All tissue used in ProSpace DBM is recovered by the tissue bank and serologically tested to ensure safety. The tissue bank performs serological testing of each tissue for HIV-1 (p24 Ag), HIV-1 DNA polymerase chain reaction (HIV-1 DNA PCR) or HIV-2, antibody to human T-lymphotropic virus type 1 and type 2 (anti-HTLV-I/II), hepatitis C virus antibody (anti-HCV) and syphilis. In addition, the donor was tested and found to be negative or non-reactive for hepatitis B surface antigen (HBsAg), hepatitis B core antibody (HBCAb), HIV antibodies type 1 and type 2 (anti-HIV-1 and anti-HIV-2), antibody to human T-lymphotrophic virus type 1 and type 2 (anti-HTLV-I/II), hepatitis C virus antibody (anti-HCV), and syphilis. The tissue bank’s evaluation included review of the tissue donor’s infectious disease test results, consent documents, donor medical history and behavior risk assessment, available relevant medical records including previous medical history, laboratory test results, existing autopsy or coronor reports (if applicable) and information from other sources or records which may pertain to donor eligibility including tissue procurement microbiological test results. The donor did not reveal risk factors for, or clinical or physical evidence of significant active infection including HIV (human immunodeficiency virus) or hepatitis infection, or risk factors for viral or prion-associated disease transmission as specified in Appendix II of the AATB standards. Serological testing: The tissue bank performs serological testing of each tissue donor at a CLIA approved laboratory utilizing FDA-licensed test kits. Donor blood samples taken at the time of recovery were tested and found to be negative or non-reactive for (at minimum): hepatitis B surface antigen (HBsAg), hepatitis B core antibody (HBCAb), HIV antibodies type 1 and type 2 (anti-HIV-1 and anti-HIV-2), antibody to human T-lymphotrophic virus type 1 and type 2 (anti-HTLV-I/II), hepatitis C virus antibody (anti-HCV) and syphilis. In addition, this donor was tested and found to be negative or non-reactive for HIV type-1 p24 antigen (HIV-1-p24 Ag), HIV-1 DNA polymerase chain reaction (HIV-1 DNA PCR) or HIV-1 NAT. The names and addresses of the testing laboratories, the listing and interpretation of all required infectious disease tests, a listing of the documents reviewed as part of the relevant medical records, and the name of the person or establishment determining the suitability of this human tissue are on file at the tissue bank and are available upon request. This allograft has been determined to be suitable for transplantation.

Viral Inactivation Validation: The methods for processing of the DBM contained in ProSPace DBM were evaluated for their viral inactivation potential. A selected panel of viruses representing various virus types, sizes, shapes and genomes were evaluated. The viral inactivation testing demonstrated suitable inactivation potential of the processing methods for a wide range of potential human viruses.

INSTRUCTIONS FOR USE

These instructions are intended as guidelines for the use of ProSpace DBM as a part of established surgical techniques. They are not intended to replace or change standard procedures for treatment of bone defects involving bone grafting and internal fixation. Procedures involving bone grafting can experience highly variable results. Factors to be considered in selecting the bone grafting material and the surgical technique to be utilized are as follows:

- Age of the patient
- Quality of the patient’s bone
- Location of the defect
- Anticipated loading conditions
- Exitation of the graft to a suitable blood supply
- Ability to achieve direct apposition of the graft to viable host bone
- Presence/addition of autogenous bone or bone marrow at the graft site
- Elimination of gaps in the graft site
- Ability to suitably stabilize the graft site
- Complete coverage of the graft material to prevent migration

For best results, extreme care should be exercised to assure the correct graft material is selected for the intended application.

TO OPEN PUTTY:
1. Peel open outer package.
2. Using sterile technique, transfer contents to a sterile field.
3. Peel open inner package and remove spatula and vial.
4. Twist off vial lid and remove putty using small spatula or other hand instrument.
5. Discard any unused portion.

TO OPEN GEL:
1. Peel open outer package.
2. Using sterile technique, transfer contents to a sterile field.
3. Peel open inner package and remove syringe.
4. Remove protective cap from syringe tip.
5. Apply pressure to the plunger to extrude gel.
6. Discard any unused portion.

PREOPERATIVE PREPARATION

Sterile technique must be maintained to minimize the risk of postoperative complications. The amount needed is based on the type of procedure and size of the defect being treated. When ProSpace DBM is being mixed with autograft, a ratio of 1:1 should be used. ProSpace DBM does not require rehydration prior to use.

Radiographic evaluation of the defect site is essential to accurately assess the extent of the defect and to aid in the selection and placement of ProSpace DBM and fixation devices.

Surgical Procedure Notes: ProSpace DBM does not possess sufficient mechanical strength to support the reduction of a graft site prior to tissue ingrowth. Therefore, anatomical reduction and rigid fixation, in all planes, should be obtained independent of ProSpace DBM.

For best results, ProSpace DBM must fill the defect and contact as much viable bone as possible.

