



# Accell Evo3<sup>®</sup> Accell Evo3c

Advanced Demineralized Bone Matrices  
Powered by Accell<sup>®</sup> Technology

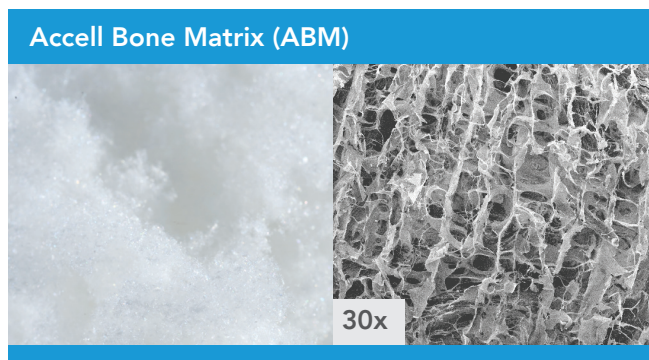


Accell Evo3<sup>®</sup> / Accell Evo3c

# Accell Evo3<sup>®</sup> / Accell Evo3c

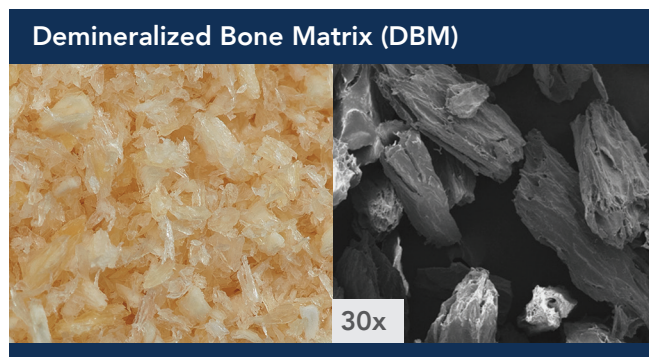
Accell Evo3<sup>®</sup> combines patented ABM and particulate DBM with a Reverse Phase Medium (RPM) carrier.

## The Accell<sup>®</sup> Advantage



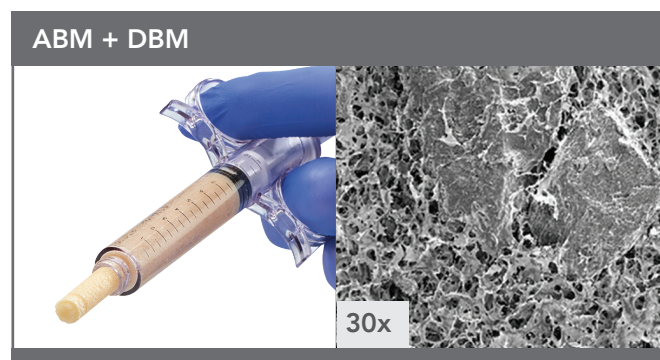
### Open structure, dispersed DBM

- Transformed from particulate DBM
- Highly porous matrix with greater surface area
- Greater exposure to bone proteins compared to DBM



### Standard, particulate DBM

- Formed by removing mineral component of cortical bone
- Dense matrix of Type-1 collagen
- Gradual access to naturally occurring bone proteins



The combination of ABM and particulate DBM provides for both immediate and sustained accessibility to naturally occurring bone proteins which are important for osteogenesis.<sup>2</sup>

## IsoTis' Patented Accell Bone Matrix

The process of demineralization retains the naturally osteoinductive elements in bone. These osteoinductive elements, including BMPs, play a critical role in the bone forming process. IsoTis manufactures both standard DBM and a proprietary dispersed form of DBM, known as ABM which has also been shown to exhibit osteoinductive potential.

