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Biologic Solutions

PrimaGen Advanced™ Allograft

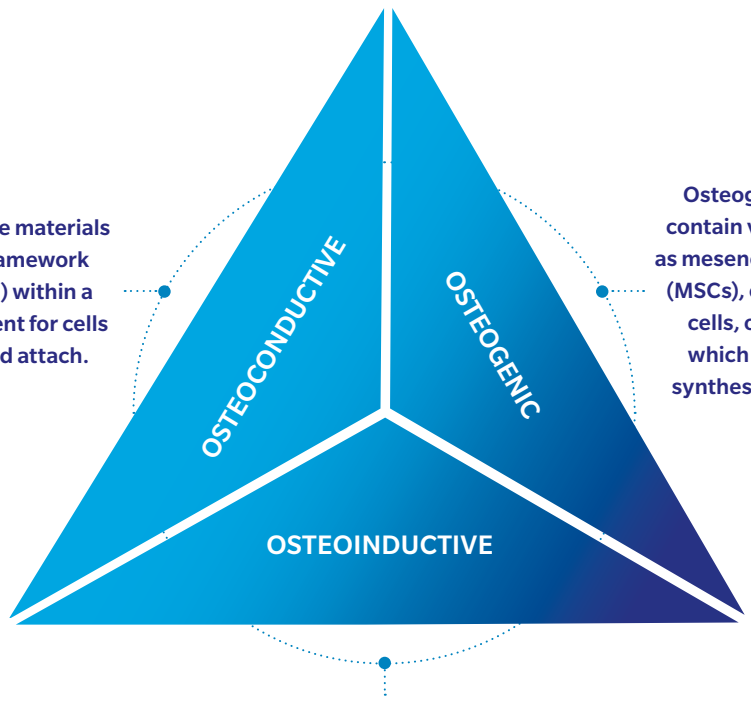
Recreating the benefits of the Gold Standard while reducing the drawbacks

The Complete Bone Remodeling Triad

Many currently available bone grafting materials have some of the features necessary for successful bone healing, but few possess all three of the components of the bone remodeling triad: osteoconductivity, osteoinductivity and osteogenicity. In an effort to provide a graft material that contains all three components without the need to harvest autograft, advanced fresh-frozen allografts were developed from cadaveric tissue to meet this medical need. These allografts retain osteoconductive and osteoinductive properties as well as naturally inherent osteogenic cells.

PrimaGen Advanced Allograft has been developed to overcome the limitations of other bone graft substitutes and designed to offer a real alternative to autograft.

Bone Remodeling Triad



Osteoconductive materials provide the framework (or scaffolding) within a bony environment for cells to infiltrate and attach.

Osteogenic materials contain viable cells, such as mesenchymal stem cells (MSCs), osteoprogenitor cells, or osteoblasts, which are capable of synthesizing new bone.

Osteoinductive materials induce bone formation in a bony or non-bony environment via the action of growth factors or signaling proteins, including Bone Morphogenetic Proteins (BMPs). These proteins simulate the conversion of progenitor cells into bone forming osteoblasts.[1,2]

The PrimaGen Advanced Allograft Process

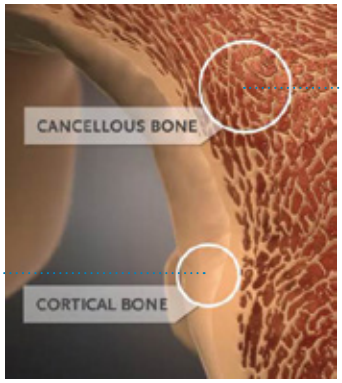
Donor processing of PrimaGen Advanced Allograft begins within 72 hours post-mortem. Processing is completed rapidly in a controlled, aseptic environment designed to protect the integrity of its viable components.

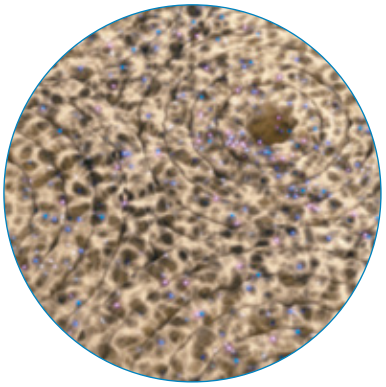
Donor processing begins within 72 hours post-mortem.

