19%)
Yes	0 (0%)	0 (0%)	1 (100%)	22 (79%)	38 (73%)	62 (84%)	13 (100%)	15.22 (81%)
Post-Processing Preservation Method								
Optisol-GS	0 (0%)	0 (0%)	1 (100%)	17 (77%)	23 (61%)	57 (92%)	11 (85%)	12.22 (80%)
Life4C	0 (0%)	0 (0%)	0 (0%)	5 (23%)	8 (21%)	5 (8%)	2 (15%)	2.22 (15%)
Cornea Cold®	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (5%)	0 (0%)	0 (0%)	0.22 (1%)
Other	0 (0%)	0 (0%)	0 (0%)	0 (0%)	5 (13%)	0 (0%)	0 (0%)	0.56 (4%)
Antifungal Supplementation?								
No	0 (0%)	0 (0%)	1 (100%)	22 (100%)	37 (97%)	53 (76%)	9 (69%)	13.67 (85%)
Yes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (3%)	17 (24%)	4 (31%)	2.44 (15%)
Recovery Procedure								
In-situ corneal excision	31 (91%)	34 (94%)	35 (100%)	40 (95%)	52 (100%)	74 (100%)	13 (100%)	35.78 (97%)
In-laboratory corneal and/or scleral excision after enucleation	3 (9%)	2 (6%)	0 (0%)	2 (5%)	0 (0%)	0 (0%)	0 (0%)	1 (3%)
Donor Site Facility								
Hospital	20 (59%)	26 (72%)	24 (69%)	23 (55%)	33 (63%)	40 (54%)	8 (62%)	22.56 (61%)
Medical examiner	2 (6%)	3 (8%)	3 (9%)	4 (10%)	5 (10%)	6 (8%)	1 (8%)	2.78 (8%)
Funeral home or mortuary	6 (18%)	4 (11%)	2 (6%)	6 (14%)	4 (8%)	16 (22%)	2 (15%)	5.11 (14%)
Other	6 (18%)	3 (8%)	6 (17%)	9 (21%)	10 (19%)	12 (16%)	2 (15%)	6.33 (17%)
	2014	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**Mean**
Endophthalmitis	**16**	**20**	**20**	**21**	**13**	**9**	**3**	**12.33**
Recipient's Age (mean)	65.73	59.8	72.75	65.57	71.17	69.33	59	67.17
Donor's Age (mean)	51.19	56.25	54.7	58.1	58	64.78	64	57.42
Donor Cause of Death								
Heart disease	6 (38%)	2 (10%)	11 (55%)	8 (38%)	4 (31%)	4 (44%)	1 (33%)	4.27 (35%)
Cancer	1 (6%)	5 (25%)	2 (10%)	1 (5%)	3 (23%)	2 (22%)	1 (33%)	1.93 (16%)
Cerebrovascular accident	1 (6%)	0 (0%)	1 (5%)	1 (5%)	2 (15%)	0 (0%)	0 (0%)	0.33 (3%)
Respiratory disease	2 (13%)	4 (20%)	1 (5%)	1 (5%)	1 (8%)	0 (0%)	1 (33%)	1.47 (12%)
Trauma	1 (6%)	3 (15%)	0 (0%)	3 (14%)	1 (8%)	0 (0%)	0 (0%)	0.87 (7%)
Toxic / Accident	0 (0%)	0 (0%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0.2 (2%)
Other	5 (31%)	6 (30%)	5 (25%)	6 (29%)	2 (15%)	3 (33%)	0 (0%)	3.27 (26%)
Mated Cases	0 (0%)	1 (5%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0.33 (3%)
Procedure Type								
Penetrating keratoplasty (includes LAK/IEK)	5 (31%)	6 (30%)	4 (20%)	2 (10%)	4 (31%)	2 (22%)	2 (67%)	3.8 (31%)
Anterior lamellar keratoplasty (includes ALK, DALK)	0 (0%)	1 (5%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0.13 (1%)
Endothelial keratoplasty: DSEK, DSAEK, DLEK	9 (56%)	11 (55%)	12 (60%)	15 (71%)	7 (54%)	2 (22%)	0 (0%)	6.93 (56%)
Endothelial keratoplasty: DMEK or DMAEK	2 (13%)	1 (5%)	4 (20%)	3 (14%)	2 (15%)	5 (56%)	1 (33%)	1.27 (10%)
Keratoprosthesis (K-Pro)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.13 (1%)
Scleral graft	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Source of Lamellar Cut								
N/A	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (22%)	2 (67%)	0.27 (3%)
Surgeon	2 (18%)	2 (15%)	5 (31%)	3 (16%)	0 (0%)	0 (0%)	1 (33%)	1.67 (19%)
Processing establishment - source eye bank	9 (82%)	10 (77%)	9 (56%)	11 (58%)	5 (56%)	4 (44%)	0 (0%)	5.13 (60%)
Other processing establishment	0 (0%)	1 (8%)	2 (13%)	5 (26%)	4 (44%)	3 (33%)	0 (0%)	1.53 (18%)
Type of Lamellar Cut								
N/A	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (22%)	2 (67%)	0.27 (3%)
Microkeratome	10 (91%)	11 (85%)	11 (69%)	15 (79%)	7 (78%)	2 (22%)	0 (0%)	6.8 (80%)
Manual Dissection	1 (9%)	2 (15%)	5 (31%)	4 (21%)	2 (22%)	5 (56%)	1 (33%)	1.47 (17%)
Tissue Preloaded								
Yes	0 (0%)	0 (0%)	0 (0%)	1 (8%)	1 (8%)	3 (33%)	0 (0%)	0.33 (12%)
No	0 (0%)	4 (100%)	1 (100%)	11 (92%)	12 (92%)	6 (67%)	3 (100%)	2.47 (88%)
Location of Tissue Transplant								
United States	13 (81%)	13 (65%)	13 (65%)	18 (86%)	10 (77%)	8 (89%)	2 (67%)	10.2 (83%)
International	3 (19%)	7 (35%)	7 (35%)	3 (14%)	3 (23%)	1 (11%)	1 (33%)	2.13 (17%)
Concordant Positive Cultures	4 (25%)	7 (35%)	4 (20%)	5 (24%)	5 (38%)	5 (56%)	1 (33%)	4.73 (38%)
Recipient Culture Results								
Achromobacter (formerly Alcaligenes)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Candida albicans	2 (13%)	1 (5%)	1 (5%)	1 (5%)	1 (9%)	1 (11%)	0 (0%)	1.2 (10%)
Candida glabrata	6 (38%)	1 (5%)	8 (40%)	6 (27%)	1 (9%)	4 (44%)	0 (0%)	3.13 (25%)
Candida parapsilosis	1 (6%)	0 (0%)	0 (0%)	0 (0%)	1 (9%)	0 (0%)	0 (0%)	0.13 (1%)
Candida tropicalis	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.2 (2%)
Candida unspecified	0 (0%)	2 (9%)	2 (10%)	2 (9%)	0 (0%)	0 (0%)	0 (0%)	0.93 (7%)
Clostridium perfringens	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (11%)	0 (0%)	0.2 (2%)
Enterobacter spp.	0 (0%)	2 (9%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (33%)	0.2 (2%)
Enterococcus faecalis	1 (6%)	2 (9%)	0 (0%)	1 (5%)	1 (9%)	2 (22%)	0 (0%)	0.67 (5%)
Enterococcus faecium	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.13 (1%)
Enterococcus spp.	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)

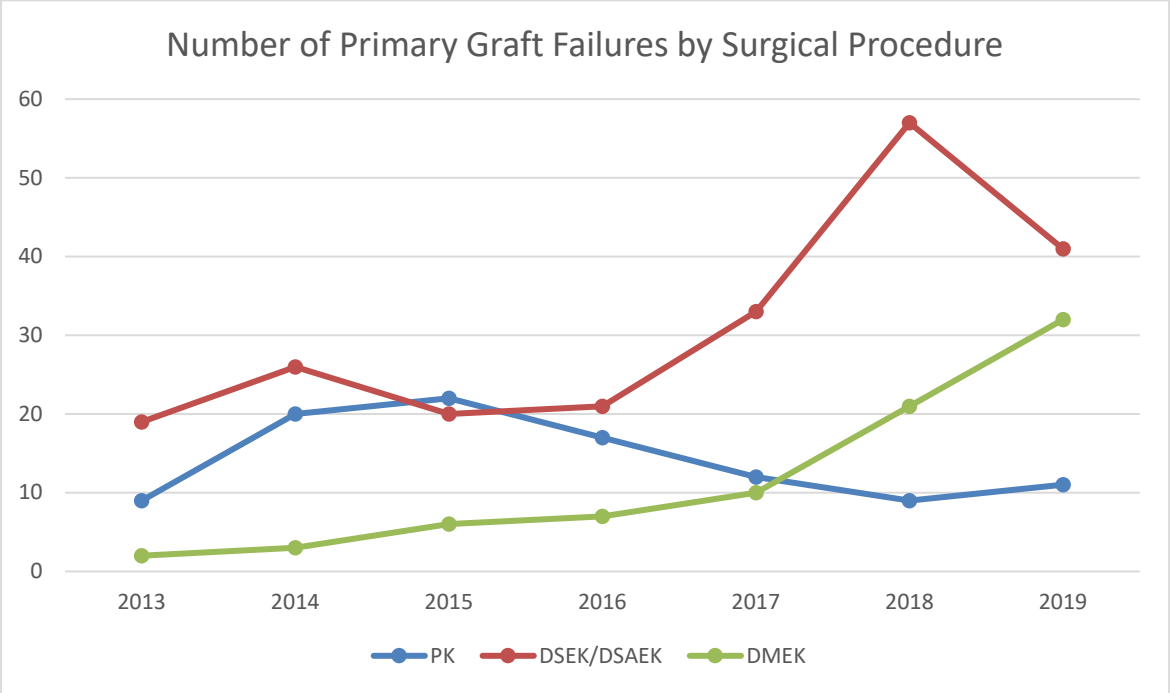
Enterococcus unspecified	0 (0%)	1 (5%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0.47 (4%)
Escherichia coli	1 (6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Haemophilus influenzae	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Penicillium spp.	0 (0%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Pseudomonas aeruginosa	0 (0%)	0 (0%)	0 (0%)	1 (5%)	1 (9%)	0 (0%)	0 (0%)	0.13 (1%)
Staphylococcus aureus	0 (0%)	0 (0%)	0 (0%)	2 (9%)	0 (0%)	0 (0%)	0 (0%)	0.27 (2%)
Staphylococcus epidermidis / coagulase negative	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Staphylococcus unspecified	0 (0%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.13 (1%)
Streptococcus agalactiae (Group B Strep)	1 (6%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.2 (2%)
Streptococcus pneumonia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Streptococcus unspecified	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.33 (3%)
Viridans streptococci (alpha hemolytic)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (9%)	0 (0%)	0 (0%)	0.13 (1%)
Yeast - non- specified	1 (6%)	0 (0%)	1 (5%)	2 (9%)	1 (9%)	0 (0%)	0 (0%)	0.4 (3%)
Other Organism	0 (0%)	1 (5%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.13 (1%)
Not done	1 (6%)	4 (18%)	3 (15%)	5 (23%)	4 (36%)	1 (11%)	1 (33%)	1.87 (15%)
No growth	2 (13%)	5 (23%)	2 (10%)	1 (5%)	0 (0%)	0 (0%)	1 (33%)	1.27 (10%)
Death to Cooling (mean hrs)	5.05	5.15	5.13	5.49	3.6	3.89	3.41	4.53
Range	1.95–14	1–13	2–15.7	1.5–17	1.5–10.5	1–6.15	2–4.81	0–19
Death to Preservation (mean hrs)	12.47	13.07	14.38	13.23	10.93	10.36	16	11.91
Range	3–22	5.25–23	6–23.58	5.75–24	4–23.83	6.8–17	14–18	2–24
Death to Surgery (mean days)	6.5	6.2	5.95	5.76	7.08	6	6.33	6.65
Range	3–14	2–11	2–10	3–13	2–13	3–8	4–10	2–128
Preservation Method								
Optisol-GS	13 (81%)	19 (95%)	19 (95%)	19 (90%)	13 (100%)	6 (67%)	2 (67%)	11.07 (90%)
Life4C	3 (19%)	1 (5%)	0 (0%)	2 (10%)	0 (0%)	3 (33%)	1 (33%)	1.13 (9%)
Eusol-C	0 (0%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Other	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Was storage solution changed after processing?								
No	0 (0%)	4 (100%)	0 (0%)	6 (50%)	7 (54%)	4 (44%)	2 (67%)	1.53 (55%)
Yes	0 (0%)	0 (0%)	1 (100%)	6 (50%)	6 (46%)	5 (56%)	1 (33%)	1.27 (45%)
Post-Processing Preservation Method								
Optisol-GS	0 (0%)	0 (0%)	1 (100%)	6 (86%)	5 (83%)	5 (100%)	0 (0%)	1.13 (85%)
Life4C	0 (0%)	0 (0%)	0 (0%)	1 (14%)	0 (0%)	0 (0%)	1 (100%)	0.13 (10%)
Other	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (17%)	0 (0%)	0 (0%)	0.07 (5%)
Antifungal Supplementation?								
No	0 (0%)	0 (0%)	1 (100%)	7 (100%)	5 (83%)	7 (100%)	3 (100%)	1.53 (96%)
Yes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (17%)	0 (0%)	0 (0%)	0.07 (4%)
Recovery Procedure								
In-situ corneal excision	16 (100%)	20 (100%)	20 (100%)	21 (100%)	13 (100%)	9 (100%)	3 (100%)	12.27 (99%)
In-laboratory corneal and/or scleral excision after enucleation	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Donor Site Facility								
Hospital	14 (88%)	13 (65%)	17 (85%)	10 (48%)	9 (69%)	5 (56%)	2 (67%)	8.4 (68%)
Medical examiner	2 (13%)	3 (15%)	0 (0%)	3 (14%)	0 (0%)	1 (11%)	0 (0%)	1 (8%)
Funeral home or mortuary	0 (0%)	4 (20%)	3 (15%)	3 (14%)	1 (8%)	0 (0%)	0 (0%)	1.2 (10%)
Other	0 (0%)	0 (0%)	0 (0%)	5 (24%)	3 (23%)	3 (33%)	1 (33%)	1.73 (14%)
	2014	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**Mean**
Infectious Keratitis	**19**	**16**	**14**	**21**	**14**	**6**	**0**	**9.2**
Recipient's Age (mean)	74.37	62.75	71.46	64.95	70.69	62.33	0	67.16
Donor's Age (mean)	48.74	54.07	51.14	54.29	59.14	49.83	0	52.47
Donor Cause of Death								
Heart disease	5 (26%)	7 (44%)	4 (29%)	6 (29%)	7 (50%)	1 (17%)	0 (0%)	3.6 (39%)
Cancer	3 (16%)	5 (31%)	1 (7%)	2 (10%)	0 (0%)	1 (17%)	0 (0%)	1.27 (14%)
Cerebrovascular accident	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.2 (2%)
Respiratory disease	0 (0%)	0 (0%)	3 (21%)	2 (10%)	1 (7%)	1 (17%)	0 (0%)	0.6 (7%)
Trauma	3 (16%)	1 (6%)	1 (7%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0.87 (9%)
Toxic / Accident	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.13 (1%)
Other	6 (32%)	3 (19%)	5 (36%)	10 (48%)	6 (43%)	3 (50%)	0 (0%)	2.53 (28%)
Mated Cases	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Procedure Type								
Penetrating keratoplasty (includes LAK/IEK)	2 (11%)	6 (38%)	4 (29%)	2 (10%)	3 (21%)	2 (33%)	0 (0%)	2.47 (27%)
Anterior lamellar keratoplasty (includes ALK, DALK)	0 (0%)	2 (13%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0.33 (4%)
Endothelial keratoplasty: DSEK, DSAEK, DLEK	16 (84%)	7 (44%)	8 (57%)	12 (57%)	9 (64%)	0 (0%)	0 (0%)	5.27 (57%)
Endothelial keratoplasty: DMEK or DMAEK	1 (5%)	0 (0%)	2 (14%)	6 (29%)	2 (14%)	4 (67%)	0 (0%)	1 (11%)
Keratoprosthesis (K-Pro)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Other (e.g. experimental surgery)	0 (0%)	1 (6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Source of Lamellar Cut								
N/A	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (33%)	0 (0%)	0.13 (2%)
Surgeon	1 (6%)	1 (11%)	0 (0%)	4 (21%)	0 (0%)	1 (17%)	0 (0%)	1 (15%)

Processing establishment - source eye bank	12 (71%)	7 (78%)	9 (90%)	8 (42%)	8 (73%)	2 (33%)	0 (0%)	4.47 (66%)
Other processing establishment	4 (24%)	1 (11%)	1 (10%)	7 (37%)	3 (27%)	1 (17%)	0 (0%)	1.13 (17%)
Type of Lamellar Cut								
N/A	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (33%)	0 (0%)	0.13 (2%)
Microkeratome	15 (88%)	8 (89%)	8 (80%)	12 (71%)	9 (82%)	0 (0%)	0 (0%)	5.27 (80%)
Manual Dissection	2 (12%)	1 (11%)	2 (20%)	5 (29%)	2 (18%)	4 (67%)	0 (0%)	1.2 (18%)
Tissue Preloaded								
Yes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (7%)	2 (33%)	0 (0%)	0.2 (8%)
No	0 (0%)	0 (0%)	3 (100%)	13 (100%)	13 (93%)	4 (67%)	0 (0%)	2.2 (92%)
Location of Tissue Transplant								
United States	17 (89%)	14 (88%)	12 (86%)	17 (81%)	10 (71%)	6 (100%)	0 (0%)	8.27 (90%)
International	2 (11%)	2 (13%)	2 (14%)	4 (19%)	4 (29%)	0 (0%)	0 (0%)	0.93 (10%)
Concordant Positive Cultures	8 (42%)	3 (19%)	1 (7%)	4 (19%)	1 (7%)	2 (33%)	0 (0%)	2 (22%)
Recipient Culture Results								
Acanthamoeba spp.	0 (0%)	1 (6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Achromobacter (formerly Alcaligenes)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Candida albicans	4 (21%)	2 (13%)	2 (14%)	5 (23%)	2 (17%)	0 (0%)	0 (0%)	1.53 (17%)
Candida glabrata	7 (37%)	1 (6%)	0 (0%)	2 (9%)	2 (17%)	1 (20%)	0 (0%)	1.13 (13%)
Candida other	0 (0%)	0 (0%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0.2 (2%)
Candida parapsilosis	0 (0%)	0 (0%)	1 (7%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0.13 (1%)
Candida tropicalis	0 (0%)	1 (6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.13 (1%)
Candida unspecified	2 (11%)	1 (6%)	0 (0%)	0 (0%)	1 (8%)	0 (0%)	0 (0%)	0.67 (7%)
Escherichia coli	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Fusarium spp.	0 (0%)	0 (0%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Herpes simplex	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (20%)	0 (0%)	0.27 (3%)
Mycobacterium chelonae	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Pseudomonas aeruginosa	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Staphylococcus unspecified	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Streptococcus agalactiae (Group B Strep)	0 (0%)	0 (0%)	0 (0%)	1 (5%)	0 (0%)	1 (20%)	0 (0%)	0.13 (1%)
Yeast - non- specified	0 (0%)	0 (0%)	0 (0%)	1 (5%)	0 (0%)	1 (20%)	0 (0%)	0.2 (2%)
Other Organism	0 (0%)	0 (0%)	1 (7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.07 (1%)
Not done	4 (21%)	6 (38%)	9 (64%)	9 (41%)	7 (58%)	0 (0%)	0 (0%)	3.07 (34%)
No growth	2 (11%)	4 (25%)	1 (7%)	1 (5%)	0 (0%)	1 (20%)	0 (0%)	1 (11%)
Death to Cooling (mean hrs)	3.7	3.31	3.77	4.99	4.53	3.25	0	3.66
Range	1–9	0.25–9	0.23–13	1–11	2–13	2–6	0–0	0–13
Death to Preservation (mean hrs)	10.61	10.97	14.43	11.23	11.89	13.24	0	11.17
Range	3.7–16	3–22	5.88–23.9	4.68–16.12	5–23.83	6.57–23.85	0–0	1.7–23.9
Death to Surgery (mean days)	5.89	6.13	5.43	5.76	6.64	4.83	0	5.53
Range	3–9	2–11	3–9	2–11	2–12	2–7	0–0	2–13
Preservation Method								
Optisol-GS	17 (89%)	13 (81%)	13 (93%)	19 (90%)	12 (86%)	5 (83%)	0 (0%)	8.2 (89%)
Life4C	2 (11%)	3 (19%)	1 (7%)	0 (0%)	2 (14%)	1 (17%)	0 (0%)	0.87 (9%)
Other	0 (0%)	0 (0%)	0 (0%)	2 (10%)	0 (0%)	0 (0%)	0 (0%)	0.13 (1%)
Was storage solution changed after processing?								
No	0 (0%)	0 (0%)	3 (100%)	4 (31%)	6 (43%)	3 (50%)	0 (0%)	1.07 (44%)
Yes	0 (0%)	0 (0%)	0 (0%)	9 (69%)	8 (57%)	3 (50%)	0 (0%)	1.33 (56%)
Post-Processing Preservation Method								
Optisol-GS	0 (0%)	0 (0%)	0 (0%)	6 (67%)	5 (63%)	3 (100%)	0 (0%)	0.93 (70%)
Life4C	0 (0%)	0 (0%)	0 (0%)	3 (33%)	0 (0%)	0 (0%)	0 (0%)	0.2 (15%)
Other	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (38%)	0 (0%)	0 (0%)	0.2 (15%)
Antifungal Supplementation?								
No	0 (0%)	0 (0%)	0 (0%)	9 (100%)	8 (100%)	4 (80%)	0 (0%)	1.4 (95%)
Yes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (20%)	0 (0%)	0.07 (5%)
Recovery Procedure								
In-situ corneal excision	19 (100%)	13 (81%)	14 (100%)	21 (100%)	14 (100%)	6 (100%)	0 (0%)	9 (98%)
In-laboratory corneal and/or scleral excision after enucleation	0 (0%)	3 (19%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.2 (2%)
Donor Site Facility								
Hospital	16 (84%)	10 (63%)	10 (71%)	18 (86%)	9 (64%)	3 (50%)	0 (0%)	6.67 (72%)
Medical examiner	1 (5%)	2 (13%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0.47 (5%)
Funeral home or mortuary	1 (5%)	1 (6%)	3 (21%)	0 (0%)	1 (7%)	0 (0%)	0 (0%)	0.73 (8%)
Other	1 (5%)	3 (19%)	1 (7%)	2 (10%)	4 (29%)	3 (50%)	0 (0%)	1.33 (14%)
Scleral Graft Infection	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0.07**
Donor Corneal Dystrophy or Degeneration	**2**	**2**	**1**	**0**	**1**	**0**	**0**	**0.6**
Mated Cases	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Donor Corneal Refractive Surgery	**0**	**0**	**0**	**2**	**0**	**0**	**0**	**0.27**
Donor-to-host Transmission of Systemic Infection	**0**	**0**	**1**	**0**	**0**	**0**	**0**	**0.4**
Malignancy	**0**	**2**	**0**	**0**	**0**	**0**	**0**	**0.2**
Other (or Multiple)	**0**	**0**	**1**	**0**	**2**	**0**	**0**	**0.27**

YEAR	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
PGF	61	78	51	31	53	53	50	54	52	31	36	31	30	50	48	45	55	87	84
Early Regraft												14	30	34	36	35	42	52	74
No. Corneal Grafts performed in U.S.	33035	32559	32240	32106	31952	33962	39391	41652	42606	42642	46196	46,684	48,229	47,530	48,792	49,869	50,934	51,294	51,336
PGF per 10,000 grafts	18.465	23.957	15.819	9.656	16.587	15.606	12.693	12.965	12.205	7.270	7.793	6.640	6.220	10.520	9.838	9.024	10.798	16.961	16.363
Early Regraft per 10,000 grafts												2.999	6.220	7.153	7.378	7.018	8.246	10.138	14.415

