READ BEFORE USING

MTF AORTIC AND PULMONIC ALLOGRAFT VALVES/CONDUITS

CAUTION: ALLOGRAFT IS FOR SINGLE USE ONLY.
ASEPTICALLY PROCESSED. PASSES USP <71> FOR STERILITY.

CAUTION: SPECIAL HANDLING INSTRUCTIONS

THIS ALLOGRAFT HAS BEEN CRYOPRESERVED AND SHIPPED IN THE VAPOR PHASE OF LIQUID NITROGEN (-100°C TO -196°C). DO NOT STORE THE PACKAGE CONTAINING THE CARDIOVASCULAR ALLOGRAFT IN LIQUID NITROGEN; THE PACKAGE MUST BE MAINTAINED IN THE VAPOR ENVIRONMENT UNTIL THAWING FOR TRANSPLANTATION DURING SURGERY.

DO NOT USE THE ALLOGRAFT IF IT HAS BEEN IMMERSED IN LIQUID NITROGEN.

WARNING: INNER CONTENTS MUST NOT BE REMOVED FROM THE OUTER FIBERBOARD BOX FOR STORAGE. HANDLE WITH CARE AS PACKAGING MATERIAL IS FRAGILE AT STORAGE TEMPERATURES. CHECK PACKAGING INTEGRITY PRIOR TO USE.

THIS HUMAN ALLOGRAFT IS RECOVERED FROM A DECEASED DONOR WHOSE LEGAL NEXT-OF-KIN HAS GIVEN PERMISSION FOR THE DONATION. THIS RECOVERY WAS PERFORMED USING ASEPTIC TECHNIQUES. PROCESSING AND PACKAGING WERE PERFORMED UNDER ASEPTIC CONDITIONS. TERMINAL STERILIZATION AGENTS WERE NOT USED IN THE PROCESS.

NO ADDITIONAL STERILIZATION STEP IS TO BE PERFORMED BY THE USER. CAUTION: RESTRICTED TO USE BY A PHYSICIAN.

DESCRIPTION

Aortic and pulmonary heart valves are two of four valves which function in a normal heart. They are located at the orifices of the aorta and pulmonary artery at their origins from the left and right ventricles respectively. Aortic valves are thicker and stronger than pulmonic valves. Each valve consists of three half-moon shaped (semilunar) flaps (also referred to as “cusps” or “leaflets”) formed by a duplication of the membranous lining of the aorta and pulmonary artery respectively, and strengthened by fibrous tissue. The membranous tissue consists of an acellular matrix (composed of proteins [collagen and elastin], acid mucopolysaccharides [proteoglycans] and other high and low molecular weight molecules) which houses cellular components (mostly fibrocytes).

Aortic and pulmonic allograft valves are procured from donor human hearts. When cryopreserved promptly after retrieval, aortic and pulmonic allograft valves are structurally similar to their counterparts in the living individual. Aortic and pulmonic allograft valves are dissected from a donor heart in a manner which preserves segments of the aorta and pulmonary trunk respectively and are referred to as valved conduits (valve/conduit).

Aortic valve/conduit

Pulmonic valve/conduit

DESCRIPTION – cont’d
Human heart valves are structures which permit the flow of blood in one direction only. When the ventricles contract (ventricular systole), the aortic and pulmonary valve leaflets are pushed open by the flow of blood from the ventricles to the aorta and pulmonary trunk respectively. When the ventricles are at rest (ventricular diastole) the aortic and pulmonary valve leaflets are pushed closed by blood rebounding off the walls of the aorta and pulmonary trunk respectively, effectively preventing the flow of blood back into the ventricles. Aortic and pulmonic allograft valves serve the same function as their counterparts in the living heart in that they permit the flow of blood in one direction only.

This allograft is a freely given anatomical gift that has been collected post-mortem from donors between the ages of newborn (minimum weight of 6 pounds) and 60 years, who have been screened for certain infections and malignant disease. The donor medical/social history is obtained and serologic testing is performed in accordance with Food and Drug Administration (FDA) requirements and the Standards of the American Association of Tissue Banks (AATB) current at the time of donation. The tissue was collected under aseptic conditions, and aseptic processing, including disinfection, was performed in a Class 100 laminar flow environment.

During packaging, tissue samples were obtained for sterility testing according to procedures in the current U.S. Pharmacopeia or Title 21 § 610.12 of the Code of Federal Regulations. This allograft is supplied in single-patient, single-use packaging consisting of two (2) pouches. The inner pouch contains the allograft suspended in cryoprotectant. The outer pouch contains the inner pouch: the exterior of the outer pouch is not sterile and must not be placed in a sterile field. The packaged allograft is stored inside a foam lined fiberboard box. This tissue was cooled at a controlled rate to the frozen state and is provided in tissue culture medium containing 10% DMSO (Dimethyl Sulfoxide) and 10% Fetal Calf Serum.