Composition

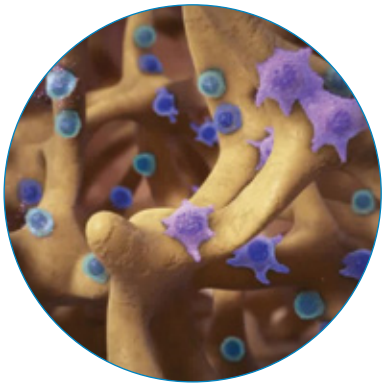
Cortical bone is processed into a fiber-like structure and demineralized, retaining a variety of osteoinductive proteins important for bone formation. The cancellous bone tissue is morselized into particulate, creating a consistent graft. The advanced, proprietary processing methods protect and retain the naturally inherent osteogenic cells.

The DBM fibers and cancellous tissue containing naturally adherent osteogenic cells are combined in a precise ratio and frozen at -70˚C in a cryoprotective solution to preserve cell viability.

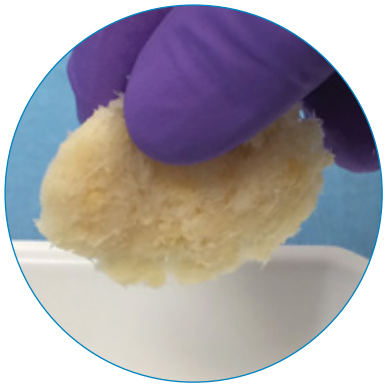




Cortical bone undergoes demineralization, which retains natural osteoinductive proteins.



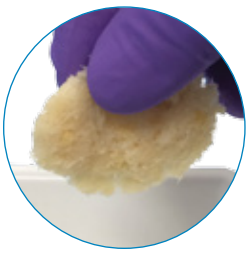
Cancellous bone containing naturally adherent osteogenic cells is processed into chips.



Both are then mixed in a 1:1 ratio and stored at -70˚C in cryoprotective solution to preserve cell viability.

Streamline Your Procedures with an Advanced Delivery System

PrimaGen Advanced Allograft is packaged in an intuitive, proprietary pre-filled delivery syringe and features a built-in filter that allows for the full preparation of the material directly inside the syringe.



Graft Consistency

In addition to being packaged in an intuitive and proprietary pre-filled delivery syringe, PrimaGen Advanced Allograft is manufactured in a way that provides optimal handling and graft consistency for better packing. The structure of the cortical fibers allows for better fluid retention and graft containment.*

A majority of bone grafting materials are made with particulate that is very granular in consistency, which, although suitable for certain applications, tends to fall apart and may not be contained very well. PrimaGen Advanced Allograft, however, utilizes a manufacturing process that creates fibers from the cortical bone, instead of particulate.

Precise Handling

The cortical fibers are demineralized and create a cohesive graft that not only stays together, but also allows for better retention of diluents such as saline.*

Removing Cryopreservative

After appropriately removing PrimaGen Advanced Allograft from its packaging, thawing can begin by submerging the syringe in a warm water bath. Thawing must be fully complete before removal of the cryoprotectant can begin.

Cryopreservative can be extracted from the syringe by simply pushing gently on the plunger.

Note: *Please see package insert for complete preparation instructions.*

Rinsing

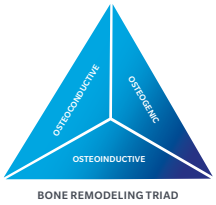
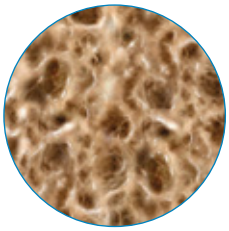
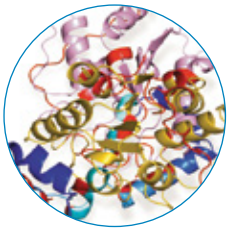
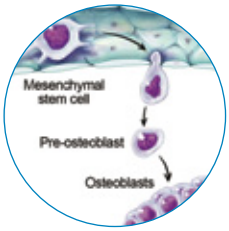
Once the preservative has been removed, draw some sterile saline into the syringe to help rinse the remaining preservative off the graft. Dispense the sterile saline by gently pushing on the plunger.