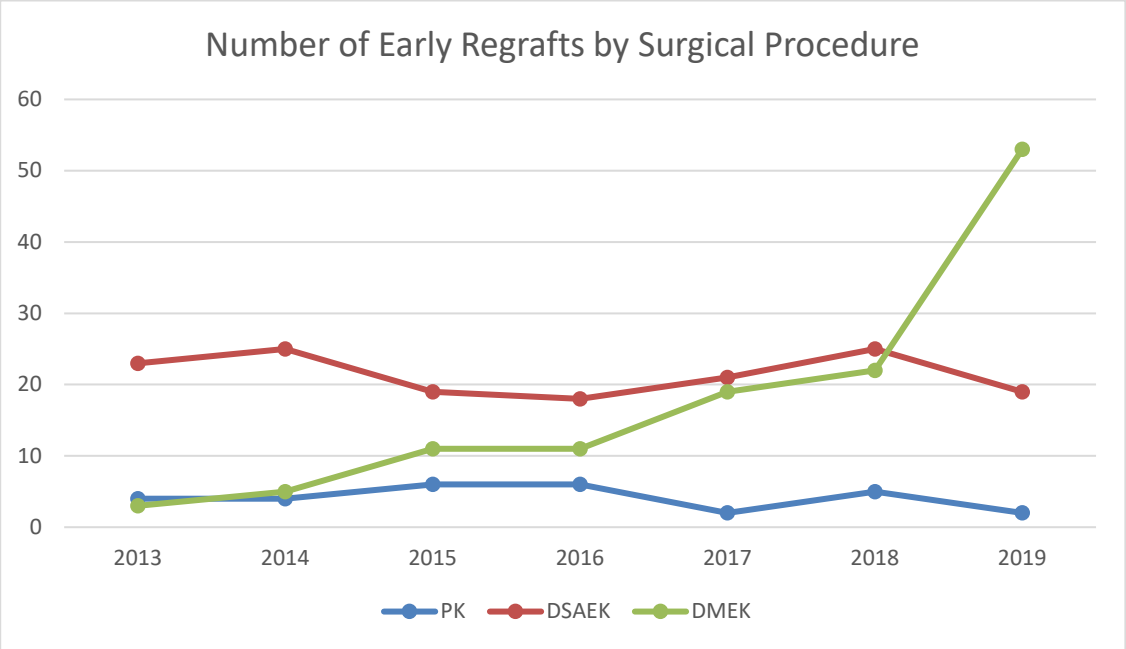


Year	2013	2014	2015	2016	2017	2018	2019
PK	9	20	22	17	12	9	11
DSAEK	19	26	20	21	33	57	41
DMEK	2	3	6	7	10	21	32
TOTAL	**30**	**50**	**48**	**45**	**55**	**87**	**84**

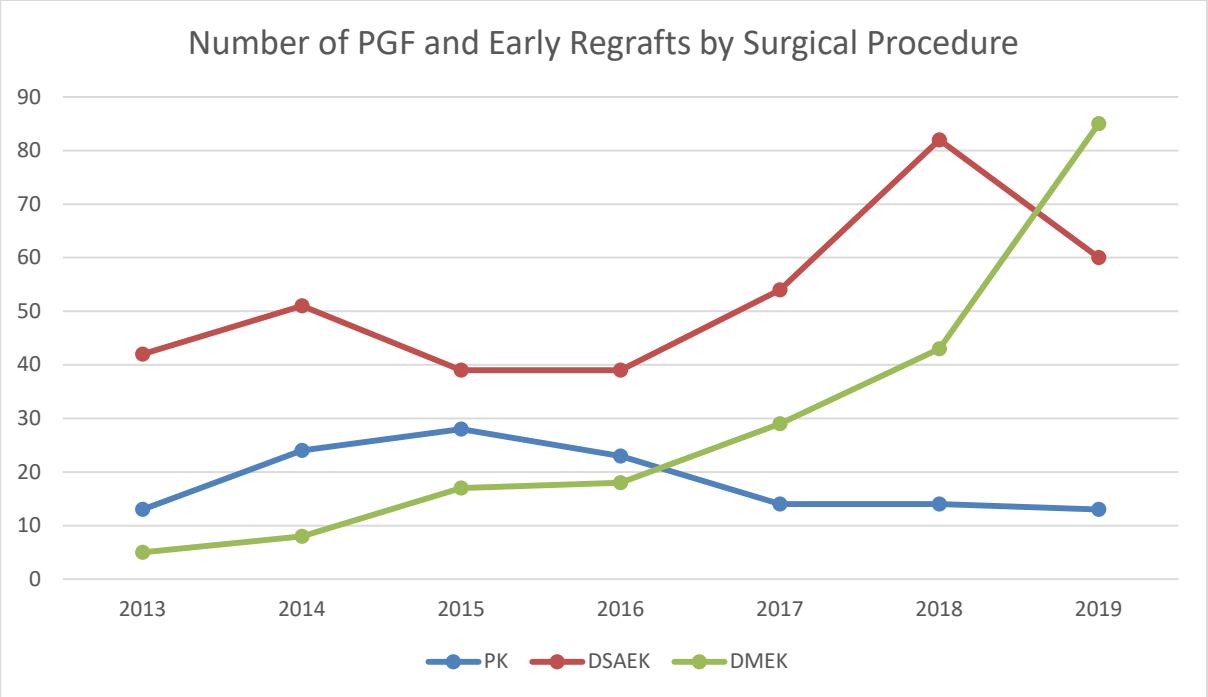


Early Regrafts

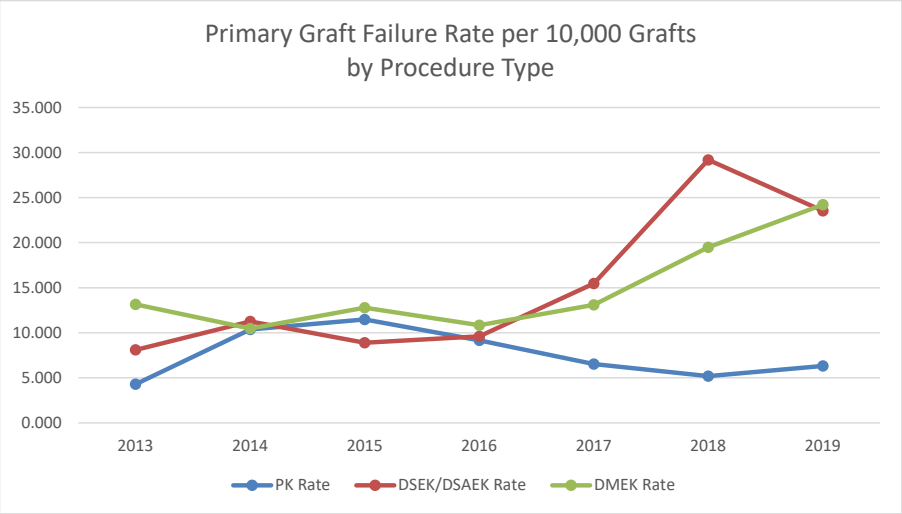
Year	2013	2014	2015	2016	2017	2018	2019
PK	4	4	6	6	2	5	2
DSAEK	23	25	19	18	21	25	19
DMEK	3	5	11	11	19	22	53
TOTAL	**30**	**34**	**36**	**35**	**42**	**52**	**74**



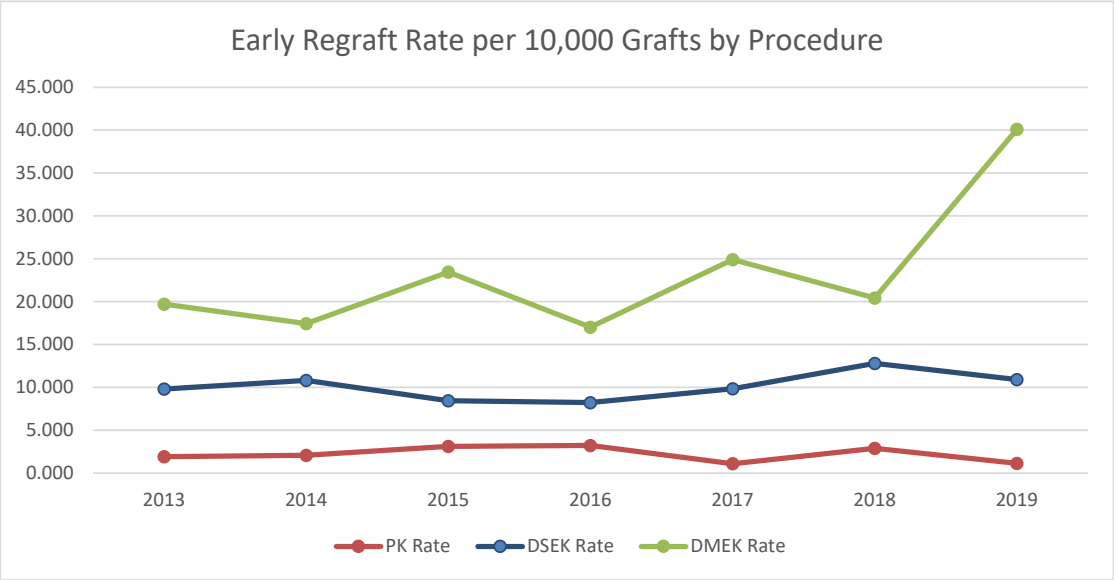
	PGF + Early Regrafts						
Year	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**
PK	13	24	28	23	14	14	13
DSAEK	42	51	39	39	54	82	60
DMEK	5	8	17	18	29	43	85
TOTAL	**60**	**84**	**84**	**80**	**97**	**139**	**158**



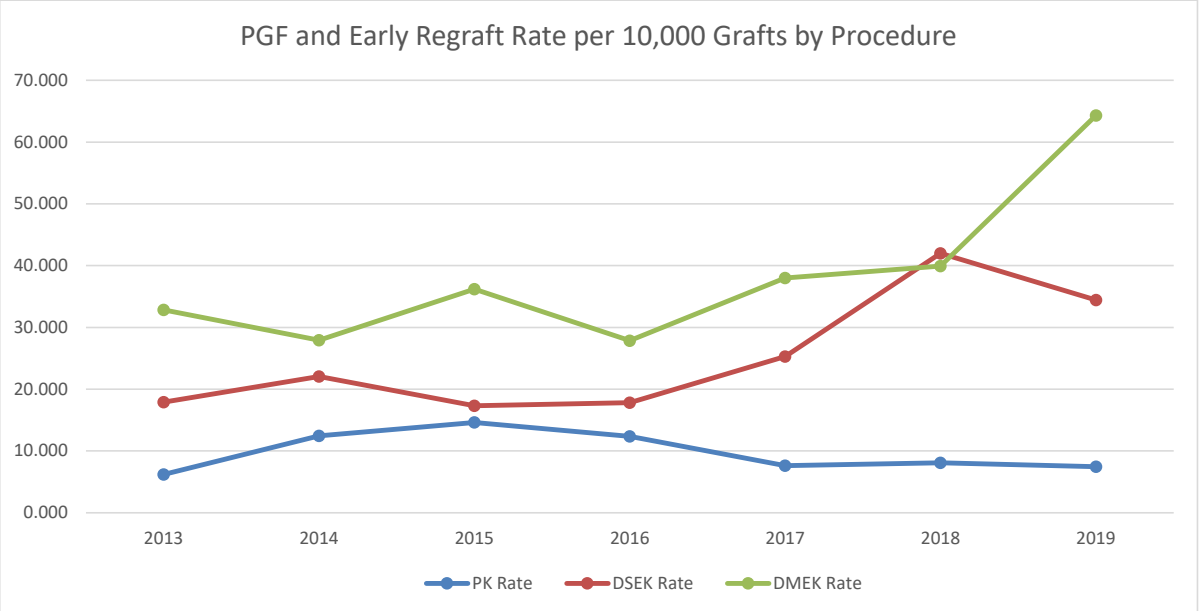
Year	2013	2014	2015	2016	2017	2018	2019
PGF following PK	9	20	22	17	12	9	11
PK Procedures	20,954	19,294	19,160	18,579	18,346	17,347	17,409
PGF rate per 10,000 PK	**4.295**	**10.366**	**11.482**	**9.150**	**6.541**	**5.188**	**6.319**
PGF following DSEK	19	26	20	21	33	57	41
DSEK Procedures	23465	23100	22514	21868	21337	19526	17,428
PGF rate per 10,000 DSEK	**8.097**	**11.255**	**8.883**	**9.603**	**15.466**	**29.192**	**23.525**
PGF following DMEK	2	3	6	7	10	21	32
DMEK Procedures	1522	2865	4694	6459	7628	10773	13,215
PGF rate per 10,000 DMEK	**13.141**	**10.471**	**12.782**	**10.838**	**13.110**	**19.493**	**24.215**



Year	2013	2014	2015	2016	2017	2018	2019
Early Regraft following PK	4	4	6	6	2	5	2
PK Procedures	20,954	19,294	19,160	18,579	18,346	17,347	17,409
Early regraft rate per 10,000 PK	**1.909**	**2.073**	**3.132**	**3.229**	**1.090**	**2.882**	**1.149**
Early Regraft following DSEK	23	25	19	18	21	25	19
DSEK Procedures	23465	23100	22514	21868	21337	19526	17,428
Early Regraft rate per 10,000 DSEK	**9.802**	**10.823**	**8.439**	**8.231**	**9.842**	**12.803**	**10.902**
Early regraft following DMEK	3	5	11	11	19	22	53
DMEK Procedures	1522	2865	4694	6459	7628	10773	13,215
Early regraft rate per 10,000 DMEK	**19.711**	**17.452**	**23.434**	**17.031**	**24.908**	**20.421**	**40.106**



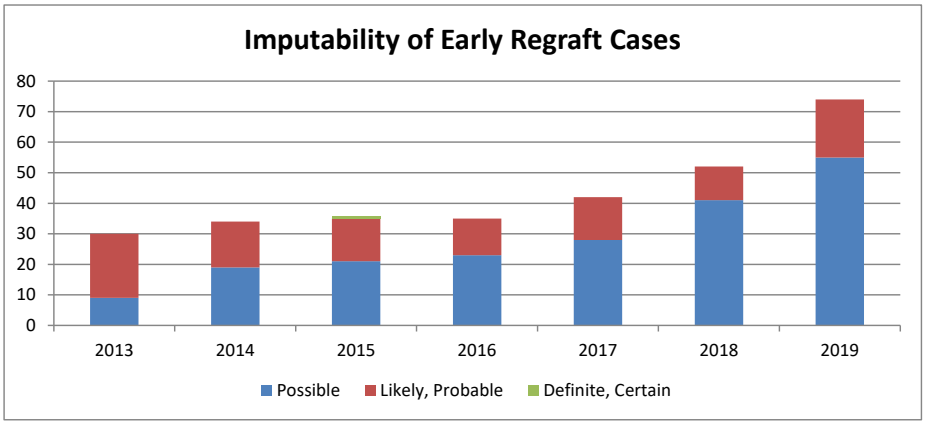
Year	2013	2014	2015	2016	2017	2018	2019
PGF + Early Regaft following PK	13	24	28	23	14	14	13
PK Procedures	20,954	19,294	19,160	18,579	18,346	17,347	17,409
PGF + Early Regraft Rate per 10,000 PK	**6.204**	**12.439**	**14.614**	**12.380**	**7.631**	**8.071**	**7.467**
PGF+ Early Regraft following DSEK	42	51	39	39	54	82	60
DSEK Procedures	23465	23100	22514	21868	21337	19526	17,428
PGF+ Early Regraft Rate per 10,000 DSEK	**17.899**	**22.078**	**17.323**	**17.834**	**25.308**	**41.995**	**34.427**
PGF+ Early Regraft following DMEK	5	8	17	18	29	43	85
DMEK Procedures	1522	2865	4694	6459	7628	10773	13,215
PGF+ Early Regraft Rate per 10,000 DMEK	**32.852**	**27.923**	**36.216**	**27.868**	**38.018**	**39.915**	**64.321**

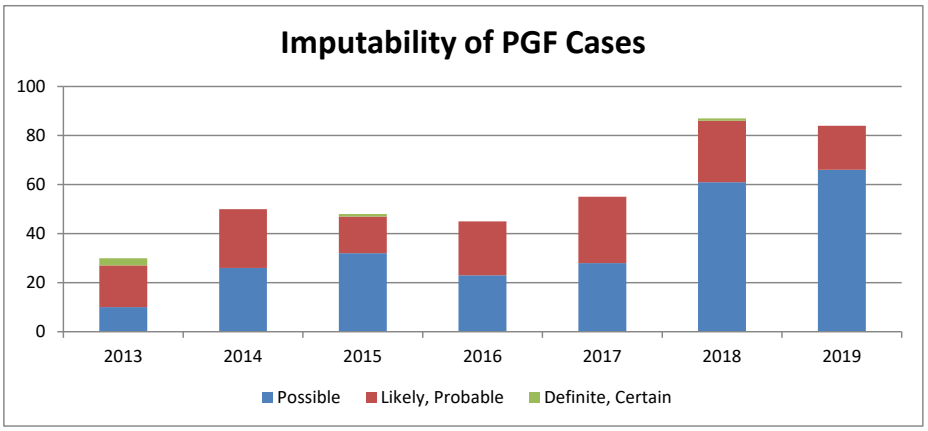


Imputability of Primary Graft Failure and Early Regraft

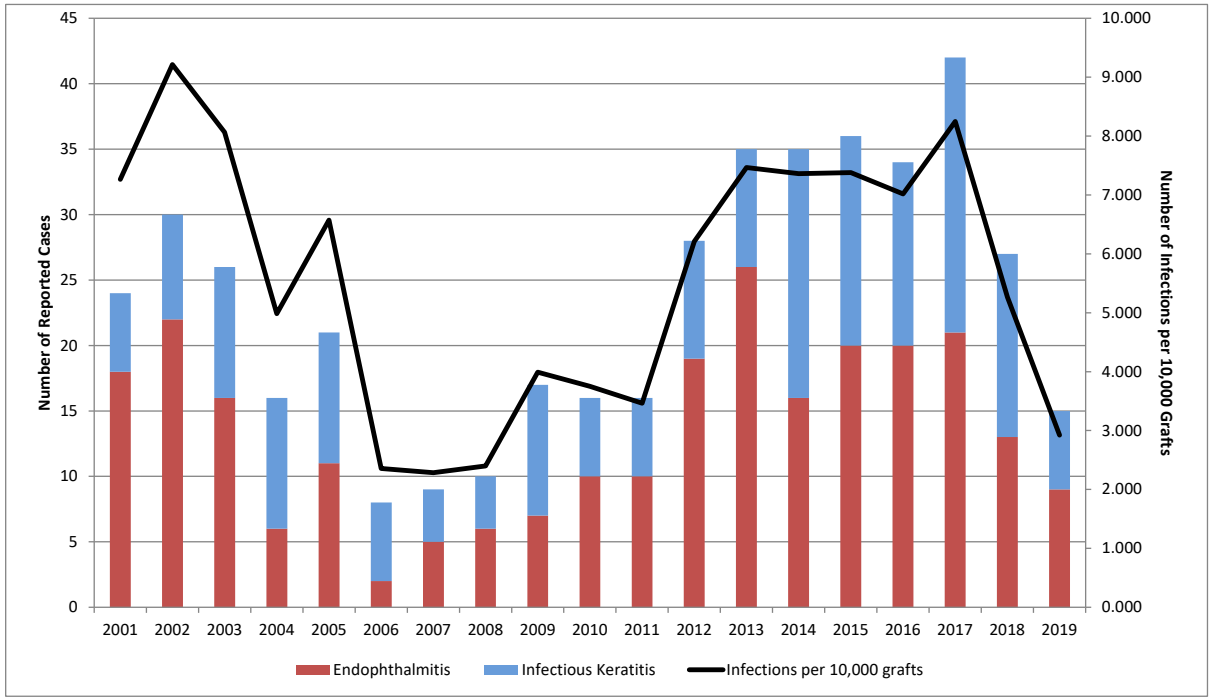
Early Regraft	2013	2014	2015	2016	2017	2018	2019
Possible	9	19	21	23	28	41	55
Likely, Probable	21	15	14	12	14	11	19
Definite, Certain	0	0	1	0	0	0	0
Total Reported	**30**	**34**	**36**	**35**	**42**	**52**	**74**

PGF	2013	2014	2015	2016	2017	2018	2019
Possible	10	26	32	23	28	61	66
Likely, Probable	17	24	15	22	27	25	18
Definite, Certain	3	0	1	0	0	1	0
Total Reported	**30**	**50**	**48**	**45**	**55**	**87**	**84**

