Certificate of Compliance

(COC-0001, Rev. 05)

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® and AmnioGuard® (both HCT/Ps) and Prokera® Classic, Prokera® Slim, Prokera® Plus and Prokera® Clear (medical devices) as 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® 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 certification under ISO 13485:2016 *(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)*

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Product Description:

- AmnioGraft® is a cryopreserved human amniotic membrane product which is aseptically processed and cell devitalized. AmnioGraft® is delivered on a non-implantable, gridded paper backing for easier handling and application.
- 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® 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 biologic 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 United States 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 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 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. Final product is tested by an independent CLIA-certified lab and is released after microbiological testing for aerobic, anaerobic and fungal organisms shows no growth. Additionally, technical review and Quality Assurance review and approval is performed before product release. Process validations of aseptic processing, container closure integrity testing of the final packaging system, and antimicrobial effectiveness of the final packaging system have been performed and found the systems 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®, 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). The storage conditions and expiration date are reflected in the labeling for these 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: BioTissue Ocular's products (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. Upon receipt, ensure the validated time on the shipper has not expired. Remove the product and store accordingly until use.

Location & Temperature	Use After Receipt
-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)

Amniotic membrane products and ultra-thick amniotic membrane products derived from umbilical cord 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) in accordance with the storage table above 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: 04/25/23 | 12:23 PM EDT
90BDEFBC8F0B44AD81541A695E914553

04/25/23 | 12:23 PM EDT

Eden Venti
Vice President of Quality
BioTissue Holdings Inc.

Date

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Certificate Of Completion

Envelope Id: 3EB0717C59274C57A8C98BB7B5D8EF84
Status: Completed
Subject: Complete with DocuSign: COC-0001 Rev. 05 (1).docx
Source Envelope:
Document Pages: 4
Signatures: 1
Certificate Pages: 1
Initials: 0
AutoNav: Enabled
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Envelope Originator:
Katia Izquierdo
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Signer Events	Signature	Timestamp
Eden Venti eventi@biotissue.com VP, QA BioTissue Holdings Inc. Security Level: Email, Account Authentication (Required)	Eden Venti Signature Adoption: Pre-selected Style Signature ID: 90BDEFBC-8F0B-44AD-8154-1A695E914553 Using IP Address: 170.55.57.82 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 4/21/2023 1:25:51 PM Resent: 4/25/2023 11:06:48 AM Viewed: 4/25/2023 12:23:21 PM Signed: 4/25/2023 12:23:48 PM

Electronic Record and Signature Disclosure:
Not Offered via DocuSign

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	4/21/2023 1:25:51 PM
Certified Delivered	Security Checked	4/25/2023 12:23:21 PM
Signing Complete	Security Checked	4/25/2023 12:23:48 PM
Completed	Security Checked	4/25/2023 12:23:48 PM

Payment Events	Status	Timestamps