Note: *Rinsing may be repeated if desired.*

Note: *Please see package insert for complete preparation instructions.*

PrimaGen Advanced Allograft should be implanted within four hours after removing the cryopreservative and replacing it with saline (allow saline to remain inside the syringe until it is ready for implantation). Once thawed, if the cryopreservative solution is not immediately decanted and replaced with sterile saline solution, PrimaGen Advanced Allograft should be implanted within two hours.

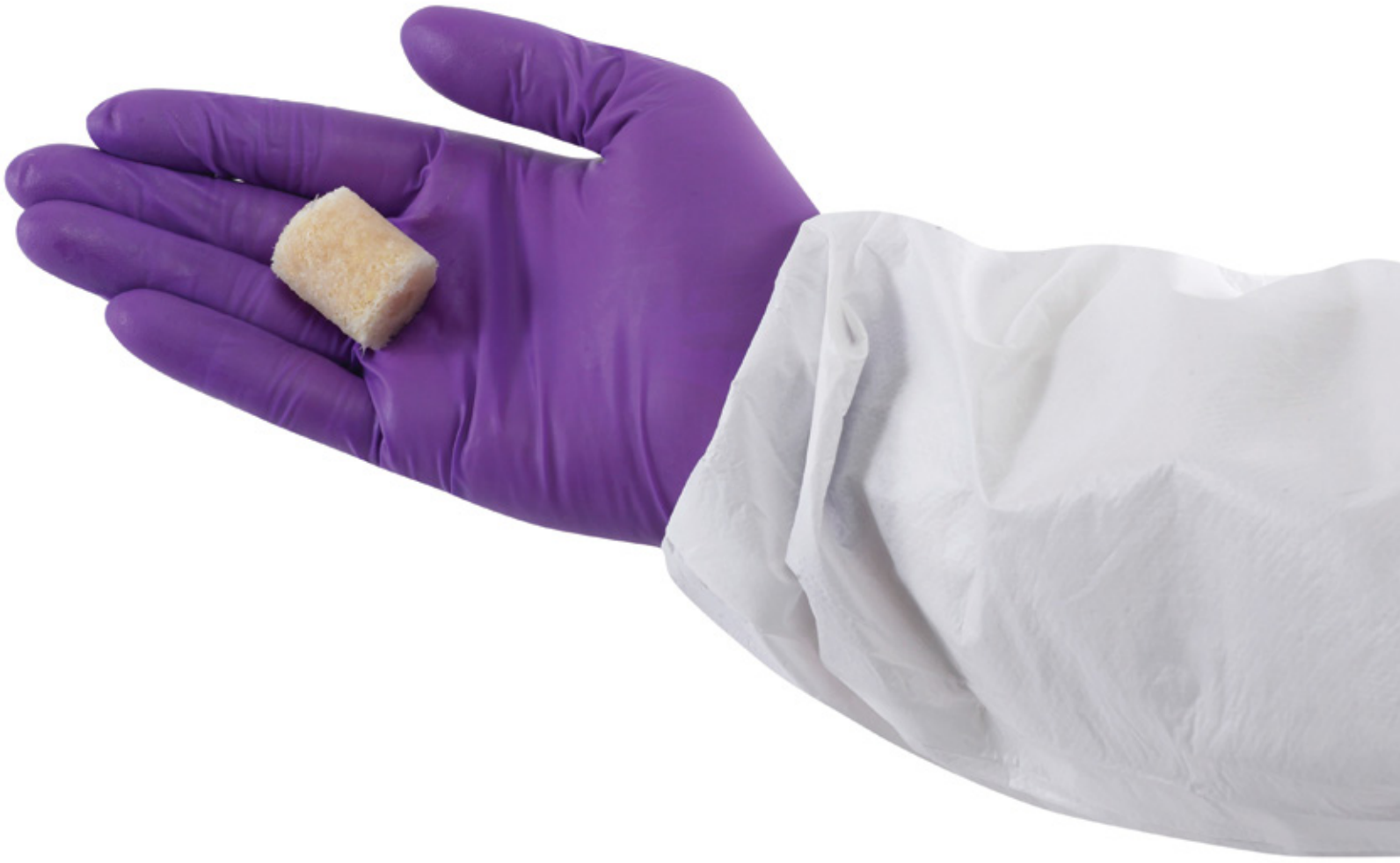
Experience Complete Bone Remodeling

Characteristic	Osteoconductivity	Osteoinductivity	Osteogenicity
 BONE REMODELING TRIAD			
Key Feature	Cancellous bone matrix offers an interconnected trabecular structure Allows for interface activity, bone in-growth and graft remodeling	Demineralized component provides additional inherent growth factors Demineralized bone has been shown to include BMP-2, 4, 6, 7, VEGF, TGF-ß, PDGF, IGF-1 and FGF[3,4]	At least 750,000 cells/cc of cancellous tissue with at least 70% cell viability* Cells include MSCs, osteoprogenitor cells and pre-osteoblasts
Benefit	Offers an optimal scaffold for bone-forming cells to migrate and remodel	Delivers proteins that will trigger the differentiation and proliferation of bone-forming cells	Provides bone-forming cells that support the fusion process
Efficacy Confirmation	Every lot contains dense cancellous bone matrix	Every lot tested for osteoinductivity	Every lot tested for *in vitro* osteogenic differentiation Cryopreserved to maintain cell viability
Test Method	Processing specifications and quality inspections ensure consistent graft composition	Athymic Rat Ectopic Bone Formation Assay/C2C12 Assay**	Osteogenic Assay Trilineage Assay Cell count with hemocytometer and trypan blue stain
Results*,**	Provides a trabecular osteoconductive scaffold with optimal graft-packing capabilities	Verifies osteoinductivity	Demonstrates the presence of MSCs and verifies the ability to differentiate into bone forming cells

Discover the PrimaGen Advanced Allograft Solution That Fits Your Procedures

PrimaGen Advanced Allograft

DESCRIPTION	CATALOG NUMBER
PrimaGen Advanced Allograft, 1cc	PSTM001