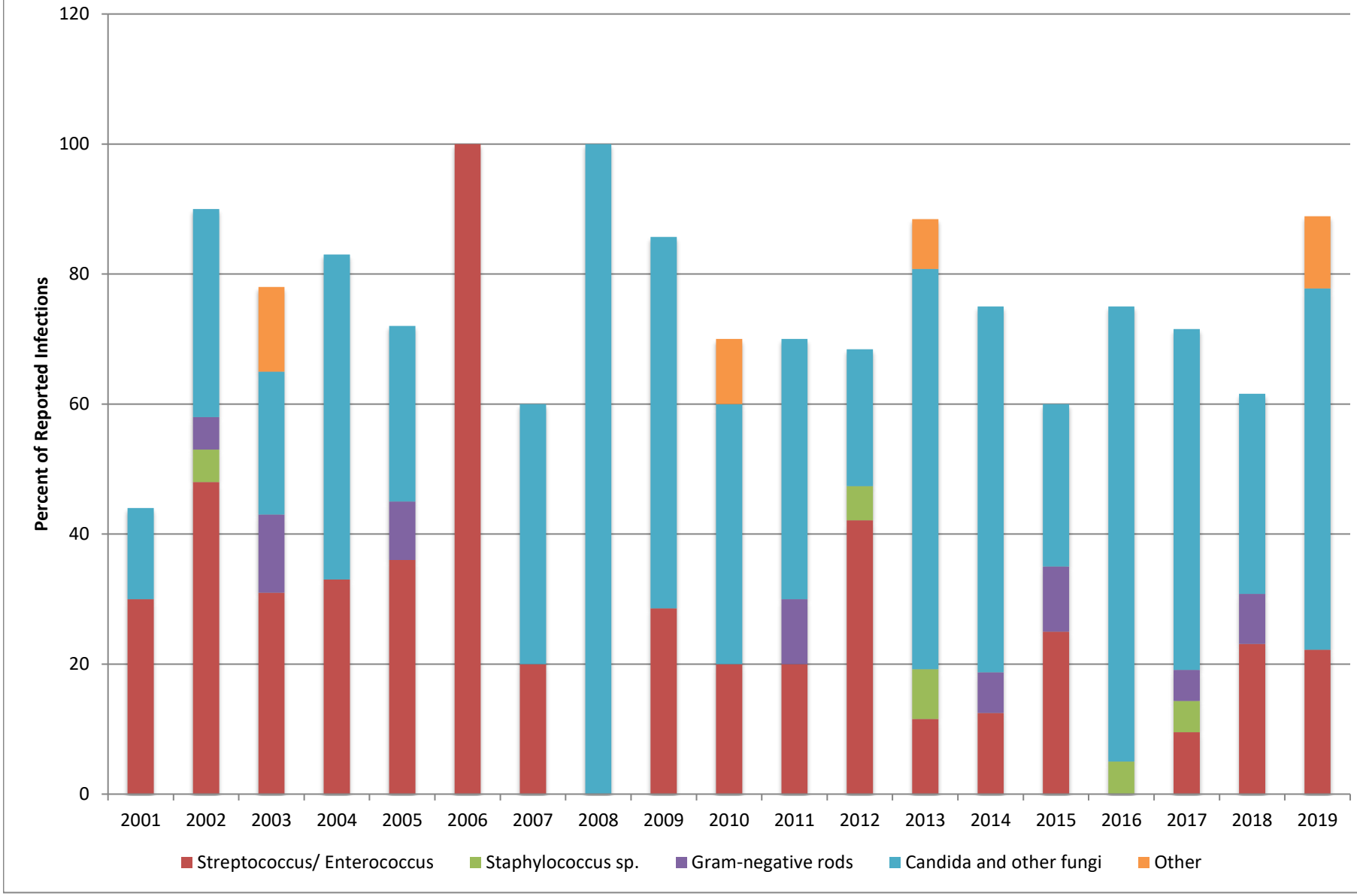




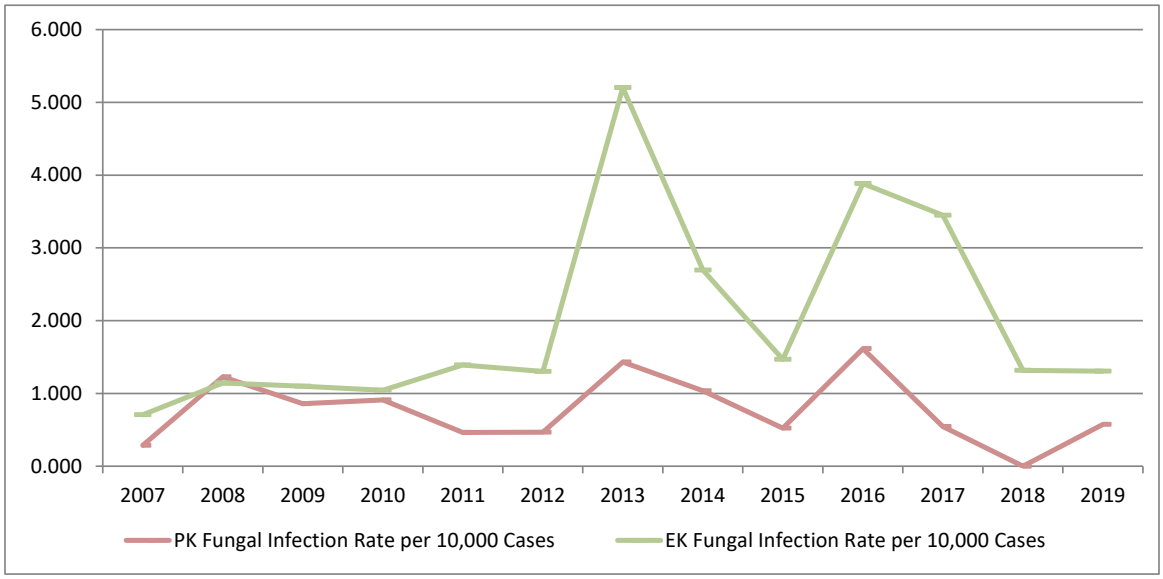
YEAR	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Endophthalm	18	22	16	6	11	2	5	6	7	10	10	19	26	16	20	20	21	13	9
Infectious Ker	6	8	10	10	10	6	4	4	10	6	6	9	9	19	16	14	21	14	6
Total Infectio	24	30	26	16	21	8	9	10	17	16	16	29	36	35	36	35	42	27	15
No. Corneal Grafts	33035	32559	32240	32106	31952	33962	39391	41652	42606	42642	46196	46,684	48,229	47,530	48792	49,869	50,934	51,294	51,336
Infections per	7.265	9.214	8.065	4.983	6.572	2.356	2.285	2.401	3.990	3.752	3.464	6.212	7.464	7.364	7.378	7.018	8.246	5.264	2.922



Endophthalmitis Pathogens



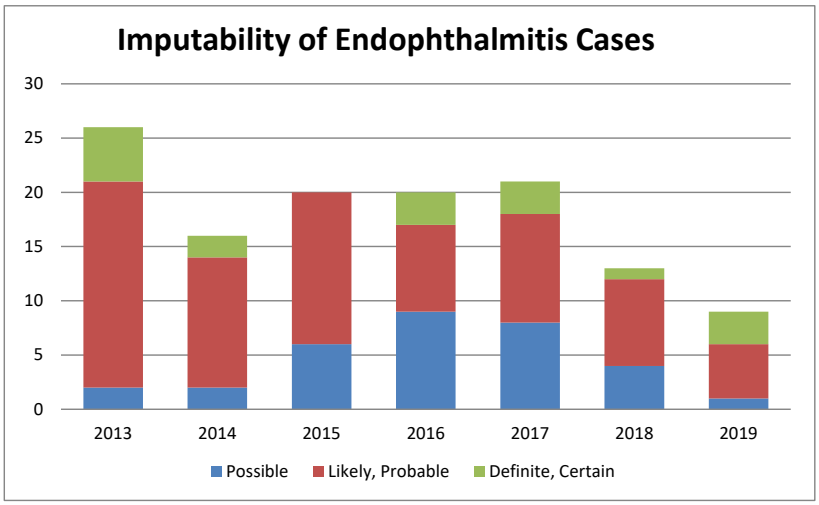
Year	Total Endophthalmitis Cases	Fungal Endophthalmitis Cases	PK Fungal Cases	EK Fungal Cases	Total Domestic PK Procedures	Total Domestic EK Procedures	PK Fungal Infection Rate per 10,000 Cases	EK Fungal Infection Rate per 10,000 Cases
2007	5	2	1	1	34806	14159	0.287	0.706
2008	6	6	4	2	32524	17468	1.230	1.145
2009	7	4	2	2	23269	18221	0.860	1.098
2010	10	4	2	2	21970	19159	0.910	1.044
2011	10	4	1	3	21620	21555	0.463	1.392
2012	19	4	1	3	21422	23049	0.467	1.302
2013	26	16	3	13	20954	24987	1.432	5.203
2014	16	9	2	7	19294	25965	1.037	2.696
2015	20	5	1	4	19160	27208	0.522	1.470
2016	20	14	3	11	18579	28327	1.615	3.883
2017	21	11	1	10	18346	28993	0.545	3.449
2018	13	4	0	4	17347	30336	0.000	1.319
2019	9	5	1	4	17409	30,650	0.574	1.305

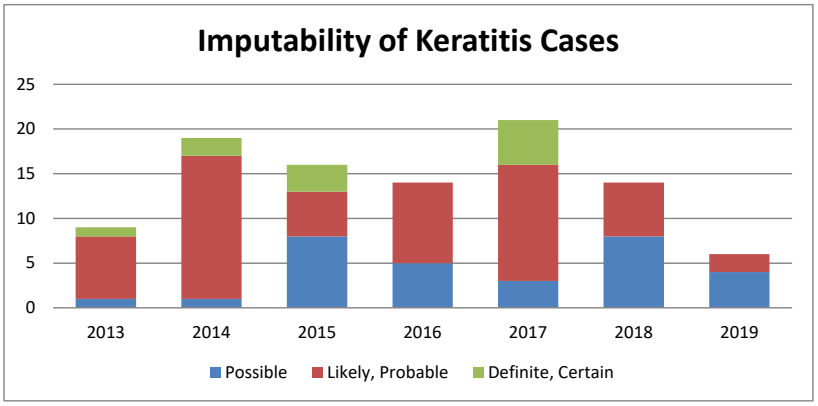


Imputability of Endophthalmitis and Infectious Keratitis

Endophthalmitis	2013	2014	2015	2016	2017	2018	2019
Possible	2	2	6	9	8	4	1
Likely, Probable	19	12	14	8	10	8	5
Definite, Certain	5	2	0	3	3	1	3
Total Reported	**26**	**16**	**20**	**20**	**21**	**13**	**9**

Keratitis	2013	2014	2015	2016	2017	2018	2019
Possible	1	1	8	5	3	8	4
Likely, Probable	7	16	5	9	13	6	2
Definite, Certain	1	2	3	0	5	0	0
Total Reported	**9**	**19**	**16**	**14**	**21**	**14**	**6**





YEAR	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Primary Graft Failure	61	78	51	31	53	53	50	54	52	31	36	31	30	50	48	45	55	87	84
Early Regraft												14	30	34	36	35	42	52	74
Endophthalmitis	18	22	16	6	11	2	5	6	7	10	10	19	26	16	20	20	21	13	9
Infectious Keratitis	6	8	10	10	10	6	4	4	10	6	6	9	9	19	16	14	21	14	6
Total Infections*	24	30	26	16	21	8	9	10	17	16	16	29	36	35	36	35	42	27	15
No. Corneal Grafts performed in U.S.	33035	32559	32240	32106	31952	33962	39391	41652	42606	42642	46196	46,684	48,229	47,530	48,792	49,869	50,934	51,294	51,336
Percent Infections	0.073	0.092	0.081	0.050	0.066	0.024	0.023	0.024	0.040	0.038	0.035	0.062	0.075	0.074	0.074	0.070	0.082	0.053	0.029
Infections per 10,000 grafts	7.265	9.214	8.064	4.983	6.572	2.356	2.285	2.401	3.990	3.752	3.464	6.212	7.464	7.364	7.378	7.018	8.246	5.264	2.922
PGF per 10,000 grafts	18.465	23.957	15.819	9.656	16.587	15.606	12.693	12.965	12.205	7.270	7.793	6.640	6.220	10.520	9.838	9.024	10.798	16.961	16.363
Early Regraft per 10,000 grafts												2.999	6.220	7.153	7.378	7.018	8.246	10.138	14.415

Endophthalmitis Pathogens	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Streptococcus/ Enterococcus	30	48	31	33	36	100	20	0	28.57	20	20	42.11	11.54	12.5	25	0	9.52	23.1	22.2
Staphylococcus sp.	0	5	0	0	0	0	0	0	0	0	0	5.26	7.69	0	0	5	4.8	0	0
Gram-negative rods	0	5	12	0	9	0	0	0	0	0	10	0	0	6.25	10	0	4.8	7.7	0
Candida and other fungi	14	32	22	50	27	0	40	100	57.14	40	40	21.05	61.54	56.25	25	70	52.4	30.8	55.6
Other	0	0	13	0	0	0	0	0	0	10	0	0	7.69	0	0	0	0	0	11.1
No growth	28	5	22	0	9	0	0	0	0	20	10	15.79	7.69	12.50	20	10	0	0	0
Not done	28	5	0	17	18	0	40	0	0	10	20	21.05	3.85	12.50	20	15	23.8	38.5	11.1

	2001	2002	2003	2004	2005	2006	2006	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Fungal	14	32	22	50	27	0	40	100	57.14	40	40	21.05	61.54	56.25	25	70	52.4	30.8	55.6
Bacterial	30	58	56	33	45	100	20	0	28.57	30	30	47.37	26.92	18.75	35	5	23.8	30.8	33.3

* Note - Includes 1 Iritis case in 2012; 1 scleral graft infection in 2013; and 1 anterior chamber reaction in 2016

POLICY & POSITION RESEARCH SUBCOMMITTEE

Eric Meinecke

From: Jennifer DeMatteo <Jennifer@restoresight.org>
Sent: Tuesday, November 26, 2019 12:24 PM
To: Aldave, Anthony
Subject: FW: Lyme Disease
Signed By: jennifer@restoresight.org

Dear Tony.

We received the email below from the Medical Director, Eye Bank Division, New Brunswick Organ and Tissue Program regarding Lyme Disease.

The Medical Advisory Board chairs would like the Policy and Position Review Subcommittee (PPRS) to review the literature about Lyme Disease and make any recommendations for the next MAB meeting. Or if they feel based on their assessment that we should bring it to MAB sooner.
Lyme disease can cause interstitial keratitis and anterior uveitis. Is not clear that there is actually active micro organisms in the Eye tissue in these diseases, but examining the data in the literature would be helpful. This bacteria is biologically similar to the one that causes syphilis.

The PPRS is relatively small, so you may wish to add additional people to your group. Currently the PPRS consists of:

Sort Name	Organization Name	E-Mail Address
Aldave Anthony	Doheny Eye & Tissue Transplant Bank	Aldave@jsei.ucla.edu
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EYE BANK ASSOCIATION OF AMERICA

Jennifer DeMatteo, MCM, CIC
Director of Regulations & Standards
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From: Christopher Seamone <cdseamone@gmail.com>
Sent: Sunday, November 24, 2019 6:48 AM
To: Jennifer DeMatteo <Jennifer@restoresight.org>
Cc: Christopher Seamone <cdseamone@gmail.com>
Subject: Lyme Disease

Dear Jennifer:

The CDC states that in the USA each year approximately 30,000 cases of Lyme disease are reported by state health departments and the District of Columbia. It has been claimed that few (< 10%) Lyme disease cases are actually reported. Thus, the CDC suggests that the number of people diagnosed with Lyme disease each year in the United States is around 300,000. These infections occur mostly in the northeastern US, but not exclusively.

In Canada, the range of Lyme disease is expanding, and it is currently endemic in areas of six provinces: British Columbia, Manitoba, Ontario, Quebec, New Brunswick, and Nova Scotia. Reported numbers of cases increased from 144 cases in 2009 to 2025 in 2017. However, again the number of cases reported underestimates the actual number of cases.

This trend in both countries will have an increasing impact on the corneal donor pool. As an eye bank medical director, I am intermittently asked to decide on suitability of donors with a recent or past history of a tick bite, or with a history of Lyme Disease.

I was wondering whether the EBAA Medical Advisory Board had developed a policy concerning potential donors with a history of a tick bite or Lyme Disease?

Thank you for looking into this matter for me.

C. D. Seamone, MD, FRCSC

Medical Director, Eye Bank Division, New Brunswick Organ and Tissue Program

Summary Report on Lyme Disease and Donor Tissue
Report of the Policy and Position Research Subcommittee

Anthony J. Aldave, MD – Chair
Paul J. Dubord, MD – Member
Adam Kaufman, MD – Member
Kristin Mathes, MA, MS – Member
Brian Philippy, CEBT – Ad hoc member

Purpose
To determine the suitability of utilizing corneas from donors with a recent or past history of Lyme Disease (LD).

Background
Although 30,000 cases of LD are reported annually, the CDC estimates that there are approximately 300,000 cases of LD in the US each year.(1-3) Infections occur predominantly in the northeastern US, although the numbers of LD cases reported elsewhere in the US and Canada are increasing.(4, 5) With this comes an increased interest and significance in determining whether LD can be transmitted via a donor cornea to the recipient.

Lyme Disease and the Cornea
The incidence and prevalence of ocular LD are not well-defined in the literature. A keratitis may develop weeks to months, or even years, following the initial infection with LD.(6-9) The typical corneal manifestation is a nummular keratitis, although corneal vascularization, edema and scarring have been reported. Other less commonly reported corneal manifestations include peripheral ulcerative keratitis, thought to be due to a secondary inflammatory response,(10, 11) and a crystalline keratopathy, confirmed by polymerase chain reaction (PCR) and electron microscopy to be due to the presence of *Borrelia garinii* in the cornea.(12) This remains the only report of the presence of a *Borrelia* species in the cornea; there are no reports of whether *Borrelia* is present in the tear film.

Lyme Disease and Corneal Transplantation
To date, there are only two reports of corneal transplantation using donor tissue from a patient with active LD at the time of death.(13, 14) Post-mortem studies of the first donor revealed positive Lyme IgM titers, reactive IgG titers, and a positive PCR, indicating active Borreliosis at the time of death. Neither of the two corneal transplant recipients developed symptoms of LD and neither seroconverted (Lyme IgM and IgG titers were negative two months following confirmation of active disease in the donor). Nevertheless, they completed a 4-6-week course of doxycycline. Subsequent follow-up findings have not been reported. Post-mortem studies of the second donor revealed pancarditis with spirochetes in the myocardium, subsequently confirmed to be *Borrelia burgdorferi*. The corneal transplant recipient died shortly after surgery of unrelated causes; neither tissue nor serum was available for analysis.

Conclusions
The consequences of transplanting a donor cornea from an individual with either active or inactive LD at the time of death are not well understood. In the only reported case of corneal transplantation using donor tissue from an individual with active LD at the time of death, the two recipients remained asymptomatic and did not seroconvert. However, spirochetes have been

demonstrated to be present in the eyelids and cornea of affected individuals,(11, 12, 15) and are known to establish persistent infections in infected individuals, including those treated with antimicrobial therapy.(16) Therefore, the EBAA Policy and Position Review Subcommittee recommends revising the EBAA Medical Standards section D1.110 EBAA Contraindications to Transplant to include:

- Lyme disease (known or suspected; active or chronic; including post-treatment Lyme Disease Syndrome (PTLDS)

As 90% of individuals with LD develop a pathognomonic erythema migrans rash, and as the Uniform DRAI contains a question regarding a rash (6f), a UDRAI Addendum is not deemed necessary.

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Report to the EBAA Medical Advisory Board
Donor Prep Subcommittee

Subcommittee Members: William Buras, Jennifer DeMatteo, Dr. Sean Edelstein, Dr. Sadeer Hannush, Kyle Mavin, Eric Meinecke (Chair), Dr. Shahzad Mian, Brian Philippy, Edwin Roberts, Ingrid Schunder, Dr. Mike Straiko, Michael Titus

At the October 10, 2019 EBAA Medical Advisory Board meeting, medical standard E1.100 was revised as follows:

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*

MAB chair, Dr. Jennifer Li, requested that a subcommittee be created to further review data on povidone-iodine prep of donor corneal tissue and report back at the next Medical Advisory Board meeting with potential further recommendations to the medical standards.

To accomplish our task, the subcommittee chose to approach this important topic in the following manner:

1. Review published literature
2. Survey of several eye bank medical directors
3. Examine specific adverse reactions related to fungal infections reported to EBAA
4. Gather information from eye banks that have done studies and implemented changes
5. Consult with infectious disease professionals
6. Re-survey eye banks on donor prep procedures

Based on the data we collected, reviewed, and discussed, our subcommittee believes that further guidance to eye banks is necessary on the use of povidone-iodine. We are recommending that E1.100 be revised as follows:

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

A 5% povidone-iodine (PI) solution shall contact the entire surface of any ocular tissue intended for transplantation at least twice between the time of the donor's death and tissue preservation (e.g. corneoscleral disc in ~~Optisol-GS~~ corneal preservation solution or whole eye in moist chamber). Regardless of how PI is administered (e.g. # of drops, a specific mL, soak, etc.), the amount must be sufficient to completely cover the corneal surface, conjunctiva, lids, and lashes. The contact time for each application should not be less than 2 minutes and not exceed 5 minutes. ~~Excess~~ Povidone-iodine solution should be irrigated from the ocular surface with a sterile eye wash/irrigating solution 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. All supplies and reagents used during the recovery and preservation process should be carefully reviewed and approved prior to use.

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:

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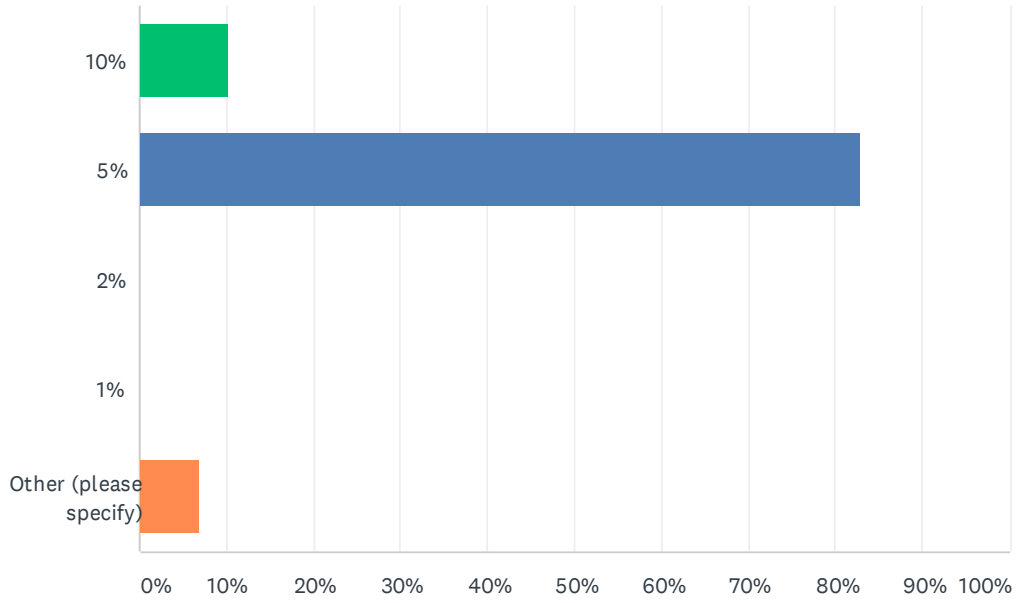
- *Active viral encephalitis or encephalitis of unknown origin*
- *Creutzfeldt-Jakob Disease (CJD)*
- *Rabies*

Our subcommittee believes the further changes to E1.100 described above provide additional guidance while also continuing to allow some flexibility to medical directors to adopt a povidone-iodine prep regime that is appropriate for their eye bank.

We would like to emphasize the importance of a high-quality donor tissue preparation prior to recovery and preservation. Eye banks should review their procedures and ensure technicians not only can follow the procedure as described in the procedure manual, but their technique be evaluated at least once annually. In addition to the ocular surface, the donor's periocular area should also be cleaned and prepped. A donor's eye lashes can also be a source of contamination so we recommend excess povidone-iodine solution should also be applied to the donor's eye lashes.

Q2 What is the concentration of povidone-iodine (PI) used during recovery?

Answered: 58 Skipped: 0

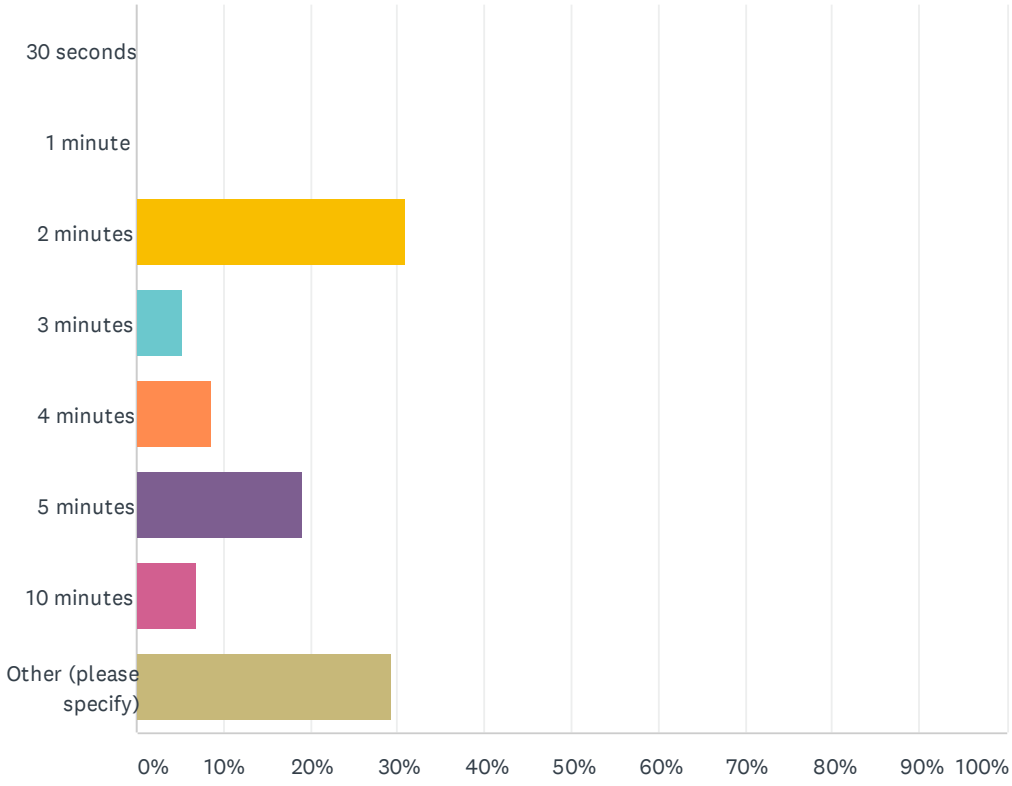


ANSWER CHOICES	RESPONSES	
10%	10.34%	6
5%	82.76%	48
2%	0.00%	0
1%	0.00%	0
Other (please specify)	6.90%	4
TOTAL		58

#	OTHER (PLEASE SPECIFY)	DATE
1	5% in the eye, 10% on surrounding skin	5/20/2020 10:44 AM
2	We are a distribution eye bank only no recoveries of donors	5/18/2020 7:07 PM
3	5% in the eye, 10% skin prep around the eye	5/13/2020 2:43 PM
4	We use 5% directly on the ocular surface and 10% around the perioribital area	5/13/2020 6:57 AM

Q3 What is the duration of PI exposure required by your procedures?

