READ BEFORE USING

CRYOPRESERVED HUMAN VEIN ALLOGRAFT

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 VASCULAR 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

This allograft is supplied in single-patient, single-use packaging consisting of two pouches, the innermost of which is filled with cryoprotectant and the allograft. The exterior of the outer pouch is not sterile and must not be placed on a sterile field. The packaged allograft is stored inside a foam-lined fiberboard box. This allograft has three dimensions: 1) length of the distended vein segment, 2) diameter of the proximal lumen of the vein, and 3) diameter of the distal lumen of the vein. The proximal end of the venous segment is identified by a prolene suture. This allograft has been cryopreserved and delivered in a liquid nitrogen dry shipper.

This saphenous vein allograft was gently flushed with a plasmalyte solution that contains Heparin, Papaverine, and Sodium Bicarbonate to dislodge blood clots and relieve the vein’s smooth muscle spasm. During processing the vein is continuously and gently flushed, inspected, the venous branches ligated and if necessary, superficial repairs made. The allograft was treated with the following antibiotics: Cefoxitin, Lincomycin, Vancomycin, and Polymyxin B. This tissue has been cooled at a controlled rate to the frozen state and is provided in tissue culture medium with 10% DMSO (Dimethyl Sulfoxide) and 10% Fetal Calf Serum.

INDICATIONS FOR USE

Human cryopreserved vein allografts may be utilized in a number of vascular reconstructive applications.
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 the surgical site
- Disease transmission
- Undesirable immune reaction to the allograft implant
- 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 Heparin, Papaverine, Polymyxin B Sulfate, Cefoxitin, Lincomycin, Vancomycin, DMSO, Sodium Bicarbonate, and Fetal Calf Serum may be present. Caution should be exercised if the recipient is allergic to any of these substances. The specific antibiotics and reagents used in the dissection and disinfection steps during processing are:

<table>
<thead>
<tr>
<th>Substance</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium Bicarbonate</td>
<td>5mEq/1000ml</td>
</tr>
<tr>
<td>Heparin</td>
<td>4 U/ml</td>
</tr>
<tr>
<td>Papaverine</td>
<td>60 µg/ml</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>240 µg/ml</td>
</tr>
<tr>
<td>Lincomycin</td>
<td>120 µg/ml</td>
</tr>
<tr>
<td>Polymyxin B</td>
<td>1000 U/ml</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>50 µg/ml</td>
</tr>
</tbody>
</table>

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 the 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 procedure. All steps must be completed prior to transplantation into the recipient. The allograft must not be refrozen after thawing.

RECOMMENDED SUPPLIES AND EQUIPMENT

<table>
<thead>
<tr>
<th>NON-STERILE</th>
<th>STERILE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Back table</td>
<td>One (1) pair sterile scissors</td>
</tr>
<tr>
<td>One (1) 5000 ml basin</td>
<td>One (1) sterile Kelly clamp, or equivalent</td>
</tr>
<tr>
<td>4000 ml warm (37°C to 42°C) normal saline for irrigation</td>
<td>One (1) pair sterile DeBakey forceps or equivalent</td>
</tr>
<tr>
<td>Insulated gloves</td>
<td>Two (2) sterile 1000 ml basins</td>
</tr>
<tr>
<td>Surgical towels</td>
<td>1000 ml cold (1°C to 10°C) (D5LR) Lactated</td>
</tr>
<tr>
<td>Thermometer</td>
<td>Ringer’s with 5% dextrose &amp; bag decanter</td>
</tr>
</tbody>
</table>

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 23 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° to 42 °C (98° 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° 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 the pouch only at the outer seams of the package.

DILUTING PROCEDURE

Diluting is a procedure that must be performed using sterile technique.

1. Open the inner pouch with sterile scissors and carefully transfer the vein and media 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. Secure a cannula to the distal end of the vein (distal end does not have the prolene suture) with 3-0 silk ligature and then gently flush with D5LR.
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.

Processed and Distributed by:

MTF

Musculoskeletal Transplant Foundation

3535 Hyland Avenue
Costa Mesa, CA 92626
USA

For orders and technical questions
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 6,111,164; US 6,432,436; US 6,437,018; US 6,448,375; US 6,548,080; US 6,554,863; US 6,830,149; US 6,854,599; US 6,911,212; US 7,019,192; and US 7,045,141. Other Patents pending.

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