PrimaGen Advanced Allograft, 5cc	PSTM005
PrimaGen Advanced Allograft, 10cc	PSTM010
PrimaGen Advanced Allograft, 15cc	PSTM015
PrimaGen Advanced Allograft, Marketing Sample	PSTM005S



Excellent Safety Profile

PrimaGen Advanced Allograft is processed via stringent donor screening, testing and sterility procedures. In addition to cytotoxicity testing and extensive lot-to-lot donor screening, PrimaGen Advanced Allograft has been validated to possess an excellent safety profile, as an allograft that does not require Human Leukocyte Antigen (HLA) typing or patient matching. Test samples of PrimaGen Advanced Allograft were shown to be immune-protective in an *in vitro* study, in which immune cells were not activated in the presence of PrimaGen Advanced Allograft.*, **

Donor screening criteria **exceeds** that of the FDA and the AATB guidelines.

Regulatory Requirements: PrimaGen Advanced Allograft is regulated by the FDA as a Human Cellular and Tissue-Based Product (HCT/P) under 21 CFR Part 1271.

Sterility: PrimaGen Advanced Allograft is processed under aseptic conditions in order to preserve the viable cells in the cancellous bone matrix and the naturally occurring bone growth factors in the demineralized bone matrix (DBM). Representative samples are sacrificed from each lot for destructive microbiological verification testing per USP <71> Sterility Tests. Results must show "no growth" after 14 days incubation in growth-promoting media.

Donor Eligibility: PrimaGen Advanced Allograft donors are accepted only after passing through stringent screening criteria exceeding those set forth by the AATB[5] and FDA. Potential donors are evaluated through a multi-step process that includes a review of medical records and a medical/social history interview with family members. All donors are subjected to communicable disease marker testing by a laboratory that is registered with the FDA in accordance with the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and 42 CFR part 493, or have met equivalent requirements as determined by the Centers for Medicare and Medicaid Services (CMS). The tissue bank's medical director determines final eligibility and acceptability after reviewing the donor screening and testing records.