Answered: 58 Skipped: 0



ANSWER CHOICES	RESPONSES	
30 seconds	0.00%	0
1 minute	0.00%	0
2 minutes	31.03%	18
3 minutes	5.17%	3
4 minutes	8.62%	5
5 minutes	18.97%	11
10 minutes	6.90%	4
Other (please specify)	29.31%	17
TOTAL		58

#	OTHER (PLEASE SPECIFY)	DATE
1	6 minutes	5/21/2020 2:17 PM
2	5 minutes per instillation, total of 10 minutes	5/20/2020 10:44 AM
3	We do 2 ocular PI preps; 5 minutes exposure time for each prep and 5 minutes between the 2 prep times; We also do a PI prep on the outside of the eye area	5/19/2020 3:56 PM
4	90 seconds	5/19/2020 9:44 AM
5	n/a	5/18/2020 7:07 PM
6	3-5 minutes, then rinse and wait 5 minutes, then another 3-5 minutes.	5/18/2020 5:31 PM
7	Two 2 minute instillations with BSS rinses after each	5/18/2020 11:57 AM
8	8 min	5/18/2020 11:07 AM
9	6 minutes: 3 min exposure,rinse, wait 3, another 3min exposure, then rinse	5/18/2020 10:53 AM
10	PI used on the outside of the eye- remains on the outter exposed layers until recovery complete	5/13/2020 2:51 PM
11	5 mins, rinse, wait 5 mins, second 5 mins	5/13/2020 9:38 AM
12	Minimum of 4 minutes - maximum of 6 minutes	5/13/2020 9:23 AM
13	2 minutes x 2	5/13/2020 6:57 AM
14	3-5 minutes, done twice for a total of 6-10 minutes	5/13/2020 6:50 AM
15	as of 1/1/2020 MS requirements, 2x3 minute preps, prior 1x3 minute prep.	5/12/2020 6:15 PM
16	6-10 minutes total	5/12/2020 5:23 PM
17	Our bank does a 5 minute exposure on the first application, followed by a complete saline rinse and immediate reapplication of the Betadine for an additional 2 minutes of exposure.	5/12/2020 5:02 PM

Q4 What is the volume of PI used during recovery?

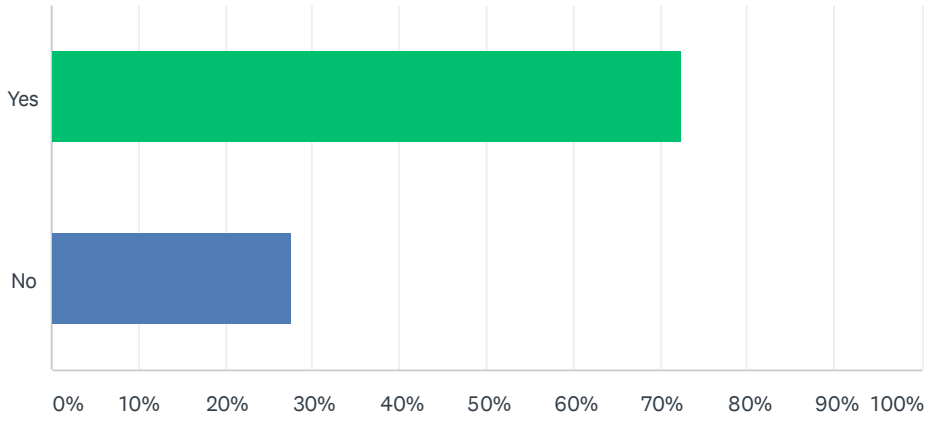
Answered: 58 Skipped: 0

#	RESPONSES	DATE
1	"two to four drops (enough to cover) Betadine 5% on each ocular surface"	5/28/2020 2:07 PM
2	(6 to 8 drops each eye) x 1 soak for 5 minutes; rinse; then (6 to 8 drops each eye) x 2nd soak for 5 minutes; rinse = about 2 mls total	5/27/2020 11:01 AM
3	0.75 cc	5/26/2020 5:17 PM
4	Prep 1-Sufficient gtts to cover ocular surface Prep 2-1.5 ml per eye	5/21/2020 9:36 PM
5	~4 oz in total. 6cc total of PI are used in each eye for the flush decontamination. (Remaining amount is used in lid/lash prep and face prep)	5/21/2020 2:17 PM
6	6ml	5/21/2020 10:25 AM
7	6 drops on each eye two times	5/20/2020 7:45 PM
8	Enough to adequately cover the entire cornea. Approximately 10 drops per cornea	5/20/2020 2:23 PM
9	We use a 5mL dropper provided by Stephens Instruments. between 5-10 drops of PI is dispensed twice with an eye wash in between. A total of 10-20 drops ~ 1-ish mL.	5/20/2020 11:14 AM
10	4 Betadine swabsticks 5 ml bottle of 5%--5-10 drops per instillation	5/20/2020 10:44 AM
11	30 ml	5/19/2020 3:56 PM
12	Minimum of 5 drops, need to ensure that the ocular surface is completely covered in PI solution.	5/19/2020 2:12 PM
13	3ml drops instilled as well as eye area swabbed with povidone iodine swab sticks. We also do a 5 minute soak of the whole globe prior to corneal excision with 10% povidone iodine diluted to 5% (50/50 mix of povidone iodine and NS.)	5/19/2020 9:46 AM
14	2.5mL	5/19/2020 9:44 AM
15	.5 oz	5/19/2020 9:27 AM
16	n/a	5/18/2020 7:07 PM
17	15 drops	5/18/2020 5:53 PM
18	We use 3mL bottle of PI and pour half (approx. 1.5mL) on each eye. Then we use a second bottle for the second application.	5/18/2020 5:31 PM
19	6 drops	5/18/2020 1:23 PM
20	30ml	5/18/2020 1:16 PM
21	1 FLuid oz plus	5/18/2020 1:04 PM
22	10-15 drops per instillation	5/18/2020 11:57 AM
23	3 cc, then another 3 cc per eye	5/18/2020 11:10 AM
24	30cc	5/18/2020 11:07 AM
25	enough to completely cover cornea, conj, and back of lids for each application	5/18/2020 10:53 AM
26	enough to cover surface and sulcus	5/18/2020 10:30 AM
27	Enough to cover the ocular surface as required by EBAA Medical Standards.	5/18/2020 10:17 AM
28	25 drops per eye each time	5/15/2020 5:45 PM
29	We prep the skin around the eye with povidone and then we apply povidone drops on the eyes surface. 2 drops superior, inferior and 2 drops central cornea, let sit for 3 minutes, Rinse and do again	5/15/2020 7:22 AM
30	Sufficient amount about 4-6 drops, enough to cover the exposed cornea and sclera.	5/14/2020 8:03 PM
31	Sufficient drops to cover the cornea, conjunctiva and palpebral fissure.	5/14/2020 4:22 PM
32	minimum of 2ml	5/14/2020 12:10 PM

33	3ml	5/13/2020 7:59 PM
34	copious	5/13/2020 3:56 PM
35	3 swab sticks per eye	5/13/2020 2:51 PM
36	10 drops	5/13/2020 2:43 PM
37	3 ml .75 ml per eye x 2	5/13/2020 2:18 PM
38	3ml	5/13/2020 1:11 PM
39	10 To 15 ML	5/13/2020 12:59 PM
40	25 drops x 2 cycles	5/13/2020 12:46 PM
41	Irrigate copiously with 5% Betadine Sterile Ophthalmic Solution (minimum 10 drops). Wait two minutes, then flush with the remaining sterile balanced saline solution. Perform this complete procedure twice.	5/13/2020 12:31 PM
42	enough to cover the cornea (aprox. 6-8 drops)	5/13/2020 12:25 PM
43	2.2 ml	5/13/2020 12:25 PM
44	3-5 drops per eye	5/13/2020 11:09 AM
45	Minimum 25 drops of 5% Betadine solution into each eye, covering the conjunctiva and cornea completely. Apply additional Betadine solution on the donor's eye lashes and lid margins.	5/13/2020 9:38 AM
46	10 ml (5 ml per PI application)	5/13/2020 9:23 AM
47	1.5 mls per eye of 5% PI	5/13/2020 6:57 AM
48	25 drops per eye per application, for a total of 50 drops per eye	5/13/2020 6:50 AM
49	2.5 mL per eye, used twice. Total volume equals 10 mL	5/12/2020 7:21 PM
50	15 drops with each of the 2 preps.	5/12/2020 6:15 PM
51	15-20 drops	5/12/2020 6:10 PM
52	For in-situ 1.5 ml X 2 wash for each eye per wash (3ml total per eye) Whole globe 1.5 ml per eye X 1 wash. Second wash done at eye bank during processing for whole globe.	5/12/2020 5:46 PM
53	3 drops	5/12/2020 5:44 PM
54	minimum of 5 mL per eye on each application	5/12/2020 5:43 PM
55	15 ml followed by 15 ml	5/12/2020 5:32 PM
56	3-5 drops in each eye; wait 3-5 minutes; rinse then repeat.	5/12/2020 5:23 PM
57	Not specified by volume but enough to completely cover the ocular surface and surroundings tissues.	5/12/2020 5:17 PM
58	However much is required to completely cover the cornea and conjunctiva.	5/12/2020 5:02 PM

Q5 Since the 2018 Povidone Iodine Survey, has your eye bank changed your policy on concentration, duration, or volume?

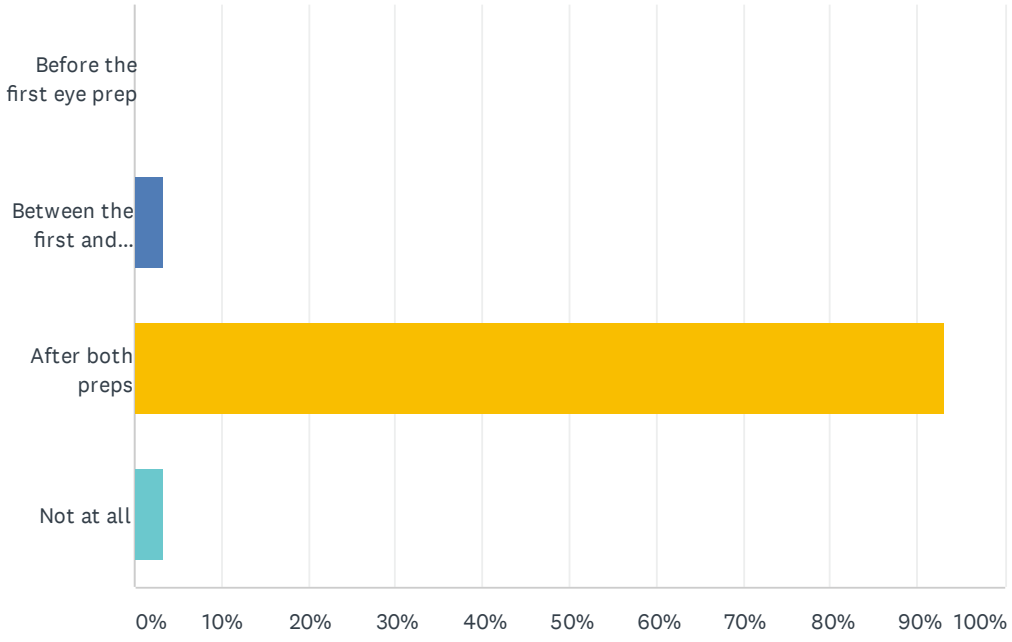
Answered: 58 Skipped: 0



ANSWER CHOICES	RESPONSES	
Yes	72.41%	42
No	27.59%	16
TOTAL		58

Q6 When do you perform conjunctiva removal?

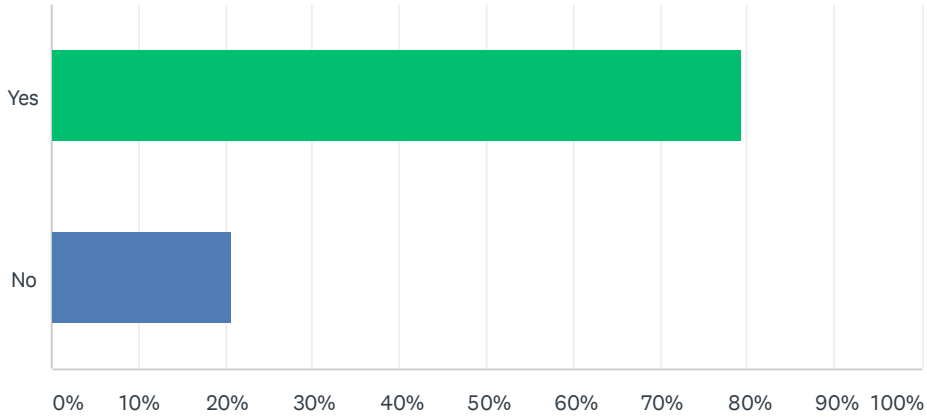
Answered: 58 Skipped: 0



ANSWER CHOICES	RESPONSES	
Before the first eye prep	0.00%	0
Between the first and second eye prep	3.45%	2
After both preps	93.10%	54
Not at all	3.45%	2
TOTAL		58

Q7 Between preps, are the donor's lids allowed to close?

Answered: 58 Skipped: 0



ANSWER CHOICES	RESPONSES	
Yes	79.31%	46
No	20.69%	12
TOTAL		58

Q8 Please list the PI product that you are using to decontaminate the ocular surface during recovery. Be as descriptive as possible: Include manufacturer name, product name, unit size, and product number, if available.

Answered: 58 Skipped: 0

#	RESPONSES	DATE
1	Krolman, Betadine 5%, 3ml, K55-57014-01	5/28/2020 2:07 PM
2	5% Betadine 5mL Krolman (droppers) K55-57014-01	5/27/2020 11:01 AM
3	Aplicare 10% Povidone-Iodine solution 2oz bottle, NDC 52380-2801-8	5/26/2020 5:17 PM
4	Prep 1-PV Eyeodine, Stephens Instruments, 5 ml Prep 2- Povidone Iodine Prep Solution 10%, MDS093940, Medline, 2 oz,	5/21/2020 9:36 PM
5	Medline PVP Prep solution (Topical antiseptic Povidone-Iodine 10%) 20z, REF MDS093940 Diluted 1:1 with Medline Sterile .9% Normal Saline, USP 100ml , 3.4oz, Reorder No. RDI30296	5/21/2020 2:17 PM
6	Krolman Betadine 5%	5/21/2020 10:25 AM
7	Betadine Solution (10% Povidine - Iodine) 1/2 fl oz (14.8 ml) Avrio Health L.P.	5/20/2020 7:45 PM
8	Alcon; Betadine 5%; 1 fluid ounce (30ml); NDC 0065-0411-30	5/20/2020 2:23 PM
9	Stephens Instruments- PV Eyeodine 5%, 5mL dropper	5/20/2020 11:14 AM
10	in a kit made up by Stephens 5% has Stephens as manufacturer 5 ml 10% swabs by Aplicare in Meriden, CT reorder # S-3111	5/20/2020 10:44 AM
11	Alcon Betadine 5% Sterile Ophthalmic Solution (Povidone Iodine Ophthalmic Solution) single use; 30ml; Product number: 0065041130	5/19/2020 3:56 PM
12	Stephens Instruments, PV Eyeodine 5%, 5ml dropper, in pre-made kits by Medline	5/19/2020 2:12 PM
13	Gtts: Krolman Betadine 5% 3ml swab sticks: PDI Povidone-iodine swabsticks 5 min soak_ Dovidine solution 450 ml 10% (diluted with 50:50 Normal saline)	5/19/2020 9:46 AM
14	PDI povidone-iodine swabsticks (3). Professional Disposals Int'l Cat# S4112S NDC 10819-3885-2	5/19/2020 9:44 AM
15	10 % in a .05 oz bottle distributed by Avrio Health	5/19/2020 9:27 AM
16	n/a	5/18/2020 7:07 PM
17	Betadine 5% PI Solution	5/18/2020 5:53 PM
18	Krolman, 3mL bottle, 5% concentration	5/18/2020 5:31 PM
19	Stephens PV Eyeodine 5% 5ml dropper	5/18/2020 1:23 PM
20	Alcon, Betadine 5% Sterile Ophthalmic Prep Solution, 30 ml; NDC0065-04111-30.	5/18/2020 1:16 PM
21	Alcon Betadine 5% 10z bottles and also Surface area around the eye PDI Swabsticks. (10%)	5/18/2020 1:04 PM
22	Alcon via Catalent Pharma Solutions - Betadine 5% Sterile Ophthalmic Prep Solution, 30ml	5/18/2020 11:57 AM
23	Whatever LEBWCO is using.	5/18/2020 11:10 AM
24	Alcon Betadine Solution 5%	5/18/2020 11:07 AM
25	Alcon, Sterile Ophthalmic Prep solution, NDC 0065 0411 30, 5%, 30 ml	5/18/2020 10:53 AM
26	Alcon ophthalmic 5% or Stephens 5% depending on supply	5/18/2020 10:30 AM
27	Stephens PV Eyodine 5%, 5 ml. dropper	5/18/2020 10:17 AM
28	Manufacturer: Alcon, Product: Betadine 5% Sterile Ophthalmic Prep Solution (povidone-iodine ophthalmic solution) Volume: 30mL Product number: 0065-0411-30	5/15/2020 5:45 PM
29	5% Betadine Preps (Small vials for drops) Krolman	5/15/2020 7:22 AM
30	Krolman, 3ml, pre-packed 5% iodine, item # K55-57014-01	5/14/2020 8:03 PM
31	Alcon, 5%, 30 ml. NDC 0065-0411-30	5/14/2020 4:22 PM
32	Stephens Instruments PV Eyeodine 5% 30 ml Dropper Bottle TN00002387	5/14/2020 12:10 PM
33	Krollman, betadine	5/13/2020 7:59 PM

34	Alcon Betadine 5% Sterile Ophthalmic Prep solution 30 ml NDC 0065-0411-30	5/13/2020 3:56 PM
35	McKesson Povidone-Iodine UPS Swabsticks (3's) MFR#987 NDC 68599-8630-4	5/13/2020 2:51 PM
36	Alcon Betadine 5% 1 Fl. Oz Vendor Item # 0065041130	5/13/2020 2:43 PM
37	Betadine 5% 3 ml Krolman Corp, K55=57014-01	5/13/2020 2:18 PM
38	Krolman K55-57014-01 5% Betadine 3ml	5/13/2020 1:11 PM
39	15 ML of 5% Betadine solution	5/13/2020 12:59 PM
40	Manufacturer: Stephens Instruments Product: PV Eyeodine 5% Unit Size: 5ml Dropper Bottle Product Number: Stephens does not provide	5/13/2020 12:46 PM
41	Sterile ophthalmic prep solution, Betadine 5%, for pre-operative prep and irrigation of the ocular and periocular surfaces, manufactured by Alcon, NDC 0065-0411-30, 30 ml single use vial	5/13/2020 12:31 PM
42	Manufacturer: Purdue	5/13/2020 12:25 PM
43	Manufacturer: Catalent Pharma Solutions, LLC Product Name: Betadine 5% Sterile Ophthalmic Prep Solution (povidone-iodine ophthalmic solution) (0.5% available iodine) Unit Size: 1 Fl. Oz.	5/13/2020 12:25 PM
44	Alcon 30 mL 5% Sterile Povidone Iodine Prep Solution NDC 0065 0411 30	5/13/2020 11:09 AM
45	PV Eyeodine 5% - Stephens Instruments, 30ml	5/13/2020 9:38 AM
46	Stephens PV Eyeodine - 5% (30ml bottle)	5/13/2020 9:23 AM
47	Krolman 5% betadine(.5% iodine) 3 mls for the ocular surface Proviodine solution 10% - Rouchier 1% free iodine NPN 00172944- used for the periorbital eye prep.	5/13/2020 6:57 AM
48	Stephens PV Iodine 5% 5ml https://stephensinst.com/pv-eyeodine/	5/13/2020 6:50 AM
49	Stephens 5mL betadine/iodine rinse in a dropper bottle that currently you have to turn the lid counter clockwise in order to puncture a hole in the bottle after removing a pull tab. Bottle itself is labeled "eyeodine"	5/12/2020 7:21 PM
50	Alcon Betadine 5% Sterile Ophthalmis Prep Solution, 30ml bottles	5/12/2020 6:15 PM
51	Alcon Laboratories Betadine 5% Ophthalmic Prep Solution, 30 mL Product ID 65041130	5/12/2020 6:10 PM
52	Krolman 5% PI single dose vials 3ml	5/12/2020 5:46 PM
53	Accutome, Betadine 5% Solution, 30 ml, AX9102	5/12/2020 5:44 PM
54	Alcon Betadine 5% Sterile Ophthalmic Prep Solution (30mL)	5/12/2020 5:43 PM
55	AlconSterile opthamolic prep solution 5% betadine	5/12/2020 5:32 PM
56	manufacturer: Aplicare product name: Three Povidone-Iodine Swabsticks unit size: 3 4in saturate swabsticks product number: NDC 52380-5101-3	5/12/2020 5:23 PM
57	We use the Krolman prepared vials of 5%	5/12/2020 5:17 PM
58	Krolman, 5% Betadine, 3mL dropper bottle, item K55-57014-01	5/12/2020 5:02 PM

Q9 Please list the saline or eye wash product that you are using to rinse away PI during recovery. Be as descriptive as possible: Include manufacturer name, product name, unit size, and product number if available.

