Certificate of Compliance

(COC-0001, Rev. 06)

This is to certify that BioTissue Holdings Inc. (parent company of BioTissue Ocular Inc. and BioTissue Surgical Inc., from hereon, collectively referred to as 'the Company') is a provider of 361 'Human Cells, Tissues and Cellular and Tissue Based Products' (HCT/Ps) as well as a medical device manufacturer and specification developer for BioTissue Ocular. BioTissue Holdings Inc. meets the requirements of the United States Food & Drug Administration (FDA) for the manufacture and distribution of AmnioGraft®, CAM360 AmnioGraft™, and AmnioGuard® (HCT/Ps) and Prokera® Classic, Prokera® Slim, Prokera® Plus and Prokera® Clear (medical devices). These products comply with the requirements specified in Current Good Tissue Practices (21 CFR Part 1271), current AATB Standards and Quality System Regulations for Medical Devices (21 CFR Part 820). BioTissue Holdings Inc. certifies that:

- ✓ Prokera Classic, Prokera Slim, Prokera Plus and Prokera Clear are cleared by the US FDA [510(k) Clearance] as Class II medical devices and by Health Canada as Class IV medical devices and follow the requirements under 21 CFR 820 and Current Good Manufacturing Practice (CGMP) regulations for medical devices
- ✓ AmnioGraft, CAM360 AmnioGraft, and AmnioGuard are regulated under 21 CFR 1271 and Section 361 of the Public Health Service Act (PHSA) and manufactured according to Current Good Tissue Practice (CGTP) regulations established by the US Food & Drug Administration (FDA)
- ✓ The Company is registered and inspected as a manufacturer and distributor with products listed with the FDA *(available upon request)*
- ✓ The Company is registered with Health Canada, respecting the Safety of Human Cell Tissues and Organs for Transplantation *(available upon request)*
- ✓ The Company is accredited by the American Association of Tissue Banks (AATB) *(available upon request)*
- ✓ The Company's facilities and Quality Management Systems are inspected by the FDA, AATB, and notified bodies performing ISO 13485:2016 and Medical Device Single Audit Program (MDSAP) certification
  (available upon request)
- ✓ The Company is compliant with AATB standards and FDA requirements for tissue processing
- ✓ The Company's Quality Management System is certified to the international standard, ISO 13485:2016 for the design and development, and manufacture of corneal inserts that incorporate the amniotic membrane for the area of ophthalmology *(available upon request)*
- ✓ The Company's Quality Management System is in compliance with the Medical Device Single Audit Program (MDSAP) recognized by the FDA and Health Canada
- ✓ The Company is licensed by California and New York State Departments of Health *(available upon request)*
- ✓ The Company is registered with Maryland, Illinois, and Oregon *(available upon request)*
- ✓ The Company has been issued a waiver by the State of Florida exempting registration and certification as a tissue bank since the Company does not procure, process, store or

distribute cadaveric tissue *(available upon request)*

Product Description:

- AmnioGraft and CAM360 AmnioGraft are cryopreserved human amniotic membrane products which are aseptically processed, and cell devitalized. These products are delivered on a non-implantable, gridded paper backing for easier handling and application. CAM360 AmnioGraft is terminally sterilized via gamma irradiation with a Sterility Assurance Level (SAL) of 10^{-6}.
- AmnioGuard is a cryopreserved ultra-thick human amniotic membrane product derived from umbilical cord, which is aseptically processed, devascularized, and cell devitalized.
- AmnioGraft and AmnioGuard are manufactured, using the CryoTek® cryopreservation process, from donated human birth tissue acquired after elective C-section delivery.
- CAM360 AmnioGraft is manufactured, using the SteriTek® preservation process, from donated human birth tissue acquired after elective C-section delivery.
- On the ocular surface, AmnioGraft exerts anti-inflammatory, anti-scarring and anti-angiogenic actions to promote wound healing, and supports epithelial adhesion and differentiation. The FDA has allowed these therapeutic claims for ocular surface use.
- Prokera Classic, Prokera Slim, Prokera Plus and Prokera Clear are corneal-epithelial devices consisting of an ophthalmic conformer that incorporates amniotic membrane (AmnioGraft). Prokera Classic, Prokera Slim, Prokera Plus and Prokera Clear are for physician use only and are intended for use in eyes in which ocular surface cells have been damaged or underlying stroma is inflamed and scarred.
- The cells of these tissues have been devitalized to reduce the possibility of graft rejection while retaining the natural biological properties.
- There is no pooling of tissues from different donors throughout the manufacturing process.

Tissue Place of Origin: Human amniotic membrane and umbilical cord tissues are only retrieved from donors within the U.S. who have donated tissue after elective Cesarean Section delivery.