ProSpace DBM must not be used to repair bone defects where complete soft tissue coverage cannot be achieved.

POSTOPERATIVE CARE

Postoperative patient management should follow the same regimen as similar cases utilizing autogenous bone grafting. Standard postoperative practices should be followed, particularly as applicable to defect repairs involving the use of fixation devices. The patient should be cautioned against early weight bearing and premature ambulation which could lead to loosening and/or failure of the fixators or loss of reduction. The length of time a defect should remain in a reduced state of loading is determined by the complexity of the defect site and the overall physical condition of the patient. Hardware should not be removed until the defect is healed.

CONTRAINDICATIONS

ProSpace DBM is contraindicated where the device is intended as structural support in load-bearing bone and in articulating surfaces. Conditions representing relative contraindications include:

- Severe vascular or neurological disease
- Uncontrolled diabetes
- Severe degenerative bone disease
- Uncooperative patients who will not or cannot follow postoperative instructions, including individuals who abuse drugs and/or alcohol
- Renal impairment
- Active or latent infection in or around the surgical site

Polymyxin Sulfate B, Bacitracin, Gentamicin and Iodine are used in processing ProSpace DBM Putty and Gel, and trace amounts may remain. Since it is impossible to quantify the levels at which any individual may have an allergic response, this product is contraindicated in patients with known sensitivity.

WARNINGS AND PRECAUTIONS

ProSpace DBM is sterile during the stated shelf life in an unopened and undamaged package. The product must be used prior to the expiration date.

Do not use if the packaging has been damaged and/or the product has been contaminated. In the event of contamination, discard the product. Damaged packaging should be returned to Aesculap, Inc.
Appropriate placement and/or fixation are critical factors in the avoidance of potentially adverse effects. As with all biological products, the tissue in ProSpace DBM has the potential to transmit infectious agents despite processing treatments, extensive donor screening, tissue selection and laboratory tests. To date, there have been no reports of experimental or clinical seroconversion using demineralized bone powder.

When filling a closed defect, care must be taken while extruding ProSpace DBM Gel from the syringe as possible pressurization of the device could result in fat embolization and/or embolization of the material into the bloodstream.

As with any surgical procedure, the possibility of infection exists.

Although the production technique is designed to eliminate antigenic properties of the product, the possibility of such a reaction is present.

Adverse outcomes potentially attributable to the product must be reported promptly to Aesculap, Inc. If any dissatisfaction with the product performance or packaging occurs, notify Aesculap, Inc. immediately and promptly return product and/or packaging.

OSTEOINDUCTIVE POTENTIAL

The osteoinductive potential of the DBM used in ProSpace DBM Putty and Gel is determined via an in vitro assay. The assay measures the alkaline phosphatase activity of myoblast cells. The level of alkaline phosphatase induction is compared to positive and negative DBM controls. Results from the assay were correlated with results from implantation of DBM into an athymic rat muscle pouch. Analysis of these results shows that the in vitro assay has been validated against the in vivo athymic rat model and predicts with at least 95% confidence the in vivo osteoinductivity of the test material. 67 out of 67 test lots that passed the in vitro assay passed the in vivo athymic rat assay via confirmation of intramuscular bone formation.

Each lot of DBM incorporated in ProSpace DBM is evaluated for osteoinductive potential using an in vitro assay. Testing each lot of DBM assures that only DBM with osteoinductive potential is used in ProSpace DBM. Although DBM used in the final product has been shown to be osteoinductive using an in vitro assay, the combination of DBM and reverse phase medium has not been evaluated for osteoinductivity; therefore, it is unknown to what extent the formulation components may alter the osteoinductivity of the DBM. Additionally, it is unknown how osteoinductivity of the DBM component, measured via the in vitro assay, will correlate with human clinical performance of ProSpace DBM.

STERILIZATION

ProSpace DBM has been sterilized by electron beam irradiation. The inner package and its contents are sterile. The package should be inspected prior to use to ensure the sterility barrier has not been compromised. This product is for single use only and should not be re-sterilized. The product must not be used beyond the stated expiration date.

DO NOT RE-STERILIZE

STORAGE

Do not refrigerate or freeze. Do not expose to extreme heat. Store at room temperature (15°C to 30°C) in a clean, dry place. It is the responsibility of the tissue dispensing service and user (facility/clinician) to maintain the product under appropriate conditions prior to use.

RECIPIENT TRACING

The clinician or hospital is responsible for maintaining recipient records for the purpose of tracing tissue post-implantation. A Graft Tracing Record has been included for completion at the time of the surgical procedure. Upon completion, the Graft Tracing Record is to be sent back to the manufacturer. If the entire tissue product was discarded, return the Graft Tracing Record and explain the reason for discard. Chart labels are provided in each package for use on the patient’s medical records. These labels provide traceability to the original tissue donor.

CAUTION: Federal (U.S.) Law restricts the use of this device to sale by or on the order of a physician.

Manufactured for:

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