Answered: 58 Skipped: 0

#	RESPONSES	DATE
1	Alcon, BSS (balanced salt solution) Sterile Irrigating Solution, 15 ml, 9017036-0119	5/28/2020 2:07 PM
2	Medi First Opthalmic Solution Eye Wash NDC47682-198-18	5/27/2020 11:01 AM
3	Medi-First Purified water, 98.3% ophthalmic solution eyewash, 4oz bottle, NDC 47682-198-18	5/26/2020 5:17 PM
4	Prep 1- Sodium Chloride irrigation solution, Vyaire, 100 ml, AL4109 Prep 2- Sterile Saline, Medline, 100ml, RDI30296	5/21/2020 9:36 PM
5	Medline Sterile .9% Normal Saline, USP 100ml , 3.4oz, Reorder No. RDI30296	5/21/2020 2:17 PM
6	Bausch & Lomb Eye Wash Irrigating Solution	5/21/2020 10:25 AM
7	Medi-First (Purified Water 98.3%) Ophtalmic Sterile Solution Eye Wash 4 fl oz (118 ml) Medique Products	5/20/2020 7:45 PM
8	Halyard; single dose saline vials; Sterile 0.9% Sodium Chloride; 15ml pink vials	5/20/2020 2:23 PM
9	Medifirst Eye Wash from Medline - OTC19818 - 118mL; NDC-47682-198-18	5/20/2020 11:14 AM
10	First Aid eye wash-4 fl oz Manufacturer is Green Guard First Aid & Safety in St., Louis. Again, made up in a kit for us by Stephens.	5/20/2020 10:44 AM
11	Medique Medifirst Purified Water 98.3% Ophthalmic Solution Eye Wash; Product Number NDC 47682-198-18	5/19/2020 3:56 PM
12	Alcon Labs, BSS Irrigating Solution, 15ml bottle (2 used in recovery), 65079515	5/19/2020 2:12 PM
13	Eye Stream eye wash 30 ml x2	5/19/2020 9:46 AM
14	First Aid Eye Wash. Purified Water, 98.3% Ophthalmic Solution 4oz Green Guard First Aid and Safety Cat# 4105 NDC 47682-410-18	5/19/2020 9:44 AM
15	Medi-First Purified Water ,98.3%, Ophthalmic Solution Eyewash , 4 oz	5/19/2020 9:27 AM
16	n/a	5/18/2020 7:07 PM
17	BSS Solution	5/18/2020 5:53 PM
18	Alcon, BSS, 15mL	5/18/2020 5:31 PM
19	Addipak 3ml Sterile 0.9% NaCl	5/18/2020 1:23 PM
20	Stephens, First Aid Eye Wash (Purified Water 98.3%) Ophthalmic Solution Eye Wash, 118 ml; NDC47682-410-18.	5/18/2020 1:16 PM
21	EyeSaline (Honeywell), 1oz bottle (#32-000451-0000) and Alcon BSS 15ml bottles.	5/18/2020 1:04 PM
22	Alcon - BSS Sterile Irrigating Solution, 15ml	5/18/2020 11:57 AM
23	Whatever LEBWCO is using.	5/18/2020 11:10 AM
24	Medifirst Eye Wash Solution 30ml Bottle x 3	5/18/2020 11:07 AM
25	PhysiciansCare® Eye Flush Solution 4 Oz. Bottle, 7-006	5/18/2020 10:53 AM
26	0.9 sterile saline 15ml addipack, per eye per rinse	5/18/2020 10:30 AM
27	Medline, Eye Wash, 1 oz, Product # 19828	5/18/2020 10:17 AM
28	Manufacturer: Medi-First Product: Ophthalmic Solution Eyewash Volume: 4 oz Product number: 47682-198-18	5/15/2020 5:45 PM
29	BSS Alcon Canada Inc.	5/15/2020 7:22 AM
30	Eye Wash - part number 19818- manufacturer- physician's care	5/14/2020 8:03 PM
31	First Aid eye wash, 4 oz., NDC 47682-410-18. Green Guard First Aid & Safety	5/14/2020 4:22 PM
32	First Aid Eye Wash Green Guard First Aid & Safety Opthalmic Solution Eyewash NDC 47682-410-18 Product #4105 4 oz(118 ml)	5/14/2020 12:10 PM

33	Winchester and Salajet	5/13/2020 7:59 PM
34	Medi-first Purified Water, 98.3% Ophthalmic Solution Eyewash 118 ml NDC 47682-198-18	5/13/2020 3:56 PM
35	Airlife 100 units (5mls amps) Sterile saline 0.9% Sodium Ref#5257 NPN#80023553	5/13/2020 2:51 PM
36	B Braun 0.9% Sodium Chloride Irrigation USP 500 mL	5/13/2020 2:43 PM
37	Medi-First Purified water 98.3% Ophthalmic Solution Eyewash Single use 4 fl oz (118 ml) Sterile Solution. 19818	5/13/2020 2:18 PM
38	Alcon 9017034-0119 BSS 15ML	5/13/2020 1:11 PM
39	Eye wash solution	5/13/2020 12:59 PM
40	Manufacturer: Alcon Laboratories Product: BSS Unit Size: 15ml Product Number: 0065079515	5/13/2020 12:46 PM
41	Sterile eye irrigating solution, Advanced Eye Relief, manufactured by Bausch & Lomb, AX17049, 4 fl oz (single use)	5/13/2020 12:31 PM
42	Sterile eye wash - 4oz container Acme United (Brand name: PhysicianCare)	5/13/2020 12:25 PM
43	Manufacturer Name: Acme United Corporation Product Name: Eyewash (Purified Water, 98.3% Ophthalmic Solution, Eyewash) Unit Size: 4 FL OZ Product Number: NDC 0924-0160-04	5/13/2020 12:25 PM
44	Medi-First (Medique Products) 98.3% Ophthalmic Sterile Solution Eyewash NDC 47682-198-28 30mL	5/13/2020 11:09 AM
45	It can vary depending on what is available and what Stephens puts in our kit. Currently we have Purified Water, 98.3% Ophthalmic Solution Eyewash (Green Guard First Aid & Safety - St. Louis, MO), 4 Fl Oz, NDC 47682-410-18	5/13/2020 9:38 AM
46	First Aid Eye Wash - Purified Water, 98.3% Ophthalmic Solution Eye Wash (4 FL OZ)	5/13/2020 9:23 AM
47	ALCON BSS 15 mls- DIN 00512990 We also use a broad spectrum atibitoic eye solution (currently using Cipro .3%)	5/13/2020 6:57 AM
48	Stephens instruments VisionPrep pack, 4ml	5/13/2020 6:50 AM
49	Medi-First purified water ophthalmic solution eyewash 4 Fl Oz	5/12/2020 7:21 PM
50	Innovacyn, Puracyn Plus Professional Formula, Wound Irrigation 120ml (use exclusively since March 2019)	5/12/2020 6:15 PM
51	Baush & Lomb Advanced Eye Relief Eye Wash, 4oz Product ID 620252	5/12/2020 6:10 PM
52	Winchester 0.9% sterile saline 30 ml vial	5/12/2020 5:46 PM
53	MediFirst, MediWash 4 fl oz, NDC 47682-198-18	5/12/2020 5:44 PM
54	Physicians Care purified water , 98.3% ophthalmic solution, eyewash (4 oz) Re-order # 7-006	5/12/2020 5:43 PM
55	Saline jet- sterile eye wash- as much as necessary. 10ml vials	5/12/2020 5:32 PM
56	manufacturer: Medi-First product: purified water, 98.3% Ophthalmic Solution Eyewash unit size: 4 fl oz product number: NDC 47682-198-18	5/12/2020 5:23 PM
57	Sterile BSS	5/12/2020 5:17 PM
58	Mylan brand sterile saline, 5mL vials, 1 vial used per eye for each rinse.	5/12/2020 5:02 PM

Q10 Any additional comments or explanations?

Answered: 36 Skipped: 22

#	RESPONSES	DATE
1	Prior to and in addition to the two PVI soaks, we also use a cotton tip applicator dipped in PVI to clean the fornices and the lid margin. 1 CTA is used for each fornix and each lid. The normal skin prep is done too.	5/26/2020 5:17 PM
2	10% solution diluted to 5% prior to application	5/21/2020 9:36 PM
3	Re Q. 7 -Eyes are allowed to close because the lids and lashes are extensively prepped with CTAs soaked in the 1:1 dilution of 5% PI solution prior to the 1 min and 5 min flush with the PI solution.	5/21/2020 2:17 PM
4	N/A	5/20/2020 7:45 PM
5	NONE	5/20/2020 2:23 PM
6	N/A	5/20/2020 11:14 AM
7	none	5/20/2020 10:44 AM
8	none	5/19/2020 3:56 PM
9	N/A	5/19/2020 2:12 PM
10	No donor tissue recoveries.	5/18/2020 7:07 PM
11	none	5/18/2020 11:57 AM
12	No	5/18/2020 11:10 AM
13	None	5/18/2020 11:07 AM
14	no	5/18/2020 10:53 AM
15	No	5/18/2020 10:17 AM
16	our policy does not specify if lids are allowed to close during the process...probably should	5/14/2020 8:03 PM
17	The betadine and eye wash can vary. Stephens builds our kits and they keep the COA's	5/14/2020 4:22 PM
18	N/A	5/14/2020 12:10 PM
19	5 additional drops of Betadine are placed on to the eye without rinsing at the time of excision. Also we use 2 lid speculums, one for each eye	5/13/2020 3:56 PM
20	10% PI used outside of the eye/ 5 % Betadine used inside of the eye -2 minute contact inside before we rinse with sterile saline	5/13/2020 2:51 PM
21	No	5/13/2020 2:43 PM
22	We have not had an increase or decrease in the number of positive rim cultures and/or adverse reactions since implementation of the additional step.	5/13/2020 2:18 PM
23	Q6/7 we remove majority of the Conjunctiva during excision. We do one eye then the other. During recovery we cut conjunctiva. Only the lid of the eye being worked on is open.	5/13/2020 1:11 PM
24	None	5/13/2020 12:59 PM
25	25 drops in contact with eye for 5 minutes, rinsed, wait 5 minutes, then 25 drops in contact with eye for 5 minutes, rinse, begin recovery.	5/13/2020 12:46 PM
26	none	5/13/2020 12:31 PM
27	ASN - performs first PI soak (with sterile eye wash rinse) prior to prepping the lids and surrounding area - then performs a sterile scrub - with double sterile gloves insert lid speculum OU - perform the 2nd PI soak & sterile eye was rinse - leaving the lid speculums inserted OU - shedding outer pair of sterile gloves	5/13/2020 12:25 PM
28	PI prep is done twice, each lasting 2 minutes.	5/13/2020 12:25 PM
29	Once the ocular surface has been prepped, we clean the lids and surrounding skin with sterile alcohol prep pads and then use 10% PI swabsticks. These swabs come from Aplicare (Reorder No S-3111)	5/13/2020 9:38 AM

30	Our eye prep is as follows- 1.5 mls of 5% betadine to each ocular surface- dwell 2 minutes; BSS flush; repeat prep- last flush is 5 mls of antibiotic eye drop to each eye-not rinsed. we also prep the periorbital area with a 10% providone solution.	5/13/2020 6:57 AM
31	The lids generally stay open in between betadine rinses, but there is nothing keeping them open.	5/12/2020 7:21 PM
32	Blind requirement for second application of PI, without defining or establishing and without studying the volume, time or concentration was not an appropriate and sceintific change to the Medical Standards and should not have been passed.	5/12/2020 6:15 PM
33	Two application of povidone-iodine are done. Each is 15-20 drops for 2 minutes.	5/12/2020 6:10 PM
34	No	5/12/2020 5:46 PM
35	Question #5 - change to prep was double application, therefore have double the exposure time and double the volume.	5/12/2020 5:43 PM
36	Nome	5/12/2020 5:17 PM

Eye banking references (year)	PI %	Contact time	Quantity applied	Irrigation after PI	Conclusions
1. Lindquist et al. (2011)	5% & 1%	2 min	4 drops	15mL saline	5% and 1% equally effective
2. Salisbury et al. (2019)	5%	5 min	X 2 separate applications	Eye wash	Double soak reduced pos. culture &infections
3. Pabon et al. (2017)	5%	3 min	flush	-	Reduced fungal contamination
4. Laubichler et al. (2016)	0.75%	3 min	bath	-	Effective decontamination
5. Pels et al. (1999)	5%	2 min	-	-	Higher PI conc. & longer immersion time wasn't more effective
6. Mindrup et al. (1993)	10%		-	-	10% extremely effective
7. Gopinathan et al. (1998)	5%	3 min	-	-	Effective decontamination
8. Li et al. (2014)	1.25%	3 min	20 mL	250 mL NSaline?	(German translation)
9. Val Luijk et al. (2012)	PI 0.5% & 0.02% chlorhex.	3 min	"rinse"	20 mL 0.9% NS	Minimized contamination and preserved K viability using both PI + chlorhex
10. Perry et al. (2020)	5%	3 min	10-15 drops	Saline rinse	Added kerasave (ampho B) to subset

Ocular surgery references (year)	PI %	Contact time	Quantity applied	Irrigation after PI	Conclusions
1. Zhang et al. (2019) -PI applied before cataract surgery	5%	2 min	irrigation	-	5% povidone-iodine for 2 min is effective & safe (vs. 30sec vs. 1 & 3.5min soak)
2. Musumeci et al. (2019) -in vitro study	0.6% vs. 5%	-	-		0.6% more rapidly bactericidal; in vitro study
3. Barroso et al. (2017)	5%	-	1 drop vs. 3 drops	-	3 drops more effective (applied 0, 20min, 28min)
4. Nguyen et al. (2017) -PI applied before cataract surgery	10%	3 min	-	-	Effective & safe in cataract surgery
5. Silas et al. (2017)	1%	30 sec x3 times	-	-	PI 1% 30sec x 3 times as effective as 5% x once
6. Grzybowski et al. (2016)			-	-	
7. Hosseini et al. (2012) -organisms from endophth thalmitis specimens	5% vs. 10%	15 min vs. 5min	-	-	5% for 15 min or 10% for 5 min equally effective
8. Levinson et al. (2018) – prep intravitreal injection	5%				Application of PI after lid speculum: most effective
9. Stranz et al. (2011) –prep before cat. surgery	0.5% and	2 min	X2 separate applic, 10min apart		Double application of PI was more effective in decontamination
10. Apt et al. (1984) -prep for ocular surgery	5%		drop		First controlled study showing efficacy of PI for ophthalmic use
11. Isenberg et al. (1985) -prep for ocular surgery	5%				Effective sterilization especially used with abx
12. Speaker et al. (1991) -prep for cataract surgery	5%				Reduced endophthalmitis rate compared
13. Dereklis et al (1994)	5%		1 drop		PI significantly reduced positive cultures compared with saline
14. Carrim et al. (2009) -prep for cataract surgery	5%	3 min			Significantly reduced positive cultures
15. Li et al. (2013) -prep for cataract surgery	10% vs. 1% & 5%		10 mL		PI 10.0% was more effective than povidone-iodine 1.0% and 5.0%
16. Quiroga et al (2010) -prep for cataract surgery	5%		10 mL		5% effectively reduces flora

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Original

Relationship between Virucidal Efficacy and Free Iodine Concentration of Povidone-Iodine in Buffer Solution

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Povidone-iodine solutions prepared to various concentrations (0.01, 0.1, 1 and 10%) with 0.2M phosphate buffer (pH 7.0) (PVP-I PB) were analyzed to determine their free iodine concentrations using membrane permeation cells, and their inactivation effects on three viruses (influenza A virus, poliovirus type 1 and *adenovirus* type 3) were examined. The free iodine concentrations in the 0.01-10% PVP-I PB were determined to be 1.84, 4.88, 1.58 and 0.17 ppm (approximate values), respectively, with the maximum obtained for the 0.1% solution. The virucidal efficacy of these PVP-I PB against poliovirus type 1 and adenovirus type 3 was found to be generally dependent on free iodine concentration, with the 0.1% solution being the most effective. Influenza A virus was inactivated with an action time of 15 s at all four concentrations examined. The results of this study suggested an association between free iodine concentration and virucidal efficacy for the 0.01-10% PVP-I PB.

Key words：Povidone-iodine / Free iodine concentration / Virucidal efficacy / Permeation cell.

INTRODUCTION

Aqueous solutions of povidone-iodine (polyvinylpyrrolidone-iodine, hereinafter called PVP-I), a conjugate of polyvinylpyrrolidone with iodine, are commonly used as antiseptics. Iodine in PVP-I maintains an equilibrium in a wide variety of forms (e.g., I_2, I^-, I_3^-, PVP-I_3^-) in solutions, with the total amount of all these forms measured as available iodine content in sodium thiosulfate titration. Above all, free iodine (I_2), which is released by PVP-I, is reported to contribute to the biocidal activity of PVP-I, with the I_2 concentration increasing with increasing dilution rate for 10% PVP-I solution, and maximizing with a dilution rate of nearly 100 fold (Gottardi, 1983). With regard to PVP-I formulations, antibacterial effects (Atemnkeng et al., 2006; Berkelman and Holland, 1982), virucidal efficacy (Kawana, 1997; Sauerbrei and Wutzler, 2010) and free iodine concentrations in PVP-I (Atemnkeng et al., 2006; Gottardi, 1983; Horn and Ditter, 1983; Pollack and Iny, 1985) have been reported; however, few studies evaluate the association between virucidal efficacy and free iodine concentration. In addition, commercially available PVP-I formulations contain multiple additives, mainly surfactants, that are diverse in terms of type, quantity and pH. It is noteworthy that some surfactants contained in such commercial formulations have been reported to exhibit potent cytotoxicity (Iwasawa and Nakamura, 2001; 2003). Assessment of free iodine concentrations and biocidal activity, seemed to indicate that some of the wide varieties of additives contained in these liquid formulations might influence the equilibrium of the iodine species in the PVP-I PB to change the free iodine

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concentrations, or have secondary effects (e.g., increase in permeability by surfactant) on the susceptibility of test microorganisms to iodine. Such an influence from additives could make it difficult to assess the association between free iodine concentration and biocidal effect. In addition, while the pH of a PVP-I solution shifts to the weakly acidic-neutral side when the solution is diluted with purified water, the 10% PVP-I solution exhibits strong acidity (pH: approx. 1.7), suggesting to be difficult in assessment of the association between free iodine concentration and biocidal effect due to the pH change at particular PVP-I concentrations. With this in mind, optionally chosen different concentrations of PVP-I PB were prepared using a pH 7 PB to avoid the influence of changes in pH and additive concentrations due to water dilution, and then assayed to clarify the relationship between the free iodine concentration and virucidal efficacy.

MATERIALS AND METHODS

Test solutions

PVP-I (PVP-Iodine, BASF Japan Ltd.) was dissolved in PB (adjusted to a pH of 7 by mixing 0.2M disodium hydrogen phosphate 12-hydrate, 7.16 g/100 mL, and 0.2M sodium dihydrogen phosphate anhydrate, 2.4 g/100 mL) to yield a 10% PVP-I PB (10 g PVP-I/100 mL), which was serially diluted 10 fold with PB to yield 1%, 0.1% and 0.01% solutions. The measured available iodine concentration of the 10% PVP-I PB was verified by titration with sodium thiosulfate.

Relationship between free iodine and absorbance (Takikawa et al., 1978)

Iodine was accurately weighed and dissolved in a 10% potassium iodine (KI) aqueous solution to yield a solution having an iodine concentration of approximately 900 ppm, and then it was diluted with a KI solution to five iodine concentrations between 1.4 and 6.8 ppm. With the KI solution (diluent for the dilutions) used for a blank determination, the absorbance at 351.5 nm ($A_{351.5}$) was determined using a 1 cm cuvette, and the relationship between iodine concentration and absorbance was examined.

Measurement of free iodine concentrations in various test solutions (Atemnkeng et al., 2006; Takikawa et al., 1978)

A high-density polyethylene membrane (DuraSeal, DIVERSIFIED BIOTECH) 0.04 mm in thickness was placed between two side-by-side membrane permeation cells for flat membranes (Permcell,VIDREX, KH-55, aperture dia.: 25 mm, membrane area: approx. 4.9 cm^2, inside volume: approx. 55 mL) (Fig.1), and a PVP-I PB was poured into the donor cell, and a KI solution into the acceptor cell. After stirring cell with a multi-stirrer at 25℃ for 20 h, $A_{351.5}$ of the KI aqueous solution in the acceptor cell was determined using a 1 cm cuvette, and the free iodine concentrations (ppm) in the various test solutions were determined using a regression line generated with the aforementioned iodine concentrations and absorbance values.

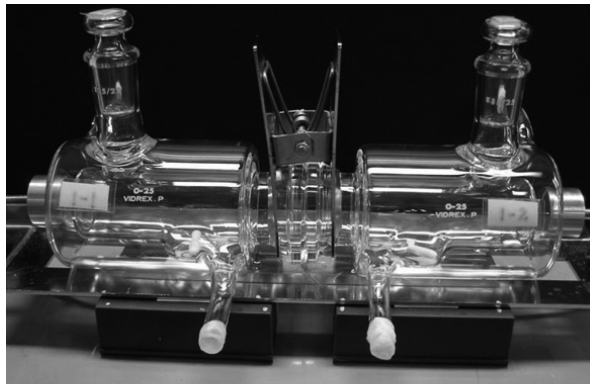

FIG. 1. Side-by-side membrane permeation cells for flat membranes used to measure free iodine. (Permcell, VIDREX, KH-55, aperture diameter: 25 mm, membrane area: approx. 4.9 cm^2, inside volume: approx. 55 mL)

Preparation of test viruses

Influenza A virus (A/PR/8/34, H1N1, ATCC VR-95) was inoculated into the allantoic cavities of embryonated chicken eggs, which were incubated at 37℃. After 2-day incubation, the virus multiplying in the allantoic fluid were harvested, and concentrated using a hollow fiber cartridge (GE Healthcare); the concentrate was subjected to sucrose density gradient centrifugation (108,000 x*g* for 3 h at 4℃) to purify the virus, which was used as the test virus (range of viral concentrations in $\log_{10}$ $TCID_{50}$ per mL: 8.7-9.5). For viral infectivity determination, Madin-Darby canine kidney (MDCK) epithelial cells were used.

Poliovirus type 1 (Poliovirus, strain sabin1 LSc 2ab, Japan Poliomyelitis Research Institute) was inoculated on vero cells. The virus-infected cells were incubated at 37℃ for 2-3 d. When approximately 90% of the cells showed CPE, a cell lysate was prepared by freezing and thawing. The cell lysate was centrifuged at 2,380 x*g* for 10 min at 4℃, and the harvested supernatant was concentrated using an ultrafiltration membrane. The concentrate was then subjected to sucrose density gradient centrifugation (108,000 x*g* for 3 h at 4℃) to purify the virus, which was used as the test virus (range of viral concentrations in $\log_{10}$ $TCID_{50}$ per mL: 8.6-8.9). For viral infectivity determination, Vero cells were used.

Adenovirus type 3 (ATCC VR-3®) was inoculated on

A549 cells. The virus-infected cells were incubated at 37℃ for 2-3 d. When approximately 90% of the cells showed CPE, a cell lysate was prepared by freezing and thawing. The cell lysate was centrifuged at 2,380x*g* for 10 min at 4℃, and the harvested supernatant was concentrated using an ultrafiltration membrane. The concentrate was then subjected to sucrose density gradient centrifugation (108,000 x*g* for 3 h at 4℃) to purify the virus, which was used as the test virus (range of viral concentrations in $\log_{10}$ $TCID_{50}$ per mL: 8.6-9.3). For viral infectivity determination, A549 cells were used.

Subculture of the cells

The cells were cultured using Dulbecco's Modified Eargle's medium (DMEM, SIGMA Aldrich), supplemented with 5-10% fetal bovine serum (FBS, SIGMA Aldrich), with passage performed every 3-4 d in a CO_2 incubator kept at 37℃ to obtain subcultured cells, which were used in the following steps.

Preparation of test solutions

Four concentrations (0.01, 0.1, 1 and 10%) of PVP-I PB solutions, prepared in the same manner as for the measurement of free iodine concentrations, were used as the test solutions.

Virus inactivation test

All of the test procedures were implemented in an indoor environment at 25℃. An aliquot of 0.1 mL of each test virus suspension was added to 0.9 mL of the test solution, and the mixture was stirred by voltexing for 5 s to initiate the exposure. After a given exposure time, a 0.1 mL sample of the mixture was collected and diluted 5 fold with a 1.6-time concentration of Dulbecco's PBS (Nissui Pharmaceutical Co., Ltd.) containing 0.5% sodium thiosulfate to stop the exposure of the test solution on the virus. This dilution was further diluted 100 fold with Dulbecco's PBS to avoid the toxicity of sodium thiosulfate on the cells. This solution was used as the sample stock solution for viral infectivity determination. Baseline infectivity titer was established by inoculating 0.2M PB with each virus, immediately collecting a sample, and assaying the sample in the same manner.