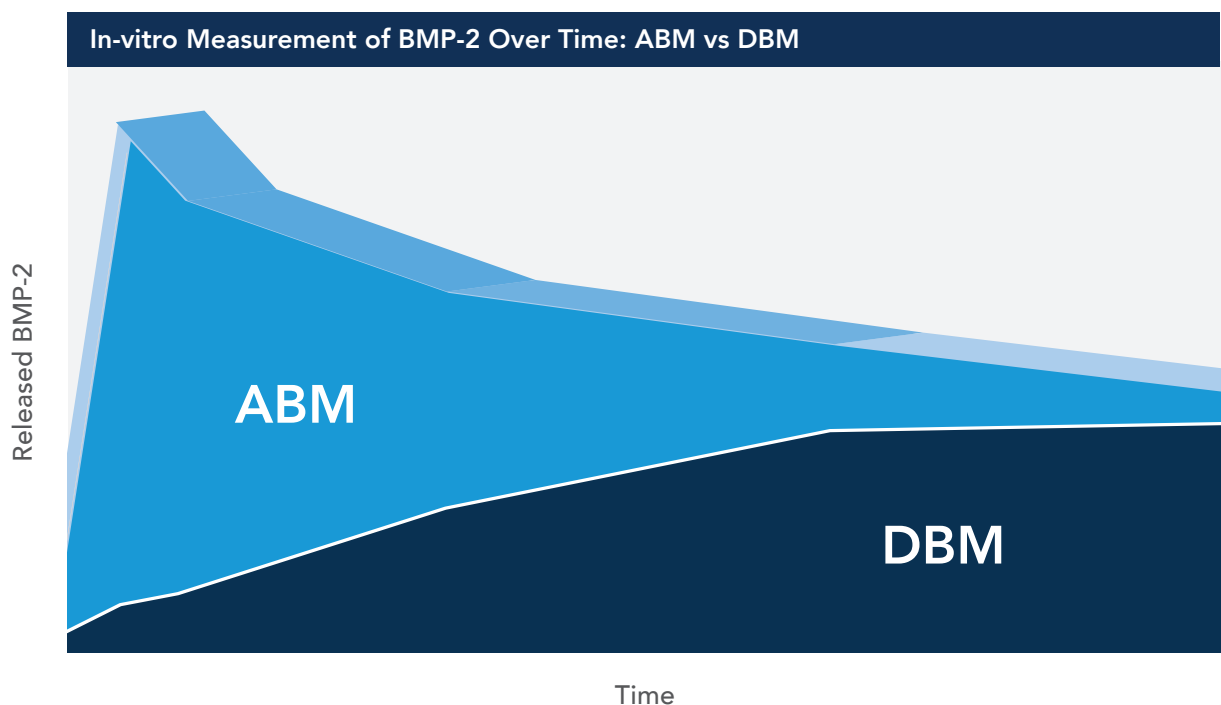
Accell Evo3 and Evo3c are designed to provide both immediate and sustained access to naturally occurring inductive bone proteins to facilitate fusion.

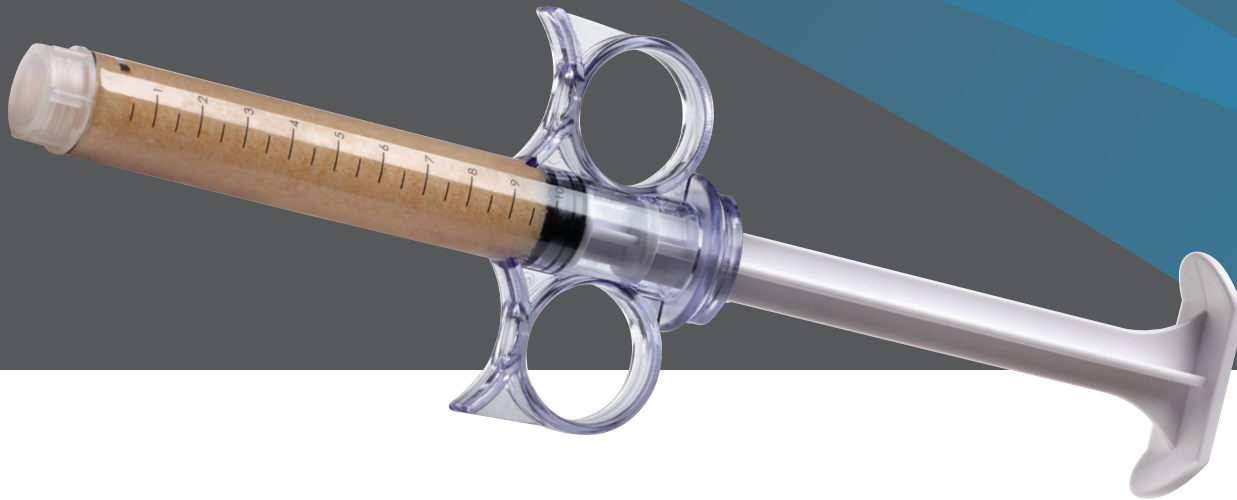
### Evaluation of Osteoinductive Potential

An *in-vitro* study was conducted to examine accessibility to bioactive proteins in ABM and DBM.<sup>2</sup> The content of BMP-2, which has been shown to be strongly correlated with osteoinductive potential *in-vivo*<sup>3</sup>, was measured over time using an Enzyme Linked Immunosorbent Assay (ELISA). The results are shown graphically below.

### Study Results

- Soluble BMP-2 was detected in ABM at an earlier time compared to particulate DBM.
- ABM's open pore structure provides earlier accessibility to bone proteins.
- DBM provides accessibility to bone proteins at later time points.