Processing: PrimaGen Advanced Allograft is processed by some of the largest tissue banks in the United States, with impeccable reputations and track records for safe tissue procurement. All tissue banks affiliated with PrimaGen Advanced Allograft are accredited by the American Association of Tissue Banks (AATB). PrimaGen Advanced Allograft is procured from human donor tissue that meets strict donor suitability requirements and is processed in a controlled environment using methods designed to prevent contamination and cross-contamination of the tissue.

See the product Instructions for Use for a complete listing of the indications, contraindications, warnings, precautions and adverse effects.

Screening Criteria for PrimaGen[5,*]	PrimaGen	AATB	FDA
Non-medical drug use	•	•	•
High-risk sexual history	•	•	•
Incarceration	•	•	•
Aesthetic needle use	•	•	•
International travel	•	•	•
Human Immunodeficiency Virus (HIV)–1 and 2	•	•	•
Hepatitis B Virus (HBV)	•	•	•
Hepatitis C Virus (HCV)	•	•	•
Transmissible Spongiform Encephalopathy (TSE)	•	•	•
Creutzfeldt-Jakob Disease (CJD)	•	•	•
Treponema Pallidum (Syphilis)	•	•	•
Neisseria Gonorrhea	•	•	•
West Nile Virus (WNV)	•	•	•
Sepsis	•	•	•
Vaccinia	•	•	•
Active genital herpes	•	•	•
Encephalitis	•	•	•
Meningitis	•	•	•
Xenotransplant recipient	•	•	•
Clostridium	•	•	•
Streptococcus Pyogenes	•	•	•
Dementia	•	•	
Malaria	•	•	
Rabies	•	•	
Clinically active tuberculosis	•	•	
Leprosy (Hansen's disease)	•	•	
Systemic mycosis	•	•	
Rheumatoid arthritis	•	•	
Systemic lupus erythematosus	•	•	
Polyarteritis nodosa	•	•	
Sarcoidosis	•	•	
Clinically significant metabolic bone disease	•	•	
Methicillin Resistant Staphylococcus aureus (MRSA)	•		
Vancomyocin Resistant Enterococcus	•		
Epstein Barr Virus	•		
Cytomegalovirus (CMV)	•		
Chagas disease	•		
Malignancy	•		
Connective Tissue diseases	•		
Collagen diseases	•		
Disease of unknown etiology	•		
Various sexually transmitted diseases	•		
Wegener's Granulomatosis	•		
Rheumatic fever	•		
Reactive Arthritis (Reiter Syndrome)	•		
Pyelonephritis	•		
Peritonitis	•		
Myasthenia Gravis	•		
Guillain-Barre Syndrome	•		
Endocarditis	•		
Anklosing Spondylitis	•		

References:

1. Khan SN, Cammisa FP Jr, Sandhu HS, Diwan AD, Girardi FP, Lane JM. The biology of bone grafting. *J AM Acad Orthop Surg.* 2005;13(1):77–86.
2. Han B, Tang B, Nimni ME. Quantitative and sensitive in vitro assay for osteoinductive activity of demineralized bone matrix. *J Orthop Res.* 2003;21(4):648–54.
3. Pietrzak WS, Woodell-May J, McDonald N. Assay of bone morphogenetic protein -2, -4 and -7 in human demineralized bone matrix. *J Craniofac Surg.* 2006;17(1):84–90.
4. Wildemann B, Kadow-Romacker A, Haas NP, Schmidmaier G. Quantification of various growth factors in different demineralized bone matrix preparations. *J Biomed Mater Res A.* 2007;81(2):437–42.
5. American Association of Tissue Banks. *Standards for Tissue Banking,* 14th ed. McLean, VA: American Association of Tissue Banks, 2016.

*Data on file.

** Pre-clinical Disclaimer: *In vitro* cellular and pre-clinical studies may not be indicative of human clinical outcomes.

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