Measurement of viral infectivity

The sample stock solution for viral infectivity determination was serially diluted with PBS 10 fold, after which 50 μL of the sample stock solution for infectivity titration or diluted virus and 50 μL of cells for viral infectivity determination in suspension in 5% FBS-supplemented DMEM were inoculated onto a 96-well microplate. Thereafter, the influenza virus and poliovirus were cultured in a 37℃ CO_2 incubator for 4 d. The adenovirus was cultured at 37℃ for 3 d, after which the medium was replaced with 0.2% FBS-supplemented DMEM, and the virus was further cultured for 3 d After completion of the cultivation, the CPE due to viral proliferation was examined under an inverted microscope, and viral infectivity ($TCID_{50}$/mL) was determined using the Reed-Muench method (Reed and Muench, 1938).

Log reduction values (LRVs) of viral infectivity were calculated using the equation: LRV = $\log_{10}$ (baseline viral infectivity ÷ viral infectivity for each exposure time)

RESULTS

pH of the test solutions

The 10% PVP-I PB solution showed an available iodine concentration of 1.02% and a pH of 6.7.

This solution was serially diluted 10 fold with PB to yield 0.01-1% solutions, all of which were found to have a pH of 7.0.

Relationship between iodine concentration and absorbance at wavelength of 351.5 nm ($A_{351.5}$)

The relationship between iodine concentration and $A_{351.5}$ is shown in Fig.2.

Values of $A_{351.5}$ for five iodine concentrations (a: 1.4, b: 2.7, c: 4.1, d: 5.5, e: 6.8 ppm) were revealed a positive correlation between iodine concentration and $A_{351.5}$, with a regression line of Y = 0.1073X + 0.0153 and a coefficient of determination of R^2 = 0.9997.

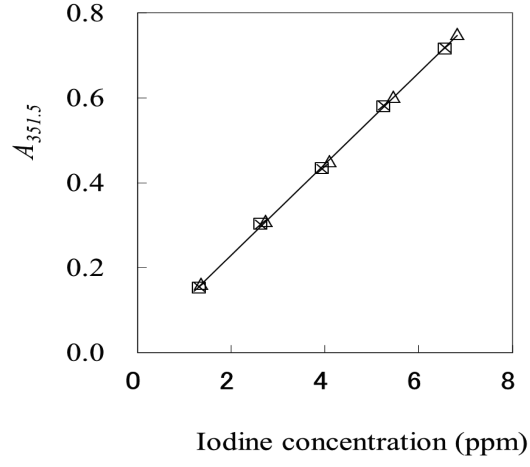

FIG. 2. Relationship between iodine concentration and absorbance at wavelength of 351.5 nm ($A_{351.5}$).
Iodine was dissolved in 10% KI aqueous solution to five iodine concentrations between 1.4 and 6.8 ppm, and its $A_{351.5}$ was measured (n=3). The measurement values at five measurement points (n=3) are indicated by □, △ and x marks respectively. Y: $A_{351.5}$, X: Iodine concentration (ppm). Regression line: Y = 0.1073X + 0.0153, R^2 = 0.9997

Measurement of free iodine concentrations in the various test solutions

Mean free iodine concentrations from three measurements are plotted in Fig.3.

Of the various test solutions, the 10% PVP-I PB solution was found to have a free iodine concentration outside the regression line range (approximate calculation from the regression line formula: 0.17 ppm); however, its 10-, 100- and 1000-fold dilutions were found to have free iodine concentrations of 1.58, 4.88 and 1.84 ppm, respectively, with the maximum obtained from the 100-fold dilution.

Virus inactivation test

The LRVs for the three viruses are shown in Tables 1, 2 and 3.

When the 0.01-10% PVP-I PB solutions were allowed to act on influenza A virus for 15 s, an infectivity titer reduction of ≥4 log was observed at all concentrations (Table 1).

When the PVP-I PB solutions were allowed to act on poliovirus, the exposure time to reach an LRV of ≥4 was determined to be 30 min for the 0.01% solution, 15 min for the 0.1% solution and 30 min for the 1% solution. With the 10% solution, even when allowed to act for 60 min, the LRV did not exceed 4 (Table 2). The virucidal efficacy (in terms of time to reach an LRV of ≥4; if there was no time difference, the virucidal efficacy was compared in terms of LRV) of the PVP-I PB solutions changed depending on the iodine concentration as follows: 0.1% > 0.01% ≥ 1% > 10%.

When the PVP-I PB solutions were allowed to act on adenovirus, the exposure time to reach an LRV of ≥4 was determined to be 5 min for the 0.01% solution, 1 min for the 0.1% solution, 5 min for the 1% solution and 60 min for the 10% solution (Table 3).

The virucidal efficacy of the PVP-I PB solutions changed depending on the iodine concentration as follows: 0.1% > 0.01% ≥ 1% > 10%.

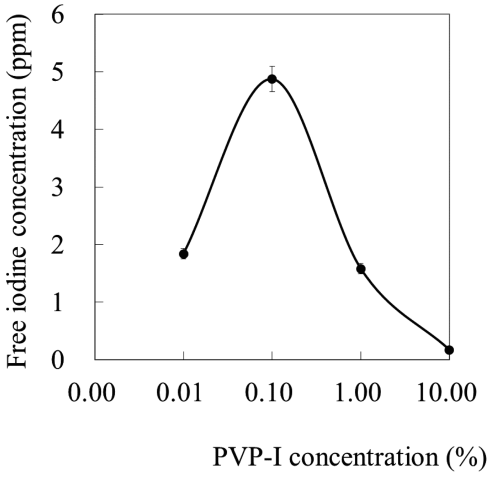

FIG. 3. Free iodine concentrations in 0.01-10% PVP-I PB solutions (n=3, mean). The vertical bars on the ● marks indicate the standard deviations of three measured values.
The iodine concentration was determined to be 1.84 ppm in the 0.01% solution, 4.88 ppm in the 0.1% solution, 1.58 ppm in the 1% solution and 0.17 ppm in the 10% solution (the 0.17 ppm value for the 10% solution was an approximation; the actual value was outside the regression line range).

DISCUSSION

In the present study, free iodine concentrations in PVP-I PB solutions and virucidal efficacy were examined under controlled conditions (as suggested from a preliminary study with 10% PVP-I aqueous solution) with the influence of pH avoided by dissolving PVP-I with PB, and likely changes in PB concentration (0.2M) due to dilution were suppressed by using a PB solution as the diluent.

There are three reported methods for measuring free iodine: extraction using the apolar solvent heptane (Pollack and Iny, 1985), equilibrium dialysis (Atemnkeng et al., 2006; Horn and Ditter, 1983) and potentiometry (Gottardi, 1983). In the present study, equilibrium dialysis was used in accordance with reported methods (Atemnkeng et al., 2006; Takikawa et al., 1978). The

TABLE 1. Virus inactivation effects (LRV[a)]) of 0.01-10%PVP-I PB on influenza A virus

Test drug		Treatment time (s)		
		15	30	60
PVP-I	10%[b)]	>4.3	n.d.[d)]	n.d.
	1%[b)]	>4.3	n.d.	n.d.
	0.1%[c)]	4.5±0.3	n.d.	n.d.
	0.01%[c)]	4.4±0.4	4.3±0.4	4.4±0.5
Negative control (0.2M PB)		n.d.	n.d.	-0.1±0.3

a: LRV = $\log_{10}$ (baseline viral infectivity÷viral infectivity obtained with each exposure time)
The LRVs were calculated from viral infectivity titers determined from 0.01-10% PVP-I PB solutions with various exposure times.
Each test consisted of two to five measurements, and each LRV value is expressed as the mean of the repeated measurements. When all measurements are lower than the limit of detection, the LRV value is indicated as ">mean LRV." For all other points, each value is expressed as the mean± standard deviation. As the negative control, only the infectivity titer following the longest exposure time with PB was measured.
b: The mean of two measurements was calculated.
c: The mean of five measurements was calculated.
d: Not determined.

TABLE 2. Virus inactivation effects (LRV[a)]) of 0.01-10%PVP-I PB on poliovirus type 1

Test drug		Treatment time (min)					
		0.25	1	5	15	30	60
PVP-I	10%	n.d.[b)]	n.d.	0.5±0.5	0.6±0.5	1.1±0.1	2.4±0.1
	1%	n.d.	0.6±0.1	0.7±0.3	2.5±0.1	>4.2	n.d.
	0.1%	0.6±0.2	0.6±0.2	2.6±0.3	>4.2	n.d.	n.d.
	0.01%	n.d.	0.6±0.2	1.7±0.4	3.6±0.4	4.2±0.1	>4.2
Negative control (0.2M PB)		n.d.	n.d.	n.d.	n.d.	n.d.	0.0

a: LRV = $\log_{10}$ (baseline viral infectivity ÷ viral infectivity obtained with each exposure time)
The LRVs were calculated from viral infectivity determined from 0.01-10% PVP-I PB solutions with various exposure times.
Each LRV value is expressed as the mean of two measurements. When both calculations are lower than the limit of detection, the LRV value is indicated as ">mean LRV."
For all other points, each value is expressed as the mean±standard deviation. As the negative control, only the infectivity titer following the longest exposure time with PB was measured.
b: Not determined.

TABLE 3. Virus inactivation effects (LRV[a)]) of 0.01-10%PVP-I PB on adenovirus type 3

Test drug		Treatment time (min)					
		0.25	1	5	15	30	60
PVP-I	10%	0.1	0.6±0.1	1.5±0.5	2.7±1.0	3.7±0.8	4.3±0.3
	1%	0.7±0.3	2.4±0.7	4.3±0.3	>4.3	n.d.	n.d.
	0.1%	2.6±0.6	4.3±0.5	>4.3	n.d.	n.d.	n.d.
	0.01%	1.6±0.5	3.5±0.3	>4.3	>4.3	n.d.	n.d.
Negative control (0.2M PB)		n.d.[b)]	n.d.	n.d.	n.d.	n.d.	0.2±0.2

a: LRV = $\log_{10}$ (baseline viral infectivity ÷ viral infectivity obtained with each exposure time)
The LRVs were calculated from viral infectivity determined from 0.01-10% PVP-I PB with various exposure times.
Each LRV value is expressed as the mean of three measurements. When all the three calculations are lower than the limit of detection, the LRV value is indicated as ">mean LRV."
For all other points, each value is expressed as the mean±standard deviation. As the negative control, only the infectivity titer following the longest exposure time with PB was measured.
b: Not determined.

membrane permeation system used was similar to a common side-by-side membrane permeation cells for flat membranes (Takikawa et al., 1978; Noda et al., 2009). Free iodine concentrations were measured using the same apparatus and a silicone membrane as in previously reported studies (Takikawa et al., 1978; Noda et al., 2009). However, both failed to assess free iodine concentrations with varied iodine or PVP-I concentrations, although some of the particular iodine or PVP-I concentrations were measured; therefore, their data did not serve for our objective. On the other hand, Atemnkeng et al. assessed free iodine concentrations in 10% solutions of two PVP-I formulations and their dilutions, using a special membrane permeation apparatus (Kontron Diapack system) and a high-density polyethylene membrane (Atemnkeng et al., 2006). The two 10% PVP-I formulations were found to have free iodine concentrations of 2.1 and 9.7 ppm, respectively, demonstrating a difference in bactericidal effect as found in free iodine concentration. They also measured free iodine concentrations in 50- to 100-fold diluted solutions from the two PVP-I formulations, reporting maximum values of 31 and 35 ppm, respectively. In our preliminary study using a permeation cell and a high-density polyethylene membrane, measurement of free iodine concentrations in PVP-I PB solutions and PVP-I formulations, diluted to optional concentrations revealed the maximum from the 100-fold dilution. Since this finding was consistent with reported results, a high-density polyethylene membrane was used as the permeation membrane for measurement of free iodine concentrations.

The free iodine concentrations in the 0.01, 0.1, 1 and 10% PVP-I PB at 25℃ (ppm, mean±standard devia-

tion) were determined to be 1.84±0.09, 4.88±0.22, 1.58±0.09 and 0.17±0.01 ppm, respectively. Hence, with regard to free iodine concentration, the PVP-I PB ranked in the descending order of 0.1% > 0.01% ≥ 1% >10%; it was revealed that these solutions showed different relationships between free iodine concentration and available iodine concentration. The free iodine concentrations we obtained were lower than those reported by Atemnkeng et al. (2006). These differences are attributable to the differences in the choice of apparatus for membrane permeation and buffer concentration, as well as the measuring time, test solution pH and other conditions. However, the relationship between the free iodine concentration and available iodine concentration we determined generally agreed with their results. While the measurement of free iodine concentrations using membrane permeation cells is generally considered to be a useful method, given the extrapolated values outside of the regression line included in the results of this study, as well as the factors affecting the measured values, further study may be necessary on the measurement method in order to obtain and confirm highly accurate and sensitive measured values.

Generally, it has been reported that viruses having an envelope (outer lipid membrane) are highly susceptible to antiseptics, non-enveloped viruses are highly resistant to antiseptics and adenoviruses, which are lipophilic, possess relatively low resistance to antiseptics despite their identity as non-enveloped viruses (Prince and Prince , 2001). In the present study, influenza A virus was chosen from among enveloped viruses, and poliovirus and adenovirus from among non-enveloped viruses, on the basis of differences in viral structure and drug resistance and other factors. The 10% PVP-I solution prepared with purified water exhibited strong acidity (pH: 1.7), resulting in infectivity titer reductions due to the pH in two (influenza virus, poliovirus) of the three viruses used in the present study (data not shown). Taking this into consideration, a specific buffer was used to prepare PVP-I solutions; the buffer selection 0.2M PB and pH (pH: 7.0) was determined in accordance with a previously reported combination (Kawana et al., 1998). Prepared with the PB solution, a 10% PVP-I PB solution was found to have a pH of 6.7, demonstrating the absence of influence of the PB solution on any test virus.

The 0.01-10% PVP-I PB solutions were found to be effective in inactivating influenza virus at all concentrations examined by reducing the infectivity titer by ≥4 log reduction when allowed to act for 15 s, with no difference in virucidal efficacy observed among the different free iodine concentrations. On the other hand, the virucidal activity against poliovirus was found to differ among the different PVP-I concentrations; the virucidal efficacy of the PVP-I PB changed depending on the iodine concentration as follows: 0.1% ≥ 0.01% ≥ 1% > 10%. Similar results were obtained with adenovirus; the virucidal activity was found to differ among the different PVP-I concentrations, with the virucidal efficacy of the PVP-I PB changing depending on the iodine concentration as follows: 0.1% ≥ 0.01% ≥ 1% > 10%. With regard to susceptibility to PVP-I PB solutions, poliovirus was found to be the most highly resistant, followed by adenovirus and influenza virus in this order, agreeing with reported data on the susceptibility of existing agents (Prince and Prince, 2001).

Kawana and colleagues (1998) examined the virucidal efficacy of PVP-I PB solutions prepared to optional concentrations against various viruses, reporting that the virucidal efficacy against three enteroviruses, including poliovirus types 1 and 3, did not depend on the available iodine concentration in PVP-I, with the drug exhibiting weaker virucidal efficacy at higher concentrations than at lower concentrations (Kawana et al., 1998). Such a virucidal efficacy not depending on PVP-I concentration has been reported in rhinovirus, a non-envelope virus, and rubella virus, an envelope virus, as well. This fact appears to be consistent with our finding of the association between virucidal efficacy against non-envelope viruses and free iodine concentration, showing that the free iodine concentration was higher in the 0.1% PVP-I PB (available iodine: 0.01%) than in the 10% PVP-I PB (available iodine: 1%), and that the virucidal efficacy was found to depend on the free iodine concentration of each solution.

While PVP-I is known to exhibit antimicrobial activity proportional to the concentration of the free iodine released, our study using non-enveloped viruses verified that the virucidal efficacy was maximized at a concentration close to that of the 100-fold dilution (PVP-I concentration: 0.1%), which produced the highest free iodine concentration. In light of existing reports and the present findings, with no molecular species other than free iodine directly involved in virucidal efficacy, PVP-I is inferred to exist chiefly as a supply source of free iodine. Attention should be paid to the fact that PVP-I, unlike other antiseptics that lose antimicrobial activity with dilution, does not always lose antimicrobial activity even when having a decreased available iodine concentration due to dilution. Although 10% PVP-I formulations are commonly used in the clinical setting, taking into account concentration reductions due to the presence of organic substances such as blood and proteins, they should not be used unless the above-described features are fully understood.

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Comparison of 5% povidone-iodine solution against 1% povidone-iodine solution in preoperative cataract surgery antisepsis: A prospective randomised double blind study

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CLINICAL SCIENCE

Comparison of 5% povidone-iodine solution against 1% povidone-iodine solution in preoperative cataract surgery antisepsis: a prospective randomised double blind study

A W Ferguson, J A Scott, J McGavigan, R A Elton, J McLean, U Schmidt, R Kelkar, B Dhillon

Br J Ophthalmol 2003;**87**:163–167

Background/aim: Povidone-iodine (PI, Betadine) is routinely used as a preoperative topical antiseptic in cataract surgery as it has been shown to reduce the incidence of postoperative endophthalmitis. However, the concentration used clinically is variable. In vitro studies have shown that PI is paradoxically more effective at lower concentration. This study was undertaken to determine if this effect was reproducible in vivo.

Methods: A prospective randomised double blind study was carried out in the ophthalmic theatre in a district general hospital. 105 patients attending for routine cataract surgery were randomly allocated to have their conjunctival fornices irrigated preoperatively with either PI 1% (group A) or PI 5% (group B). Conjunctival swabs were taken, in identical fashion, both before and 1 minute after irrigation. The number and species of bacterial colonies cultured from each swab was counted. The difference in the median number of bacterial colonies from pre-irrigation to post-irrigation cultures was then compared between the groups.

Results: Bacterial cultures were gained from 100 patients (33 male, 67 female, mean age 74 years, range 30–95 years). Group B (5% PI) showed a decrease in median colony forming units (CFU) pre-irrigation from 100 to 40 CFU post-irrigation (a drop of 60%). This was greater than in group A (1% PI) where the reduction was 120 CFU pre-irrigation to 100 CFU post-irrigation (a drop of 16.7%) (Mann-Whitney test, $p<0.05$). At higher initial bacterial loads (CFU pre-irrigation >1000), the difference in median between the two groups became larger as the number of pre-irrigation bacteria increased. In group B pre-irrigation CFU reduced from 3340 to 110 post-irrigation (a drop of 96.7%) compared with group A: 5000 CFU pre-irrigation to 3000 post-irrigation (a drop of 40%) (Mann-Whitney test, $p=0.0014$).

Conclusion: Despite in vitro evidence of higher bactericidal efficacy of PI at more dilute concentrations, 5% PI is more effective than 1% PI in decreasing the human conjunctival bacterial flora in vivo, particularly in the presence of heavier initial bacterial load.

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Although the incidence of endophthalmitis following cataract surgery is rare at about 0.1%,[1 2] it remains a serious postoperative complication with a potentially poor visual prognosis. Various methods of prophylaxis have been used in an effort to minimise the risk of postoperative endophthalmitis, but the designs of studies with sufficient power to measure their efficacy are hampered by the large sample sizes required to produce a statistically significant result. In a recent comprehensive literature review of various prophylactic techniques, Ciulla *et al* found preoperative irrigation with povidone-iodine (polyvinylpyrrolidone-iodine; PI) to be the most strongly recommended technique based on the current clinical evidence (the strength of povidone-iodine was not specifically mentioned).[1]

Povidone-iodine has been shown to be effective against a wide range of bacteria, as well as fungi, protozoa, and viruses.[3–5] Although some bacteria have demonstrated a "pseudo-resistance" to povidone-iodine, this is presumed to be due to their ability to coat themselves in a protective extracellular matrix.[4 6] This inhibition is inversely proportional to the povidone-iodine concentration.[7] It is not inhibited by normal saline or water solutions.[8]

The ideal concentration of povidone-iodine for maximal efficacy is not clarified. Povidone-iodine stock solution is 10%, comprising 90% water, 8.5% povidone-iodine, 1% available iodine, and iodide.[3] Previous studies have shown that 5% povidone-iodine effectively decreases the bacterial flora of the ocular surface and adnexae,[9–12] and thus theoretically decreases the risk of endophthalmitis, while other large studies have demonstrated 5% povidone-iodine to directly decrease the incidence of endophthalmitis.[1 13]

More dilute concentrations have been studied in vivo in dogs' eyes where 0.2% povidone-iodine was shown to be equally as bactericidal as 1% and 5% povidone-iodine.[14] In human eyes, in a small study, 0.02% povidone-iodine irrigation has been found to be equally bactericidal compared to 5% povidone-iodine drops.[9]

There has been no study to compare more dilute concentrations of povidone-iodine with 5% povidone-iodine in the human eye while controlling other variables such as method or length of irrigation. We therefore conducted a prospective randomised double blind comparative study of the effect of 5% povidone-iodine against 1% povidone-iodine on the bacterial flora of the human conjunctiva, using an identical and clinically relevant method of application, to see if the increased bactericidal effect of lower concentrations seen in vitro was reproducible in vivo.

METHODS

Ethical approval for the study was obtained from the Forth Valley Health Board ethics of research committee. The supply of povidone-iodine in randomised aliquots of either 1% or 5%

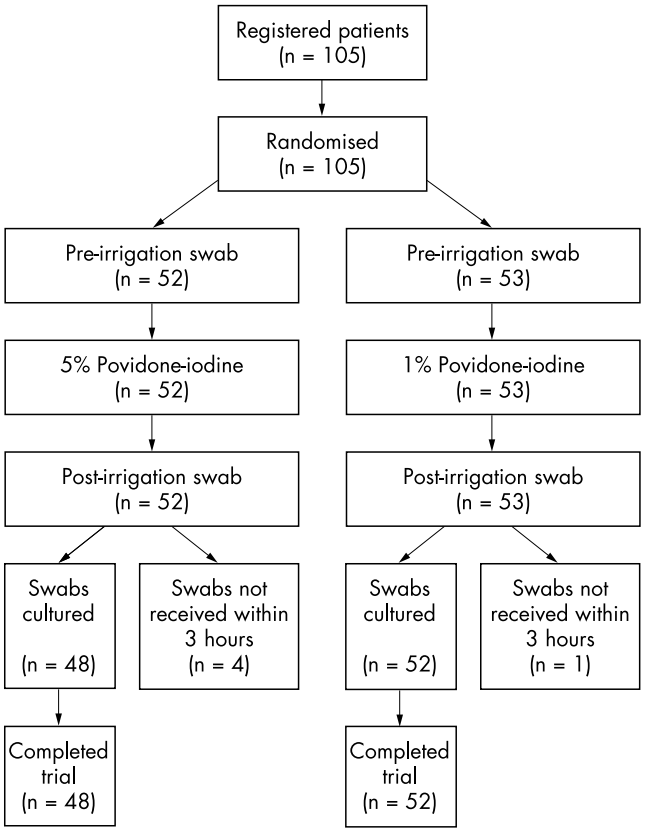

Figure 1 Flow chart describing progress of patients through trial.

dilution was sourced from a nearby pharmaceutical laboratory. Aliquots were supplied in identical smoked glass bottles, numbered from 1 to 105.

Patients attending for routine cataract surgery at Stirling Royal Infirmary were invited to take part in the study, via a written information sheet accompanying their letter of appointment to attend for pre-assessment. Informed consent was then obtained from those agreeing (105 in total) at the pre-assessment visit 1 week before their operation. Exclusion criteria were current eye infection, use of topical or systemic antimicrobial agents, allergy to iodine, previous intraocular surgery, and pregnancy.

Our standard preoperative preparation was carried out on each patient: three applications of single dose units of proxymetacaine hydrochloride 0.5%, cyclopentolate 1%, phenylephrine 2.5%, and diclofenac sodium 0.1% were applied to the operative eye 1 hour before surgery.