- ✓ The Company acquires birth tissue (placenta, amniotic membrane and umbilical cord) through an internal acquisition program or contracts directly with FDA-registered acquisition partners *(available upon request)*
- ✓ Tissue is acquired after elective C-section from mothers birthing live, healthy babies

Donor Suitability, Selection & Testing:

- This tissue was procured from a donor that was determined to be eligible based on the results of donor screening and testing. HCT/P donor eligibility and placenta suitability, which is based on the results of donor screening at delivery for infectious, malignant, neurological & auto-immune diseases and for other exposures or social habits, has been determined and documented by BioTissue Holdings Inc.
- A blood specimen, drawn within ± 7 days of donation, has undergone serological testing by a laboratory registered with the FDA to perform donor testing and certified to perform such testing

on human specimens in accordance with the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and 42 CFR Part 493, or that has met equivalent requirements as determined by the Centers for Medicare and Medicaid Services (CMS). The donor has been tested for the following infectious diseases, and the results were non-reactive:

- HIV-1 & HIV-2 Antibody
- HIV-1 (RNA-NAT)
- Hepatitis B Surface Antigen (HBsAg)
- Hepatitis B Core Antibody (HBcAb)
- Hepatitis B (HBV, DNA-NAT)
- Hepatitis C Antibody (HCVAb)
- Hepatitis C Virus, HCV (RNA-NAT)
- Syphilis (RPR)
- HTLV I & II Antibody (HTLV I/II Ab)
- West Nile Virus (WNV, RNA-NAT)

Process Controls: Final product is processed for BioTissue Ocular in the Company's GMP Clean Room Facility using aseptic methods under ISO Class 5 Biological Safety Cabinets. The final product is tested by an independent CLIA-certified lab and is released after microbiological testing for aerobic, anaerobic, and fungal organisms shows no microbiological growth. Additionally, technical review and Quality Assurance review and approval is performed before product release. Aseptic process validations and container closure integrity testing of the final packaging system have been performed and were found to be acceptable.

Labeling & Traceability: Each finished product (HCT/P or medical device) is assigned and labeled with a unique identification code that relates the final product to the donor. There is a system established and maintained to track the final product from the consignee to the donor and from the donor to the consignee or final disposition.

Stability: BioTissue Ocular's products (AmnioGraft, CAM360 AmnioGraft, AmnioGuard, Prokera Classic, Prokera Slim, Prokera Plus and Prokera Clear) are preserved in validated and patented storage solutions. Validation studies have been conducted to establish the expiration date of these amniotic membrane products when stored between -80°C - 4°C (-112°F – 39.2°F). Validation studies have also been conducted to establish the expiration date of CAM360 AmnioGraft when stored between -20°C – 25°C (-4°F – 77°F). The storage conditions and expiration date are reflected in the labeling for BioTissue Ocular's products. Validation studies include analysis of tissue sections followed by morphological staining of test and control tissue samples, as well as package and container closure integrity testing of final packaging systems.

Packaging/Shipping: See individual Product Inserts for packaging information. The shipping containers have been validated via simulated and actual shipping condition testing. These studies also provide objective evidence that the package integrity is maintained throughout transit therefore providing sufficient protection to the product during the transportation process.

Storage: AmnioGraft, AmnioGuard, Prokera Classic, Prokera Slim, Prokera Plus, and Prokera Clear are stored at cold temperature storage before shipping to retain their natural function and integrity. These cryopreserved amniotic membrane products are shipped in a shipper validated to hold the required temperature during shipping.

CAM360 AmnioGraft is stored at controlled room temperature (20°C - 25°C, 68°F - 77°F) before shipping and shipped in a validated shipping container.

Upon receipt of a BioTissue Ocular product, ensure the validated time on the shipper has not expired, if applicable. Remove the product and store it accordingly until use.

Product	Location & Temperature	Use After Receipt
AmnioGraft, AmnioGuard, Prokera Classic, Prokera Slim, Prokera Plus, Prokera Clear	-80°C – 4°C (-112°F – 39.2°F) Example: ultra-low temperature freezer, standard freezer, or standard refrigerator	Within the expiration date printed on product packaging (shelf-life is 2 years from date of manufacture)
CAM360 AmnioGraft	-20°C – 25°C (-4°F – 77°F)	Within the expiration date printed on product packaging (shelf-life is 1 year from date of manufacture)

In accordance with the storage table above, AmnioGraft, AmnioGuard, and Prokera products exposed to controlled room temperature (20°C - 25°C, 68°F - 77°F) for up to 6 hours may be returned to cold temperature storage (-80°C - 4°C, -112°F - 39.2°F) as long as the packaging remains unopened and intact.

Voluntary Correction/Removal Procedures: The Company has detailed procedures in place to respond appropriately to product concerns that may affect the health and safety of the patient. The current tracking system facilitates any correction or removal event that may occur. All affected customers will be immediately notified by verbal or electronic communication. Formal written notification will also be issued.

Refer to BioTissue Ocular's individual Product Inserts for more details.

DocuSigned by:
Eden Venti
Signer Name: Eden Venti
Signing Reason: I approve this document
Signing Time: 06/03/24 | 11:51 AM EDT
90BDEFBC8F0B44AD81541A695E914553

06/03/24 | 11:51 AM EDT

Eden Venti
Vice President of Quality
BioTissue Holdings Inc.

Date