**INDICATIONS FOR USE**

Aortic and pulmonic valve allografts are used for left and right ventricular outflow tract procedures. As described in the literature, the following properties have been reported for allograft heart valves.

1. The heart valve allograft is dissected from a heart and is comprised of the valve, a portion of the vascular conduit and myocardium.
2. The heart valve allograft has been cryopreserved in tissue culture medium containing fetal calf serum and a cryoprotectant dimethyl sulfoxide (DMSO).
3. Reported heart valve allograft failures have included those which exhibited valvular insufficiency and disappearance of valve leaflets.
4. The heart valve allograft performs as a substitute for an autologous heart valve.

Aortic and pulmonic allografts have a wide range of uses in cardiovascular repair surgery. They are used to repair or replace both congenital and acquired cardiac valve dysfunctions. The aortic valve allograft, or valved conduit, is typically used in left ventricular outflow tract procedures. The pulmonic valve allograft, or valved conduit, can be used in both left and right ventricular outflow tract procedures.

Common congenital abnormalities for which allograft valves/valved conduits can be and have been used include, but are not limited to, the following:

1. Tetralogy of Fallot
2. Transposition of the great vessels
3. Truncus arteriosis
4. Valve atresia/stenosis
5. Hypoplastic (left) heart syndrome
6. Congenital valve malformations/disorders such as: Bicuspid valve or floppy aortic valve

Some acquired conditions for which allograft valves/valved conduits can be and have been used include, but are not limited to, the following:

1. Calcific valve stenosis
2. Atherosclerotic valve stenosis/insufficiency
3. Rheumatic heart disease
4. Endocarditis
5. Failure of prosthetic/bioprosthetic/allograft valve
6. Infection of prosthetic/bioprosthetic/allograft valve.
7. Hypertensive heart disease
8. Aortic dissection with valvular incompetence
9. Aortitis with valvular incompetence
10. Annular ectasia

CONTRAINDICATIONS

Tissues distributed by MTF are contraindicated in the following circumstances:

- Infection in or around the intended surgical site
- Previous adverse reactions/outcome to use of allograft vascular products
- Fever
- Uncontrolled diabetes
- Pregnancy
- Inability to cooperate with and/or comprehend post-operative instructions

ADVERSE EFFECTS

Possible adverse effects of using human tissues include but are not limited to:

- Infection in or around surgical site
- Disease transmission
- Undesirable immune reaction to the allograft implanted
- Failure of the allograft to perform as expected
- Adverse reaction to trace amounts of processing agents

Within the United States: Adverse outcomes attributable to the tissue must be promptly reported to MTF.
Outside of the United States: Adverse outcomes attributable to the tissues must be promptly reported to your local representative.

CAUTIONS

Trace amounts of Polymyxin B Sulfate, Cefoxitin, Lincomycin, Vancomycin, DMSO and Fetal Calf Serum may be present. Caution should be exercised if the recipient is allergic to any of these substances. The specific antibiotics used in the disinfection steps during processing are:

- Cefoxitin 240 μg/ml
- Lincomycin 120 μg/ml
- Polymyxin B 1000 U/ml
- Vancomycin 50 μg/ml

Extensive medical screening procedures have been used in the selection of all tissue donors for MTF. Transmission of infectious diseases such as HIV or Hepatitis, as well as a theoretical risk of the Creutzfeldt-Jakob (CJD) agent, may occur in spite of careful donor selection and serological testing.

TISSUE INFORMATION

ALL ALLOGRAFTS ARE FOR SINGLE PATIENT USE ONLY. The allografts are not terminally sterilized. Each allograft is aseptically processed and the finished product passes USP <71> for sterility. Do not subject allografts to additional sterilization procedures. Do not use portions of an allograft from one container on multiple patients. If allograft is not implanted, do not refreeze. Dispose of excess or unused tissue in accordance with recognized procedures for discarding regulated medical waste materials.

ANY DAMAGED ALLOGRAFT PACKAGING (FIBERBOARD BOX, INNER AND OUTER POUCHES) AND INVOLVED ALLOGRAFT MUST BE RETURNED TO MTF FOR INSPECTION. CONTACT MTF FOR INSTRUCTIONS ON HOW TO RETURN DAMAGED PACKAGING OR UNUSED ALLOGRAFTS.

PREPARATION OF THE CRYOPRESERVED ALLOGRAFT FOR USE
Before use, the allograft must be thawed and the cryoprotectant must be diluted out of the tissue according to the Musculoskeletal Transplant Foundation’s Thawing and Diluting procedures. All steps must be completed prior to transplantation into the recipient. The allograft must not be refrozen after thawing.