For each participant, a swab from the inferior conjunctival fornix, of the eye to be operated on, was taken with a sterile cotton tipped applicator in the anaesthetic bay before local anaesthesia and surgery. In order to reduce operator sampling bias, a standardised swabbing technique was used for all study patients. The swab was then inoculated in a bijou bottle containing 2 ml of tryptone soya broth with 0.5% sodium thiosulphate broth. The ocular surface of the same eye was then irrigated with one of the randomised aliquots of povidone-iodine by dripping 2 ml of the solution from a syringe directly on to the eye over 1 minute. After a further minute a second swab was taken in identical fashion to the first. Both swabs were labelled with the number of the randomised povidone-iodine aliquot used, as well as "A" or "B" for the pre-irrigation and post-irrigation swabs respectively. The patient's details were kept separately with the same number. Inoculated swabs were transferred directly to the microbiologist for culture within 3 hours of being taken (see Fig 1). By this method and to reduce bias, the swabber/irrigator and the microbiologist were blinded to the povidone-iodine concentration used.

On completion of the sampling for the study, routine operative protocol was followed: all patients subsequently received local anaesthesia by sub-Tenon's injection (bupivacaine 0.75% and lignocaine 2%) either inferonasally or inferotemporally. Honan's balloon was not used. Patients were then taken into the operating room where they received further preoperative cleansing of the ocular surface and periorbital skin with 5% povidone-iodine immediately before surgery, as in the guidelines for cataract surgery issued by the Royal College of Ophthalmologists[15] (normal practice for the department is to irrigate the eye with 5% povidone-iodine in the anaesthetic room before and after anaesthesia, with formal re-preparation after transfer to the operating theatre). Patients then proceeded to phacoemulsification and posterior chamber lens implantation.

On reaching the microbiology laboratory, samples were vortexed for 30 seconds. Subsequently, 100 µl aliquots were spread onto: (1) a chocolate blood agar plate which was incubated for 48 hours in 10% carbon dioxide; (2) an anaerobic basal agar containing 5% horse blood which was incubated for 48 hours in an anaerobic cabinet (Na 80%, H_2 10%, CO_2 10%); after which colony forming units (CFU) were counted in both plates. A further 100 µl was incubated into fastidious anaerobic broth that was incubated for 7 days, and then subcultured anaerobically and in 10% carbon dioxide.

Colonies were counted by hand, using an illuminated colony counter when large numbers of colonies were present. The number of colonies on each plate was converted to number of bacteria per 2 ml of tryptone soya broth (equal to number of bacteria per eye) using the equation:

Total CFU per eye = (CFU on plate per amount of solution plated) × (volume of original solution)

Bacterial species were identified using conventional biochemical and biophysical reactions.

The sample size of 100 had 80% power to detect as significant at the 5% level a true mean difference in normally distributed outcomes of 0.65 standard deviations. For counts of CFU, which were approximately normally distributed after logarithmic transformation, this corresponded to a fourfold change in levels. To enable logarithmic transformation a count of 10 was arbitrarily assigned when no CFU were detected (being less than half the minimum detectable CFU count, and where the number of CFU was too large to count (that is, CFU >8000) a count of 16 000 was assigned (that is, double the maximum countable number). Numbers of CFU counted ranged from 10 to 16 000 after logarithmic transformation in each treatment group, both before and after irrigation. Raw data were used for qualitative analysis, but logarithmic transformation was employed for quantitative statistical data analysis to correct the extreme skewness in these numbers.

The two treatment groups were compared using Mann-Whitney tests for numbers of CFU; and χ^2 tests with Yates's correction for presence or absence of specific bacteria. Multiple linear regressions were used to compare the two groups between pre-irrigation and post-irrigation CFU, using the logarithms of the counts.

RESULTS

In all, 105 patients were recruited, but the swabs from five patients were not received by the laboratory within 3 hours of sampling and so were not cultured and therefore excluded (see Fig 1). The code for the correlation of patient with the dilution of povidone-iodine used for each patient was not broken until all microbiological data were complete.

The results of the pre-irrigation and post-irrigation cultures on 100 patients were available for analysis; 67 patients were female and 33 were male. The mean age was 74 years (range 30–95; SD 10.4 years). Forty eight patients received 5% povidone-iodine and 52 patients received 1% povidone-iodine. The two groups showed no statistical difference with respect to age ($p=0.7$, unpaired t test) or sex ($p>0.999$, Yates's corrected χ^2).

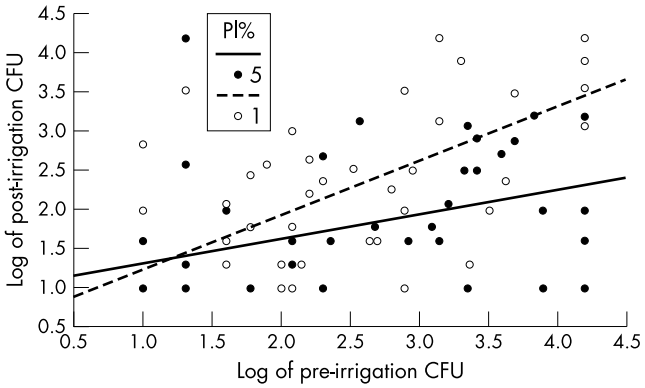

Figure 2 Plot of post-irrigation against pre-irrigation CFU on a logarithmic scale to base 10.

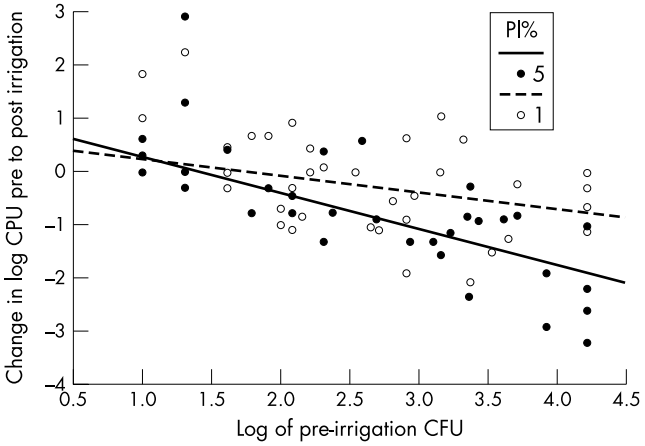

Figure 3 Plot of change in logarithm to base 10 of CFU between pre-irrigation and post-irrigation assessments against logarithm of pre-irrigation CFU.

No patient in the study developed postoperative endophthalmitis or surgical complication as a result of the study, nor suffered any adverse reaction to the irrigation fluid or swabbing procedure.

Qualitative data

The number of CFU decreased following irrigation with povidone-iodine in 84 of the 100 cultures. Of the 16 cultures that showed an increase in CFU, 10 were in the 1% group and six in the 5% group (no statistical difference between the groups). The median CFU in the 1% PI group changed from 120 before irrigation to 100 after irrigation (a drop of 16.7%) and from 100 before irrigation to 40 after irrigation in the 5% PI group (a drop of 60%). The difference in post-irrigation CFU between the two groups was significant (Mann-Whitney U; $p<0.05$).

Quantitative data

As the CFU varied over four orders of magnitude, further analysis was done after logarithmic transformation, and Figure 2 shows a plot of (log) post-irrigation CFU against pre-irrigation CFU, with separate regression lines fitted to each group. An interaction test in a multiple linear regression showed that the slope of the line for the 5% PI group was significantly less than that for the 1% PI group ($t = 2.79$, 96 degrees of freedom, $p=0.006$). Multiple linear regression analysis of the *change* in log CFU, showed that the gradient of the line for 5% PI was significantly steeper in this case (Fig 3). This implies that the 5% PI dosage was especially effective relative to the 1% dose in the context of high initial levels of CFU. Indeed, among those with pre-irrigation CFU >1000, the difference was even more significant: 1% PI subgroup median CFU changed from 5000 pre-irrigation to 3000 post-irrigation (40% reduction); and 5% PI subgroup changed from 3340 pre-irrigation to 110 post-irrigation (96.7% reduction) ($p=0.0014$). Conversely, the difference in CFU in the subgroup with pre-irrigation CFU <1000 showed no statistically significant difference ($p=0.12$)

Table 1 Number (%) of patients with specific bacteria in each treatment group before and after irrigation

	Pre-irrigation		Post-irrigation	
	1% PI	5% PI	1% PI	5% PI
Coagulase negative staphylococci	33 (63)	26 (54)	31 (60)	19 (40)
Micrococcus	6 (11)	5 (10)	4 (8)	3 (6)
Moraxella	0 (0)	1 (2)	0 (0)	0 (0)
Proteus	3 (6)	2 (4)	3 (6)	1 (2)
Staph aureus	5 (10)	9 (19)	5 (10)	5 (10)
α Haemolytic streptococci	5 (10)	5 (10)	2 (4)	3 (6)
Corynebacterium	2 (4)	1 (2)	0 (0)	1 (2)
Peptococcus	1 (2)	2 (4)	1 (2)	0 (0)
Klebsiella	0 (0)	1 (2)	0 (0)	0 (0)
E coli	1 (2)	0 (0)	1 (2)	0 (0)

Bacterial species

Table 1 summarises the results for prevalence of bacteria species in each treatment group before and after irrigation. The type of bacteria isolated were consistent with the bacterial flora found in previous studies.[9–12] None of these either before or after irrigation showed a significant difference between the treatment groups. Twenty six of the 100 cultures were "sterile" (yielded no cultured organism) before irrigation, and 22 of these were also "sterile" following irrigation. The total number of "sterile" cultures post-irrigation was 34. Where post-irrigation bacteria were present, the same species were also present in the pre-irrigation cultures in 95 of 100 cultures. Coagulase negative staphylococci (CNS) were present pre-irrigation and post-irrigation in 29 patients (88%) treated with 1% PI and 18 (69%) of those treated with 5% PI; this difference between the two groups approached significance (Yates, $p=0.07$), while the counts for post-irrigation CNS without pre-irrigation CNS were low in both groups at 2 (10%) and 1 (4%) respectively.

DISCUSSION

Povidone-iodine has been shown to be bactericidal against a wide range of bacteria, and is also effective against fungi, protozoa, and viruses.[3–5] Povidone is hydrophilic and acts as a carrier of the iodine moiety to cell membranes. Once the povidone-iodine complex reaches the cell wall, the free iodine released is rapidly cytotoxic, killing the prokaryotic cell within 10 seconds.[4] Further free iodine is released from the povidone-iodine complex as free iodine is used up, until the available iodine is exhausted. The free iodine concentration has been shown to increase with more dilute concentrations of povidone-iodine, with a maximal free iodine concentration of 24 parts per million at 0.7%.[3] This paradoxical effect follows a "bell curve": concentrations less than 0.05% lose their povidone-iodine complex characteristics and behave like aqueous iodine. Correspondingly, the in vitro bactericidal efficacy of povidone-iodine has been shown to increase at more dilute concentrations of 0.1 to1%, with relatively faster killing rates.[16]

Previous studies have shown that 5% povidone-iodine effectively decreases the bacterial flora of the ocular surface and adnexae,[9–12] and thus theoretically decreases the risk of

endophthalmitis. Other large studies have demonstrated 5% povidone-iodine to directly decrease the incidence of endophthalmitis, although, as noted by the authors, the design of these studies is not ideal: Schmitz *et al* acknowledge the limitations of their retrospective survey design[17]; Speaker and Menikoff conducted a prospective parallel trial, however it was not randomised and antibiotic prophylaxis was an uncontrolled variable.[13]

Our results show a significant difference in bactericidal activity in vivo between 5% and 1% povidone-iodine, with 5% povidone-iodine demonstrating more activity overall. Interestingly, there is no statistical difference between the two strengths with low initial bacterial loads—the difference becomes more marked *only* as the initial load of bacteria increases. This is in contrast with results seen in vitro.[16] In vivo, known inhibitors of povidone-iodine (blood, pus, fat, glove powder[7] as well as protein containing solutions[8]) may be present and may have a role of altering bactericidal efficacy, or the dose or volume of the povidone-iodine may vary depending on the contact time and retention within the conjunctival fornix.

Nevertheless, Roberts *et al* demonstrated, in dogs' eyes in vivo, that 0.2% povidone-iodine (continuous ocular irrigation and periocular scrub for 2 minutes followed by soak for 2 minutes) was equally as bactericidal as 1% and 5% povidone-iodine.[14] Grimes *et al*, in a small study of human eyes of 22 patients, again found 0.02% povidone-iodine irrigation (duration not specified) to be equally bactericidal as 5% povidone-iodine drops.[9] The discrepancies between our results and previous studies may be explained by the povidone-iodine concentration, or the mode or duration of application. Povidone-iodine 1%, although initially more bactericidal, has a lower reservoir of available iodine which is exhausted when the bacterial load is increased. The study in dogs' eyes[14] irrigated the ocular surface with povidone-iodine for a total of 4 minutes (compared to 1 minute in our study), which would allow the available iodine reservoir to be continually replenished and so avoid this problem. We used 1 minute as our time of irrigation as this was closer to the actual time we currently spend irrigating the ocular surface in the anaesthetic room (although the total time the povidone-iodine is in contact with the ocular surface before the operation commences is approximately 4–5 minutes). Irrigating the ocular surface for a longer period may therefore show an improvement in the performance of 1% povidone-iodine (with results similar to those seen in the dogs' eye study). Confirmation of the minimum time of irrigation for each concentration would need to be studied with further prospective randomised studies and was outside the scope and resources of our study. There may be an optimum concentration/time balance which provides acceptable reduction in CFU count, in a reasonable and practical application time without ocular toxicity.

Our results do raise the question of whether an even higher (for example, 10%) concentration would prove even more effective as a bactericidal agent and in a shorter time, but at the risk of toxicity. In many units, 5% povidone-iodine is diluted from hospital stock solution (10%) povidone-iodine (Betadine). The choice of 5% povidone-iodine, as opposed to the 10% stock solution, was based on concerns over the toxicity of the undiluted form[12] and the evidence base to support the use of 5% povidone-iodine. The comparative bactericidal effect of the stock solution (10%) povidone-iodine was not studied in this trial. This product has a typical free iodine concentration of one part per million (0.0001 %), being in a state of dynamic equilibrium with the povidone-iodine complex.

The documented toxicity of topical povidone-iodine is largely limited to conjunctival irritation (incidence of 0.4%)[3] (and from one of the author's personal experience certainly most unpleasant in an unanaesthetised eye!). Keratoconjunctivitis sicca has also been reported.[18] Contact dermatitis is less common (0.04%); however, the risk of a reaction is increased tenfold in the presence of allergy to shellfish or iodine.[3] Although it is not common, the incidence of a conjunctival reaction seems to be directly related to the concentration of povidone-iodine used.[12 18] This may be explained by the pH of povidone-iodine solution, which becomes less acidic with dilution[14 16] and thus more closely approximates the pH of the conjunctiva.

Wille evaluated corneal swelling and endothelial cell loss with specular microscopy following cataract surgery; he did not show any increased corneal damage when povidone-iodine was used.[19] Unfortunately the strength of povidone-iodine used was not mentioned in the study. MacCrae *et al* studied rabbit corneas after application of 10% povidone-iodine and showed moderate transient corneal oedema at 5 minutes, which had resolved by 3 hours,[20] while Tsunoda found the cytotoxicity of povidone-iodine in vivo in rats was less than in vitro.[21]

The cytotoxicity of povidone-iodine on fibroblasts and polymorphonuclear lymphocytes is also directly related to the concentration,[3 14] with concentrations as low as 0.5% retarding wound healing in rabbit models by 24 hours.[22] Intravitreal injection of povidone-iodine in rabbit eyes causes retinal oedema and necrosis, again in a dose dependent fashion[23] and therefore intraocular contamination must be viewed with concern. Establishing the correct therapeutic ratio of concentration dose and time is important, and reducing concentration of the irrigating fluid would be seen as an advantage, but not at the expense of inadequate bacterial kill.

We chose to take our samples before the injection of any local anaesthesia as povidone-iodine is known to be inhibited by blood,[7] and in our experience a small amount of subconjunctival haemorrhage is not uncommon following sub-Tenon's injection. This inhibition is worth considering in current preoperative antisepsis methods (regardless of strength used) as our study shows residual conjunctival bacteria present in 66% of post-irrigation cultures. It would therefore seem prudent to irrigate the ocular surface before local anaesthesia to avoid inhibition of povidone-iodine and thus minimise the presence of conjunctival bacteria, and to extend the effective time before surgical entry into the eye.

A total of 16% of cultures showed an increase in the number of bacteria following irrigation, with 4% showing a new species. These cases occurred in both groups, which would indicate this result may an artefact. Possible sources would be sampling errors of small numbers of bacteria missed by the first swab, or mechanical release of bacteria from the lid margins by the mechanical action of taking the swab. This effect has been noted in previous studies where irrigation with normal saline has caused an increase in the number of bacterial species cultured.[24] We have included all culture results in our analysis none the less.

None of our patients developed postoperative endophthalmitis, but the study is of too low a power to draw conclusions from this. A truly sterile conjunctival fornix is probably not achievable, but reduced external load probably reduces anterior chamber contamination and allows natural defence mechanisms (for example, defensins) not to become overloaded.

SUMMARY

In conclusion therefore, this study supports the use of 5% povidone-iodine in everyday clinical use. Up to 96.7% bacterial kill is achieved with only 1 minute of irrigation. Despite in vitro evidence to the contrary, with a short irrigation time 5% povidone-iodine is more effective than 1%, particularly in the presence of large numbers of bacteria. Exact times and concentrations of povidone-iodine to establish optimum therapeutic ratios require further studies.

ACKNOWLEDGEMENTS

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wish to thank Professor P Aspinall for statistical advice while devising the study; Dr K Kumar and Dr C Scarlett for their contributions in data collection; Drs JD Huggan, AT Crawford, JA Scott, and T Saboor for permission to include patients under their care; Maisie Martindale, clinical pharmacist at Stirling Royal Infirmary, and Tayside Pharmaceuticals at Ninewells Hospital, Dundee for the production of the test solutions, and the staff of the ophthalmic theatre at Stirling Royal Infirmary for their patience.

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Competing interest: None.

This study was presented at the annual meeting of the Scottish Ophthalmological Club on 8 March 2002.

The authors declare no competing or proprietary interest in Betadine or other products.

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NEW BUSINESS

LIONS VISIONGIFT

2201 SE 11th Avenue, Portland OR 97214
27-43 Wormwood Street, Suite 100, Boston MA 02210
800.843.7793 **VisionGift.org**

April 22, 2020

Dear Drs. Li and Chamberlain,

Lions VisionGift (LVG) has discovered a need to request postoperative information on endothelial keratoplasties sooner after surgery than is currently required by the Medical Standards. This will require a change to M1.500 Recipient Follow-up Information. Additionally, we'd like the ability to perform an investigation on graft failures and ocular infections related to the tissue that was imported from another eye bank. Currently, the Standards instruct the source eye bank to perform the investigation. LVG would like the ability to perform investigations on graft failures and ocular infections on tissue we distributed. This will require a change to G1.000 Quality Assurance.

Currently, Medical Standards and Accreditation documents stipulate that postoperative information must be sought between 3-6 months post-surgery. We would like the flexibility to seek it sooner than three months, preferably at 4 weeks.

For endothelial keratoplasties that fail within days to a couple weeks post-transplant, transplanting surgeons have determined a need for regraft in short periods of time. These can be categorized as Early re-grafts vs. primary graft failures but still fall under the need for tissue investigation. In many cases, a regraft has been performed it by the time we seek the 3-6mo postop data.

We feel that it is better to establish an early reporting system to collect data on early graft failures that are associated in particular with DMEK surgery. Performing an investigation on a graft failure where the transplanting surgeon attributes the failure to the tissue closer to the date of the surgery has benefits:

1. Reduction in recall error: the circumstances of the surgery will be fresher in the mind of the surgeon.
2. Increased reporting rate: if a second graft has been placed and is doing well (which is the usual scenario) the surgeon may be less motivated to report distant graft complication.
3. There is a benefit to the processing staff and the surgeon to identify factors in both tissue processing and surgeon technique that may be addressed earlier.

In most cases, LVG imports tissue from another eye bank and that tissue will undergo additional processing prior to distribution. Allowing for the distributing eye bank to perform the investigation on tissue-related graft failures and ocular infections gives us the opportunity to work directly with the reporting/transplanting surgeon to learn what, if anything, went wrong with the tissue we processed. It also allows for consistent data collection.

The Medical Standards apply the investigation policy to all adverse reactions. Changing the Standards and Accreditation documents to reflect this request requires us to delineate investigations of adverse reactions that are related to ocular infection and biological disfunction to reports of systemic infection. The latter necessarily need to be investigated by the eye bank that made the eligibility determination.

Data collection on adverse events including post-keratoplasty infection, primary graft failures, and early re-grafts was prominent topic of discussion moderated by Marian Macsai at the Fall 2019 MAB meeting in San Francisco. EBAA members present agreed on the need to explore better mechanisms collect data on surgery outcomes. We feel that our suggestions here are a step in that direction by tracking down earlier results on transplant surgeries.

Thank you for your consideration.

Kind regards,

Kristin Mathes
COO – Lions VisionGift

M1.500 Recipient Follow-Up Information

4. Each distributing establishment must request postoperative outcome information between three and six months after transplant from the consignee concerning possible adverse reactions on all cornea tissue, except long term preserved, used for human transplantation that was distributed to the consignee by that bank. The distributing eye bank may seek postoperative information sooner than this for endothelial keratoplasties, but no sooner than 4 weeks.. This request must be addressed to the transplanting surgeon and delivered separately from the documentation that accompanies the eye tissue. For special research studies where postoperative outcomes are monitored by other means, by recommendation of the Medical Advisory Board and approval by the EBAA Board of Directors, eye bank solicitation of postoperative outcome information and documentation of such solicitation (under M1.400 item 25) will not be required.

G1.000 Quality Assurance

…

(on page 25 of Oct19 MS) 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~~ notify the source eye bank of the adverse reaction information ~~to the source eye bank~~, which made the donor eligibility determination.

For adverse reactions involving biological dysfunction or ocular infection~~.~~, t~~T~~he ~~source~~ distributing bank must perform an investigation to determine imputability of the tissue, which must include the input of the source eye bank. The distributing eye bank ~~and~~ must report the adverse reaction information within 30 days to the EBAA office for review by the Medical Advisory Board.

For adverse reactions involving systemic infection in a recipient, the source eye bank must perform an investigation to determine imputability, which must include input from the processing and/or distributing eye bank. In accordance with FDA 1271.350, adverse reactions involving a relevant communicable disease must be reported to the FDA within 15 calendar days of receipt of the information if the adverse reaction is fatal, life-threatening, results in permanent impairment or damage or requires medical or surgical intervention. Any deviation reported to a regulatory public health authority will also be reported to EBAA.

For adverse reactions involving systemic infection in a recipient, ~~T~~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.

From:	Matthew Arnett
To:	Jennifer Li; Eric Meinecke
Subject:	MAB Agenda Item Submission
Date:	Monday, May 18, 2020 9:39:18 AM
Attachments:	G1.000 Quality Assurance.docx G1.XXX Supply Management (Final Draft).docx

Good Morning Dr. Li and Mr. Meinecke,

My name is Matthew Arnett and I am the current Chair of the Quality Assurance Committee.

Over the past several years, the Quality Assurance Committee has been working on quality-specific procedures for the EBAA Procedures Manual. This year, we have completed two more that we would like to submit to the Medical Advisory Board for consideration.

The first is a rewrite of G1.000 Quality Assurance. We have updated this procedure to include additional information as well as add more reference information.

The second is a new procedure for managing supplies and qualifying vendors. This is a new procedure for the Manual.

If you have any questions or concerns, please let me know. Otherwise, I thank you for your consideration of these items.

- Matt

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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:

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

   B. Actively supporting, cooperating and assisting the QAP and QA personnel.

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

   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.

7. The Quality Manager or designee is responsible for:

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

   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.

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

E1. EBAA Med Stds – E1.100 Recovery

E2. FDA 21CFR1271.215 Recovery

aseptically excise ocular tissue

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 C 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 how to recall tissue from consignee.	M1. EBAA Med Stds - G1.300 Tissue Recall 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. Establish ment 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.XXX 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***
1. 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).	1. 21 CFR 1271.210(a)
2. 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.	2. 21 CFR 1271.210(a)
3. 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	

4. A designated individual(s) will inspect the supply and pay particular attention to the following:
    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.)

