biotissue®

Certificate of Compliance

(COC-0001, Rev 04)

This is to certify that TissueTech Inc. (parent company of Amniox Medical, Inc. and Bio-Tissue, 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 Bio-Tissue, Inc. TissueTech, 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®, PROKERA® Slim, PROKERA® Plus and PROKERA® Clear (medical devices) as specified in Current Good Tissue Practices (21 CFR Part 1271), FDA Guidance Documents, current AATB Standards and Quality System Regulations for Medical Devices (21 CFR Part 820). TissueTech, Inc. certifies that:

- ✓ The Company is registered as a manufacturer and distributor with products listed with the US FDA *(available upon request)*
- ✓ AmnioGraft and AmnioGuard are designated by the FDA as Tissue Products (HCT/Ps)
- ✓ Bio-Tissue holds a Drug Master File on file with the FDA for its HCT/P – AmnioGraft
- ✓ PROKERA, PROKERA Slim, PROKERA Plus and PROKERA CLEAR are Class II medical devices cleared by the FDA [510(k) clearance] and Class IV medical devices regulated by Health Canada *(available upon request)*
- ✓ The Company is accredited by the American Association of Tissue Banks (AATB) *(available upon request)*
- ✓ 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) by the FDA and Health Canada.
- ✓ The Company contracts directly with FDA-registered acquisition partners *(available upon request)* for the acquisition of Birth Tissue (Placenta, Amnion and Umbilical Cord) and does not second source tissue or products
- ✓ Tissue is acquired after elective C-section from mothers birthing live, healthy babies.
- ✓ The Company's facilities and Quality Management Systems are periodically inspected by the FDA and by qualified external auditors
- ✓ The Company is licensed by the States of New York and California Departments of Health *(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 registered with Maryland, Illinois, and Oregon *(available upon request)*
- ✓ The Company is compliant with AATB and FDA guidelines for tissue processing
- ✓ 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 AmnioGuard are Bio-Tissue trademarks for processed and cryopreserved human Amniotic Membrane tissue retrieved from donated birth tissue after elective Cesarean Section delivery. These Amniotic Membrane products are currently designated by the FDA as a tissue product under PHS Act 361 HCT/P (human cells, tissues and cellular and tissue-based products).
- AmnioGraft has therapeutic actions that promote anti-scarring, anti-inflammation and anti-angiogenesis and pain reduction. It supports epithelial healing in addition to serving as a physical barrier against the external environment on the ocular surface. The FDA has allowed these therapeutic claims for ocular surface use.
- PROKERA, 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. PROKERA, PROKERA Slim, PROKERA Plus and PROKERA Clear are corneal-epithelial devices consisting of an ophthalmic conformer that incorporates amniotic membrane (AmnioGraft). PROKERA, 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. They can be used as grafts for ocular reconstruction procedures.
- The cell activity of these tissues has been inactivated to reduce the possibility of graft rejection while retaining the natural biologic properties.

Tissue Place of Origin: Human amniotic membrane tissues are only retrieved from donors within the United States who have donated tissue after elective Cesarean Section delivery.

Donor Suitability, Selection & Testing: Birth tissue is recovered aseptically after elective Cesarean Section from mothers birthing live, healthy babies. Mothers donate the tissue under full informed consent. The mothers are screened at delivery for infectious, malignant, neurological and auto-immune diseases and other exposures or social habits to determine the suitability for human transplantation. The suitability of the donation is determined by reviewing medical records and history of possible transmissible diseases (via a standard questionnaire) and reviewing physical examinations that have been performed. Mothers are serologically tested by an independent CLIA-certified lab at the time of delivery and must be found non-reactive using FDA-licensed, approved, or cleared test kits for the following tests:

- HIV 1 (NAT-RNA)
- HIV 1 & 2 (antibody)
- Hepatitis B (NAT)
- Hepatitis B surface antigen (HBsAg)
- Hepatitis B core antibody (HBcAb)
- Hepatitis C Antibody (HCVAb)
- Hepatitis C antibody, HCV (NAT-RNA)
- HTLV 1 & 2 antibodies
- Syphilis
- West Nile Virus (WNV, RNA-NAT)

Process Controls: Final product is processed for Bio-Tissue 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 once microbiological testing for aerobic, anaerobic and fungal organisms shows no growth. Additionally, technical review and Quality Assurance approval is performed before product release. Process validations of aseptic processing, container and 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. With the exception of the human tissue, all materials and reagents used to process the tissue products are sterile.

Labeling & Tracking: 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/Solutions: Bio-Tissue's products (AmnioGraft, AmnioGuard, PROKERA, PROKERA Slim, PROKERA Plus and PROKERA Clear) are preserved in validated and patented storage media made of Dulbecco's Modified Eagle Medium and Glycerol (1:1) containing Ciprofloxacin and Amphotericin B. Cryopreservation is vital for maintaining the integrity and biologic activity of Amniotic Membrane. The biological functions are retained with this cryopreservation method. Validation studies have been conducted to establish the expiration date of these amniotic membrane products when stored between 4°C and -80°C. The storage conditions and expiration date are reflected in the labeling for these products. Validation studies included analysis of frozen sections followed by morphological staining of test and control tissue samples, as well as package and container closure integrity validation of final packaging systems.

Packaging/Shipping: See individual Product Inserts for packaging information. The shipping containers (NanoCool systems) have been validated via simulated and actual shipping condition testing. The validation studies concluded that the shipping containers currently in use for final product distribution and shipment effectively maintain temperatures below 21°C for up to 72 hours when tested against the ISTA-7D seventy-two (72) hour summer profile (standard shipper) and for up to 96 hours when tested against the ISTA-7D seventy-two-hour (modified to 96 hours) summer profile (long haul shipper). 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: Bio-Tissue's products (AmnioGraft, AmnioGuard, PROKERA, PROKERA Slim, PROKERA Plus and PROKERA Clear) are stored at -80°C (-112°F) before shipping to retain their natural function and integrity. These cryopreserved Amniotic Membrane products are shipped in validated NanoCool shipping systems. If the unit is not used immediately, the following guidelines should be followed for the storage of Bio-Tissue's products:

Usage after receipt of Tissue	Storage Temperature	Acceptable Storage Location	Storage Time
Few hours after package arrival	Below 21°C (Below 69.8°F)	Unopened insulated shipping container	Within the expiration date on outer shipping box
Long Term Storage	-80°C – 4°C (-112°F – 39.2°F)	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 exposed to controlled room temperature (20°C to 25°C) for up to 6 hours may be returned to cold temperature storage 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 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 Bio-Tissue's individual Product Inserts for more details.

Sherry Saurini

Sherry Saurini
Vice President of Quality
TissueTech, Inc. & its Subsidiaries

06 July 2020
Date