**RECOMMENDED SUPPLIES AND EQUIPMENT**

### NON-STERILE
- Back table
- One (1) 5000 ml basin
- 4000 ml warm (37°C to 42°C) normal saline for irrigation
- Insulated gloves
- Surgical towels
- Thermometer

### STERILE
- One (1) pair sterile scissors
- One (1) sterile Kelly clamp, or equivalent
- One (1) pair sterile DeBakey forceps, or equivalent
- Two (2) sterile 1000 ml basins
- 1000 ml cold (1°C to 10°C) (D5LR) Lactated Ringer’s with 5% dextrose & bag decanter

**INSTRUCTIONS FOR USE**

The following procedure has been developed to assure the proper thawing rate and passive dilution of cryoprotectant from the allograft. Maintenance of the saline bath in the range of 37°C to 42°C allows the allograft to approach physiologic temperatures in a controlled fashion. Exposure of the allograft to temperatures above this range may damage the tissue.

The two-step dilution protocol reduces cryoprotectants from the allograft, from the original amount of 10% to minimal levels. These steps and final placement of the allograft into the recipient's heparinized blood will help rehydrate the tissue toward an iso-osmotic state.

1. The entire thawing/dilution process should take approximately 22 minutes.
2. During the thaw procedure, when the frozen cryoprotectant inside the pouch has turned to slush and the entire allograft is freely moveable within its pouch by visual examination, immediately begin the dilution phase of the process.
3. Once the allograft is ready for transplantation, it is recommended that it be immersed in the recipient's own heparinized blood. In pediatric cases where patient blood volume is critical, the allograft may be maintained on cold D5LR. **Do not allow the allograft to dry out.**

   **NOTE:** The use of recipient's own heparinized blood as a final rinsing fluid serves two purposes. First, it allows the allograft to return to a more complete osmotic balance before transplantation. Second, it will also further reduce the amount of residual calf serum in the allograft added during cryopreservation; calf serum has been suggested to be a heterologous antigen.
4. If either the inner or outer pouch shows evidence of failure, immediately contact MTF, or if outside of the United States, immediately contact your local representative. Do not use the allograft if both pouches show evidence of failure.

**THAWING PROCEDURE**

The thawing procedure is a non-sterile procedure performed on a back table by OR circulating staff. Prior to removing the allograft from its cryogenic storage location, assemble all needed equipment and coordinate the timing of the allograft preparation for implantation with the surgeon.

1. Assemble the large 5000 ml basin, 4 liters of saline and a surgical towel on a non-sterile back table.
2. While wearing insulated gloves, retrieve the allograft, in fiberboard box, from VAPOR phase LN₂ storage and bring into the operating room. Open the fiberboard box and remove the pouch.
3. Carefully wipe the frost from the outer pouch with a towel to verify the allograft label information and
inspect the pouch for seal integrity. IF THE OUTER POUCH SHOWS EVIDENCE OF FAILURE, IMMEDIATELY CONTACT MTF.

4. Return the pouch to the open box and allow for initial warming at room temperature for six (6) minutes. Prepare the thawing bath.

5. Pour three (3) liters of warm saline into the large basin and maintain 37°C to 42°C (98°F to 108°F) by referencing a suitable thermometer for the duration of the thawing procedure. Retain 1000 ml of warm saline for later use.

6. Slowly immerse the pouch in the warm saline bath and continue to thaw the allograft for approximately five (5) minutes, adding additional warm saline as necessary to maintain 37°C to 42°C. Gentle swirling of the bath will help to facilitate heat transfer from the graft and expedite thawing.

7. While the graft is thawing, set up the sterile field for the dilution step.

8. When the cryoprotectant media around the allograft appears SLUSHY (do not allow the media to completely thaw), remove the allograft package from the warm saline and gently blot dry with a towel.

   NOTE: Open the corner spot welds near the word PEEL and completely dry the peel pouch at the initiation point.

9. The circulating nurse opens the outer peel pouch by separating and grasping both flaps between thumb and forefinger and peeling apart until the inner pouch is retrievable. Be careful not to contaminate or damage the sterile inner pouch.

   NOTE: Make sure to initiate the peeling sequence at the location identified by the "ARROW" and "PEEL".

10. Aseptically present the allograft to the scrub nurse who will retrieve the inner sterile pouch with the Kelly clamp

    NOTE: Do not puncture the inner pouch. Handle pouch only at the outer seams of the package.

DILUTING PROCEDURE
Diluting is a procedure that should be performed using sterile technique.

1. Open the inner pouch with sterile scissors and carefully transfer contents into the empty sterile 1000 ml basin.

2. Slowly add approximately 500 ml of the D5LR to the sterile 1000 ml basin containing the allograft and cryoprotectant media. Do not direct the solution onto the allograft. Add the remaining contents to the second sterile 1000 ml basin.