4. 21 CFR 1271.210(a-b)

5. 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

5. 21 CFR 1271.210(d) and C3.300

6. 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
7. Affix a Released Supply identifier to the item
8. Place the supply in the designated appropriate storage location
9. 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

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

10. Store all supplies according to manufacturer's instructions – pay attention to any environmental requirements (such as storage temperature or humidity)

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**

LIONS VISIONGIFT

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May 22, 2020

Jennifer Li, MD
Chair, Medical Advisory Board
Eye Bank Association of America
1101 17th Street NW, Suite 400
Washington DC 20036

Dear Dr. Li,

I suggest a change to our Medical Standards policy M1.600. The standard refers to a Board policy, which is confusing. I suggest, for the sake of clarity, we update the standard to allow for a better understanding of the requirement. After all, statistical reporting is required to provide supporting data for our biovigilance efforts. Additionally, it aids the MAB in making evidence-based decisions. In other words, this is essential information to our field and the ultimate safety of recipients. As such, I propose the following:

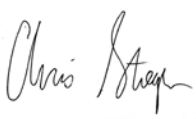
M1.600

Each eye bank shall report statistics to the EBAA ~~in accordance with a policy established by the EBAA Board~~.
Each source eye bank shall report information on surgical technique, indications for surgery, and destination country.

EBAA shall maintain an electronic reporting system through which member eye banks must submit their statistical data. Eye banks shall fully submit their operational data no later than 30 days following the end of March, June, September and December. Data to be submitted will be defined by the EBAA Statistical Ledger and the reporting system.

Thank you for your consideration.

Sincerely,



Chris Stoeger, MBA, CEBT
Chief Executive Officer

Eric Meinecke

From: Jennifer DeMatteo <Jennifer@restoresight.org>
Sent: Friday, May 29, 2020 3:26 PM
To: Eric Meinecke
Subject: FW: Medical Standards Corrections
Signed By: jennifer@restoresight.org

From: Brian Philippy <brianp@lionseyebank.org>
Sent: Thursday, March 12, 2020 5:54 PM
To: Jennifer Li <jennifer.yh.li@gmail.com>; Jennifer DeMatteo <Jennifer@restoresight.org>
Subject: Medical Standards Corrections

Dear Chair,

Review of the EBAA Medical Standards suggests a few minor corrections and addition to definitions may be in order.

- **Distributing Eye Bank**. The entity that provides tissue to a consignee, such as an international eye bank intermediary, unaccredited domestic eye bank, third-party distributor, or transplantation surgeon (whether agency, institution, organization, or researcher). A **process** must be in place to ensure the principles of tracking, traceability, and adverse event reporting.
- **Donation Identification Number (DIN).** A unique identification of a donation/recovery event. The DIN contains three elements: The Facility Identification Number (FIN); a two-digit year code; and a ~~unique six-digit sequence number~~ Product Code assigned by the facility.
- **Product Code.** A unique six-digit sequence assigned by the facility from a list of codes established by ICCBBA. Product Codes have been defined for unique combinations of tissue type, tissue sub-type, storage solution, anatomic position, and processing executed.

Thank you for your consideration.

Sincerely,

Brian Philippy, BChE, BS, CEBT
Director of Transplant and Research
Lions Medical Eye Bank & Research Center of Eastern Virginia, Inc.
(231) 584-3618 (office)
(757) 636-5563 (mobile)

The Lions Medical Eye Bank and Research Center of Eastern Virginia, Inc. is a non-profit transplant agency which provides the opportunity to donate eye tissues, health care professionals the means to end blindness and patients the ability of clearly seeing form, color, and motion.

COVID-19

INFORMATIONAL ALERT:

UPDATED GUIDANCE AND COVID-19 SCREENING RECOMMENDATIONS

May 14, 2020

The EBAA Policy & Position Review Subcommittee of the Medical Advisory Board continues to update guidance and screening recommendations as the COVID-19 pandemic continues to evolve rapidly. Developments in our understanding of this novel SARS-CoV-2 virus and in our ability to screen donors should allow for the continued provision of safe corneal tissue to patients during this time. As we again proceed with elective corneal transplantation procedures across the US, the safety of corneal tissue may be supported by the following:

1. There have been no reported cases of transmission of SARS-CoV, MERS-CoV, or any other coronavirus via transplantation of ocular tissue.
2. Current Medical Standards of the EBAA requires use of a double povidone iodine donor prep; povidone iodine has documented in vitro viricidal activity against coronaviruses.
3. Increased testing of patients in the hospital and outpatient settings for SARS-CoV-2, and greater understanding of COVID-19 symptoms will enhance donor screening and the safety of donor tissue.
4. Medical Director review for final determination of donor eligibility in certain cases allows for further assessment of the full clinical picture and/or case specific scenarios.
5. Donor eligibility criteria remain fluid and complex during the COVID-19 pandemic. Current guidance is more clearly presented in table format for use by eye banks and Medical Directors.

DONOR ELIGIBILITY CRITERIA

PCR Test Status[1]	COVID-19 Signs[2]	COVID-19 Symptoms[3]	Plausible Alternative Etiology of Signs or Symptoms	Close Contact[4]	Eligibility
Positive (in last 28 days)	Yes or No	Yes or No	Yes or No	Yes or No	**Not Eligible**
Negative (post-mortem or recent pre-mortem)	Yes	Yes or No	Yes	Yes or No	**Medical Director Review**
			No	Yes or No	**Not Eligible**
	No	Yes	Yes	Yes or No	**Medical Director Review**
			No	Yes or No	**Not Eligible**
		No	N/A	Yes	**Medical Director Review**
				No	**Eligible**
Not done	Yes	Yes or No	Yes or No	Yes or No	**Not Eligible**
	No	Yes	Yes	Yes	**Not Eligible**
				No	**Medical Director Review**
			No	Yes or No	**Not Eligible**
		No	N/A	No	**Eligible**

[1]RT-PCR SARS-CoV-2 test performed 28 days prior to or less than 24 hours after death. If performed, but result is indeterminate or inconclusive, then donor should be deferred.

[2]Development of one of the following signs consistent with possible COVID-19 infection within the 28 days prior to death:

- ARDS
- Pneumonia
- Pulmonary computed tomography (CT) showing "ground glass opacities" (regardless of whether another organism is present)

[3]Development of acute symptoms consistent with COVID-19 infection within the 28 days prior to death:
One of the following:

- Cough
- Shortness of breath/difficulty breathing

Or

Two of the following:

- Fever
- Chills
- Repeated shaking with chills
- Muscle Pain
- Headache
- Sore throat
- New loss of taste or smell

[4]Close contact is defined by the CDC as:

a) being within approximately 6 feet (2 meters) of a COVID-19 case for a prolonged period of time; close contact can occur while caring for, living with, visiting, or sharing a health care waiting area or room with a COVID-19 case; ***OR***
b) having direct contact with infectious secretions of a COVID-19 case (e.g., being coughed on).

IF such contact occurs while not wearing recommended personal protective equipment (PPE).

DONOR TESTING

At this time, the EBAA is not requiring eye banks to perform post-mortem nasopharyngeal (NP) RT-PCR testing for SARS-CoV-2. However, a negative PCR result may be necessary (in addition to a Medical Director Review) to release certain tissue (see Donor Eligibility Table). The decision to not require post-mortem NP RT-PCR testing for SARS-CoV-2 is based on several considerations including the variable false negative rates of current RT-PCR testing, ranging between 2-22%. Additionally, diagnostic RT-PCR tests for SARS-CoV have not been validated for cadaveric donors and are not intended for donor screening. Currently, the FDA does not recommend the use of laboratory tests to screen asymptomatic blood or plasma donors.[5]

The EBAA acknowledges that other associations, hospital systems, eye banks, departments of health, or governments may require that all donors be tested for COVID-19. Eye banks need to establish a protocol to ensure access to testing notification and results obtained by partner agencies. Results of such testing must be communicated to end-users on Tissue Report Forms or other supporting documents.

Eye banks *may* consider post-mortem testing of donors using currently available nasopharyngeal (NP) RT-PCR testing for SARS-CoV-2. Again, these tests have not been validated for cadaveric samples. If testing is performed, results must be obtained prior to release for transplantation and reported to end-users on Tissue Report Forms or other support documents. Tissue from donors with indeterminant, invalid, or inconclusive results should not be released for transplant. SARS-CoV-2 testing may reduce, but does not eliminate, the potential of transplanting tissue from a donor with COVID-19. Post-mortem testing must be performed within 24 hours of death. Considerations that may help guide the decision to initiate wide-spread donor testing should include epidemiologic factors such as the prevalence of disease within the recovery area, and the availability of supplies (e.g. swabs, viral transport media, reagents, etc.).

Finally, the EBAA does not suggest serologic testing for COVID-19 antibodies. Viral RNA can still be detected in patients despite development of antibodies against SARS-CoV-2.[6,7]

DONOR PREP

A recently published review[8] looked at the persistence of coronaviruses on inanimate surfaces as well as their inactivation with biocidal agents. Their review of the literature found that povidone iodine (0.23 - 7.5%) readily inactivated coronavirus (SARS-CoV and MERS-CoV) infectivity by approximately 4 $\log_{10}$ or more in vitro, with exposure times ranging between 15 seconds and 1 minute. Although we must be careful to extrapolate too much from these findings to the novel coronavirus, SARS-CoV-2, these results certainly support the current EBAA standards for ocular surface prep prior to recovery.

Current EBAA Medical Standard **E1.100 Recovery** requires double exposure of povidone-iodine to the entire surface of the ocular tissue. This would result in rapid viricidal activity against coronaviruses and reduce the likelihood that COVID-19 may be transmitted through corneal transplantation.

The European Centre for Disease Prevention and Control (ECDC) considers this a disinfection or microbial inactivation step that is validated for enveloped viruses. However, it is not known if infectious virus particles are present inside ocular surface cells or within deeper layers of the ocular tissue that may or may not be eliminated by povidone-iodine preparations.

[5]Kampf G, Todt D, Pfaender S, et al. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. *J Hosp Infection*. 2020 Mar;104(3):246-251.

[6]Updated Information for Human Cell, Tissue, or Cellular or Tissue-based Product (HCT/P) Establishments Regarding the Coronavirus Disease 2019 Pandemic". *US Food & Drug Administration*, US Department of Health & Human Services, 1 April 2020, https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/updated-information-human-cell-tissue-or-cellular-or-tissue-based-product-hctp-establishments.

[7]To KK, Tsang OT, Leung WS, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *Lancet Infect Dis.* 2020 Mar 23. doi: 10.1016/S1473-3099(20)30196-1.

[8]Zhao J, Yuan Q, Wang H, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. *Clin Infect Dis*. 2020 Mar 28. doi: 10.1093/cid/ciaa344.

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	January
I. Death Referrals	
A. Total death referrals received by eye bank or entity on behalf of eye bank	
B. Death referrals determined eligible to donate for transplant intent	
II. Tissue Recoveries	
A. Total donors	0
1. Donors recovered not found on a donor registry, nor known to have first-person consent documentatio	
2. Donors recovered found on a donor registry or known to have first-person consent documentation	
B. Eyes and/or corneas recovered with intent for surgical use	
C. Eyes and/or corneas recovered for other uses	
CALCULATION A: Total eyes and/or corneas recovered	0
Validation A: This cell should be less than or equal to 2.	
III. Donor Profiles	
A. Age Profile	
1. Donors aged under one year	
2. Donors aged 1 to 10	
3. Donors aged 11 to 20	
4. Donors aged 21 to 30	
5. Donors aged 31 to 40	
6. Donors aged 41 to 50	
7. Donors aged 51 to 60	
8. Donors aged 61 to 70	
9. Donors aged 71 to 80	
10. Donors aged over 80	
CALCULATION B: Total donors by age	0
Validation B: This value should equal zero.	0
B. Sex Profile	
1. Male	
2. Female	
CALCULATION C: Total donors by sex	0
Validation C: This number should be zero.	0
C. Cause of Death Profile	
1. Heart Disease	
2. Cancer	
3. Cerebral Vascular Accident	
4. Respiratory Disease	
5. Trauma	
6. Other	
CALCULATION D: Total donors by primary cause of death	0
Validation D: This value should be zero.	0
IV. Eligibility and suitability for tissues recovered with intent for surgical use	
A. Reasons tissues were not released (more than one reason per tissue may apply):	
1. Donor eligibility:	
a. Positive or reactive test for communicable disease agent or disease (Tests run by donation	0
i. HIV Antibody (HIV I/II Ab)	
ii. HIV Nucleic Acid Test (HIV NAT)	
iii. Hepatitis B Surface Antigen (HBsAg)	
iv. Hepatitis B Core Antibody (HBcAb)	
v. Hepatitis B Nucleic Acid Test (HBV NAT)	
vi. Hepatitis C Antibody (HCV Ab)	
vii. Hepatitis C Nucleic Acid Test (HCV NAT)	
viii. Syphilis (RPR, VDRL, FTA, etc.)	
ix. HTLV Antibody (HTLV I/II Ab)	
x. West Nile Virus Nucleic Acid Test (WNV NAT)	
xi. Other positive or reactive test for communicable disease	
b. Other communicable disease testing issue	
c. Medical record or autopsy findings	0

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i. Dementia/Neurological Issues	
ii. Sepsis (determined by positive blood cultures)	
iii. Sepsis (determined by other indicators)	
iv. Plasma dilution	
v. Unknown cause of death	
vi. Other	
d. Medical/social history interview:	0
i. Travel	
ii. Dementia/Neurological Issues	
iii. Other	
e. Body Exam	
2. Tissue suitability	0
a. Epithelium	
b. Stroma	0
i. Prior refractive surgery	
ii. Scar	
iii. Infiltrate	
iv. Foreign body	
v. Other	
c. Descemet's membrane	
d. Endothelium	
3. Quality issue	0
a. Storage	
b. Labeling	
c. Processing	
d. Supply or reagent	
e. Environmental control	
4. Other reason prior to tissue release	
B. Total eyes and/or corneas intended for transplant but not released for transplant	
CALCULATION E: Total eyes and/or corneas released for transplant	0
Validation E1: This cell should read, "Valid." The value is valid when the number of reasons for not releasing tissue is greater than or equal to the number of corneas not released for transplant.	Valid
C. Reasons released tissues were not transplanted (more than one reason per tissue may apply):	
1. Transportation issue	
2. Surgeon issue	
3. Recipient issue	
4. Returned and unable to place again	
5. Donor information not available at time of tissue release	
6. Expired or unable to place tissue	
7. Tissue damaged during processing (tissue was released for transplant prior to cut)	
8. Other reason after release of tissue	
D. Total eyes and/or corneas released for transplant but not used for transplant	
Validation E2: This cell should read, "Valid." The value is valid when the number of reasons for released tissue is not transplanted is greater than or equal to the number of corneas released but not transplanted.	Valid
V. Intermediate-Term Tissue Distribution of Source Eye Bank Corneas	
A. Intermediate-term preserved corneas processed into corneal segments (into separate containers for use in multiple recipients)	
B. Number of corneal segments produced from whole, intermediate-term preserved corneas processed into segments (into separate containers for use in multiple recipients)	
C. Intermediate-term preserved corneas, cornea segments or whole eyes, transplanted domestically for:	0
1. PK	
2. EK	0
a. DSEK, DSAEK, DLEK	
b. DMEK or DMAEK	
c. PDEK	

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d. Other EK	
3. ALK	0
a. DALK (Deep Anterior Lamellar Keratoplasty)	
b. SALK (Superficial Anterior Lamellar Keratoplasty)	
c. Other ALK (e.g. peripheral, eccentric, etc.)	
4. KLA	
5. Keratoprosthesis (K-Pro)	
6. Glaucoma shunt patch or other non-keratoplasty use	
7. Other Keratoplasty (e.g. experimental surgery type)	
8. Unknown or Unspecified	
D. Intermediate-term preserved corneas, cornea segments or whole eyes, transplanted internationally for:	0
1. PK	
2. EK	0
a. DSEK, DSAEK, DLEK	
b. DMEK or DMAEK	
c. PDEK	
d. Other EK	
3. ALK	0
a. DALK (Deep Anterior Lamellar Keratoplasty)	
b. SALK (Superficial Anterior Lamellar Keratoplasty)	
c. Other ALK (e.g. peripheral, eccentric, etc.)	
4. KLA	
5. Keratoprosthesis (K-Pro)	
6. Glaucoma shunt patch or other non-keratoplasty use	
7. Other Keratoplasty (e.g. experimental surgery type)	
8. Unknown or Unspecified	
CALCULATION K: Total intermediate-term preserved corneas, cornea segments, and whole eyes used for KERATOPLASTY	0
CALCULATION L: Total intermediate-term preserved eyes and/or corneas used for TRANSPLANT	0
VI. Long-Term Preserved Tissue Preservation and Distribution of Source Eye Bank Tissue	
A. Long-term preserved corneas or whole eyes PRESERVED for transplant	
B. Long-term preserved corneas, cornea segments, or whole eyes DISTRIBUTED for:	0
1. Keratoplasty	
2. Glaucoma shunt patching	
3. Other surgical uses	
C. Long-term preserved corneas, cornea segments, or whole eyes FORWARDED to another entity for final distribution	
D. Sclera or sclera segments PRESERVED for transplantation	
E. Sclera or sclera segments DISTRIBUTED for:	0
1. Prosthesis following enucleation	
2. Glaucoma shunt patching	
3. Other surgical uses	
F. Sclera or sclera segments FORWARDED to another entity for final distribution	
CALCULATION M: Total eyes and/or corneas transplanted and long-term preserved for transplant	0
Validation M: This cell should be zero.	0
VII. Tissue Provided for Non-Surgical Uses	
A. Tissues provided for research (all tissue types)	
B. Tissues provided for physician or technician training (all tissue types)	
VIII. Tissue Processing for Transplant by My Eye Bank	
A. Eye Processing (does not include in situ excision)	0
1. Processed for cornea preservation (corneas only)	
2. Processed for sclera preservation (incl. cornea/sclera preservation, sclera preservation from poles removed after in situ excision, etc.)	
3. Processed for other ocular materials (regardless of cornea or sclera preservation)	
B. Cornea Processing	0

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1. Processed by microkeratome	
2. Processed by laser	
3. Processed by manual dissection (e.g. DMEK, DMAEK, cornea dissection for long-term preservation)	
4. Processed by transfer into long-term preservation (incl. sectioned tissue only once)	
5. Processed by other methods	
IX. Countries of Destination	
A. Country: (Home Country - Domestic)	
B. Country:	
C. Country:	
D. Country:	
E. Country:	
F. Country:	
G. Country:	
H. Country:	
I. Country:	
J. Country:	
K. Country:	
L. Country:	
M. Country:	
N. Country:	
O. Country:	
P. Country:	
Q. Country:	
R. Country:	
S. Country:	
T. Country:	
U. Country:	
V. Country:	
W. Country:	
X. Country:	
Y. Country:	
Z. Country:	
Validation X (Domestic count): This cell should be zero.	0
Validation Y (International count): This cell should be zero.	0
X. Indications for Penetrating Keratoplasty	
A. Post-cataract surgery edema	0
1. Domestic - Post-cataract surgery edema	
2. International - Post-cataract surgery edema	
B. Ectasias/Thinnings	0
1. Domestic - Ectasias/Thinnings	
2. International - Ectasias/Thinnings	
C. Endothelial Dystrophies	0
1. Domestic - Endothelial Dystrophies	
2. International - Endothelial Dystrophies	
D. Repeat corneal transplant	0
1. Domestic - Repeat corneal transplant	
2. International - Repeat corneal transplant	
E. Other degenerations or dystrophies	0
1. Domestic - Other degenerations or dystrophies	
2. International - Other degenerations or dystrophies	
F. Refractive	0
1. Domestic - Refractive	
2. International - Refractive	
G. Microbial keratitis	0
1. Domestic - Microbial keratitis	
2. International - Microbial keratitis	

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H. Mechanical (non-surgical) or chemical trauma	0
1. Domestic - Mechanical (non-surgical) or chemical trauma	
2. International - Mechanical (non-surgical) or chemical trauma	
I. Congenital opacities	0
1. Domestic - Congenital opacities	
2. International - Congenital opacities	
J. Pterygium	0
1. Domestic - Pterygium	
2. International - Pterygium	
K. Non-infectious ulcerative keratitis, thinning, or perforation	0
1. Domestic - Non-infectious ulcerative keratitis, thinning, or perforation	
2. International - Non-infectious ulcerative keratitis, thinning, or perforation	
L. Other causes of corneal opacification or distortion	0
1. Domestic - Other causes of corneal opacification or distortion	
2. International - Other causes of corneal opacification or distortion	
M. Other causes of endothelial dysfunction	0
1. Domestic - Other causes of endothelial dysfunction	
2. International - Other causes of endothelial dysfunction	
Z. Unknown, unreported, or unspecified	0
1. Domestic - Unknown, unreported, or unspecified	
2. International - Unknown, unreported, or unspecified	
CALCULATION N: Total indications for penetrating keratoplasty	0
Validation N1 (Domestic indications): This value should be zero.	0
Validation N2 (International indications): This value should be zero.	0
XI. Indications for Anterior Lamellar Keratoplasty	
B. Ectasias/Thinnings	0
1. Domestic - Ectasias/Thinnings	
2. International - Ectasias/Thinnings	
D. Repeat corneal transplant	0
1. Domestic - Repeat corneal transplant	
2. International - Repeat corneal transplant	
E. Other degenerations or dystrophies	0
1. Domestic - Other degenerations or dystrophies	
2. International - Other degenerations or dystrophies	
F. Refractive	0
1. Domestic - Refractive	
2. International - Refractive	
G. Microbial keratitis	0
1. Domestic - Microbial keratitis	
2. International - Microbial keratitis	
H. Mechanical (non-surgical) or chemical trauma	0
1. Domestic - Mechanical (non-surgical) or chemical trauma	
2. International - Mechanical (non-surgical) or chemical trauma	
I. Congenital opacities	0
1. Domestic - Congenital opacities	
2. International - Congenital opacities	
J. Pterygium	0
1. Domestic - Pterygium	
2. International - Pterygium	
K. Non-infectious ulcerative keratitis, thinning, or perforation	0
1. Domestic - Non-infectious ulcerative keratitis, thinning, or perforation	
2. International - Non-infectious ulcerative keratitis, thinning, or perforation	
L. Other causes of corneal opacification or distortion	0
1. Domestic - Other causes of corneal opacification or distortion	
2. International - Other causes of corneal opacification or distortion	
Z. Unknown, unreported, or unspecified	0

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1. Domestic - Unknown, unreported, or unspecified	
2. International - Unknown, unreported, or unspecified	
CALCULATION O: Total indications for anterior lamellar keratoplasty	0
Validation O (Domestic Indications): This value should be zero.	0
Validation O (International Indications): This value should be zero.	0
XII. Indications for Endothelial Keratoplasty	
A. Post-cataract surgery edema	0
1. Domestic - Post-cataract surgery edema	
2. International - Post-cataract surgery edema	
C. Endothelial Dystrophies	0
1. Domestic - Endothelial Dystrophies	
2. International - Endothelial Dystrophies	
D. Repeat corneal transplant	0
1. Domestic - Repeat corneal transplant	
2. International - Repeat corneal transplant	
M. Other causes of endothelial dysfunction	0
1. Domestic - Other causes of endothelial dysfunction	
2. International - Other causes of endothelial dysfunction	
Z. Unknown, unreported, or unspecified	0
1. Domestic - Unknown, unreported, or unspecified	
2. International - Unknown, unreported, or unspecified	
CALCULATION P: Total indications for endothelial keratoplasty	0

LATE ADDITIONS

FOR INFORMATION & REVIEW