3. Allow the cryoprotectant to passively dilute from the allograft for 10 minutes, swirling occasionally.

4. Using the sterile DeBakey forceps, transfer the allograft to the second sterile basin containing 500 ml of D5LR and periodically swirl basin for the final two (2) minutes of the dilution phase.

5. Gently and periodically flush with D5LR. The allograft may be maintained in this solution or in the recipient's own heparinized blood on cooling slush. Do not allow the allograft to dry out.

DONOR SCREENING & TESTING

Prior to donation, the donor’s medical/social history is screened for medical conditions or disease processes that would contraindicate the donation of tissues in accordance with current policies and procedures approved by the MTF Medical Advisory Board.

Donor blood samples taken at the time of recovery were tested by a CLIA licensed facility for:

- Hepatitis B surface antigen
- Hepatitis B core antibody
- Hepatitis C antibody
- HIV-1/2 antibody
- HTLV-I/II antibody
- Syphilis

In addition to the testing listed above, HIV Nucleic Acid Amplification Testing (NAT) was performed. Furthermore, donors recovered on or after May 1, 2004 were tested for HCV utilizing the HCV NAT testing method. The results of all serological testing were negative. This allograft tissue has been determined to be suitable for transplantation.
The infectious disease test results, consent, current donor medical history interview, physical assessment, available relevant medical records to include previous medical history, laboratory test results, autopsy and coroner reports, if performed, and information obtained from any source or records which may pertain to donor suitability, have been evaluated by an MTF physician and are sufficient to indicate that donor suitability criteria current at the time of procurement have been met. This tissue is suitable for transplantation. The donor suitability criteria used to screen this donor are in compliance with the FDA regulations published in 21 CFR Part 1270 and Part 1271 Human Tissue Intended for Transplantation, as applicable. All procedures for donor screening, serologic and microbiologic testing meet or exceed current standards established by the American Association of Tissue Banks.

PACKAGING AND LABELING

This allograft must not be used under any of the following conditions:

- If the container or seal is damaged, not intact or has any physical damage
- If the container label or identifying bar code is severely damaged, not readable or is missing
- If the inner or outer pouch is not intact
- If the expiration date shown on the container label has passed
- If the final container is not labeled
- If the Cryopreserved allograft has NOT been stored at -100°C or colder

If either the inner or outer pouch shows evidence of damage, or the storage conditions or container seals have been compromised, contact MTF or, if outside of the United States, immediately contact your local representative. Any damaged allograft packaging (fiberboard box, inner and outer pouches) and allograft must be returned to MTF for inspection.

STORAGE

**WARNING: Use insulated gloves when handling the package.**

Store this cryopreserved allograft in its fiberboard box at -100°C or colder. The cryopreserved allograft is shipped and must remain stored in a liquid nitrogen “vapor phase” cryoenvironment (-100°C to -196°C), **but not immersed in liquid nitrogen**. Do not store or use the cryopreserved allograft beyond the listed expiration date. Handle with care as packaging material may become brittle at storage temperatures; do not drop the frozen allograft. Check packaging integrity prior to use. It is the responsibility of the transplant facility or clinician to maintain the tissue intended for transplantation in the appropriate recommended storage conditions prior to transplant.

PATIENT RECORD

Tissue recipient records must be maintained by the consignee and transplant facility for the purpose of tracing tissue post-transplantation to facilitate the investigation of actual or suspected transmission of communicable disease and take appropriate and timely corrective action. A TissueTrace® Tracking Form and peel-off labels have been included with each package of tissue. Record the patient name, the name and address of the transplant facility, allograft tissue information (using the peel-off labels) and comments regarding the use of the tissue on the TissueTrace Tracking Form. **Within the United States:** Once completed, the bottom page of the form should be returned to MTF using the self-addressed, postage paid mailer. Copies of this information should be retained by the transplant facility for future reference. **Outside of the United States:** Once completed, the bottom page of the form should be returned to the local allograft representative or provider. Copies of this information should be retained by the hospital for future reference.
REFERENCES


(7) Current Standards for Tissue Banking, AATB, McLean, VA.


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Within the United States: 1.800.272.5287  
Outside of the United States: 1.714.708.1300

All recovery, processing and distribution costs were paid for by MTF, a non-profit organization.

CAUTION: Federal (US) law restricts this allograft to sale, distribution and use by or on the order of a physician

These tissue forms may be covered by one or more of the following US Patents: US 5,284,655; US 5,290,558; US 5,728,159; US 6,025,538; US 6,030,635; US 6,099,529; US 6,111,164; US 6,155,756; US 6,162,225; US 6,326,018; US 6,432,436; US 6,437,018; US 6,448,375; US 6,508,830; US 6,548,080; US 6,554,863; US 6,761,739; US 6,830,149; US 6,854,599; US 6,998,135; US 7,019,192; US 7,044,968. Other patents pending.

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