## Superior Handling<sup>1</sup>

The optimized formulation of Accell Evo3 contains ABM and DBM combined with a unique poloxamer RPM. The result is a graft material with exceptional handling and containment characteristics.

The unique RPM carrier becomes more viscous at body temperatures, while it is less viscous at room temperature. Because of the RPM's thermoreversible property, Accell Evo3 is:

- Moldable at the time of application
- Packable into virtually any size or shape defect
- Mixable with other grafting materials
- Irrigation-resistant



The unique thermoreversible RPM carrier allows Accell Evo3 to resist irrigation and graft migration.



The optimized formulation of Accell Evo3 results in a robust, moldable putty that does not stick to surgical gloves.

# FEATURES

Accell Evo3<sup>®</sup> combines patented Accell<sup>®</sup> Bone Matrix (ABM) and particulate Demineralized Bone Matrix (DBM).



## Accell<sup>®</sup> Bone Matrix x 3

- Accell Evo3 contains three times more ABM than the previous generation of Accell Demineralized Bone Matrix products.\*
- This patented, dispersed form of DBM offers significantly increased surface area, which provides access to the naturally occurring bone proteins contained in DBM.



## Superior Handling

Accell Evo3 incorporates a poloxamer Reverse Phase Medium, a biocompatible carrier. This unique thermoreversible carrier allows Accell Evo3 to meet the needs of challenging surgical applications where robust handling is essential.

- At room temperature, Accell Evo3 is malleable and easily extruded from the syringe.
- At body temperature, Accell Evo3 is more viscous, resists irrigation and minimizes graft migration.



## Custom, Ready-to-Use Syringe

The ergonomic syringe design and large diameter opening facilitates easy handling and extrusion of the graft. Accell Evo3 and Evo3c are ready for implantation directly from the syringe. They do not require any cumbersome or time-consuming preoperative preparation, such as thawing or mixing.



## IsoTis DBM: An Expert Approach to DBM Processing

IsoTis controls the processing of DBM and ABM from start to finish in its state-of-the-art facility. Each lot is tested in a validated *in vitro* assay to verify osteoinductive potential.<sup>1</sup>



## Safety Through E-Beam Sterilization

IsoTis utilizes electron beam (e-beam) sterilization to ensure product sterility. IsoTis' sterilization process has not been shown to impact the osteoinductive potential of DBM.<sup>1</sup> All products are e-beam sterilized as the last step in manufacturing prior to being shipped.



## Cancellous Bone

Accell Evo3c contains cancellous chips that complement the osteoconductive scaffold by providing a natural porous structure that facilitates tissue and vascular ingrowth. Cancellous bone is resorbed naturally by being incorporated into new bone during the remodeling process.<sup>1</sup>

\*Compared to Accell Connexus<sup>®</sup>

## Evolution of DBM to Accell Evo3®

### 1st Generation: DBM

**Early 1990s** – First-generation DBM formulations combined standard processed particulate DBM with an inert carrier for easy handling and graft containment.

### 2nd Generation: DBM + ABM

**2002** – A patented process was developed to transform particulate DBM into a dispersed form of DBM. This patented ABM is blended with traditional particulate DBM and an inert carrier to create our second-generation products.

### 3rd Generation: Accell Evo3

**2008** – With Accell Evo3®, IsoTis optimized the formulation of ABM, DBM, and RPM. This third-generation product includes three times the amount of ABM as compared to second-generation products with even better handling.

### Accell Evo3

Reference	Description	Size
02-5000-010	Putty (syringe)	1cc
02-5000-025	Putty (syringe)	2.5cc
02-5000-050	Putty (syringe)	5cc
02-5000-100	Putty (syringe)	10cc

### Indications for Use

Accell Evo3 is intended for filling voids and gaps in the skeletal system that are not intrinsic to the stability of the bony structure. The product is indicated for use as a bone graft extender in the spine, extremities and pelvis. Accell Evo3 may also be used as a bone void filler in the posterolateral spine, extremities and pelvis. The voids or gaps may be surgically created defects or the result of traumatic injury to the bone.

Accell Evo3c is intended for filling voids and gaps in the skeletal system that are not intrinsic to the stability of the bony structure. Accell Evo3c is indicated for use as a bone graft extender in the posterolateral spine, extremities and pelvis, or as a bone void filler in the extremities and pelvis. The voids or gaps may be surgically created defects or the result of traumatic injury to the bone.

### Warnings

- The product must be used prior to the expiration date.
- For single use only.
- Do not re-sterilize.
- Do not use if packaging has been damaged and/or the product has been compromised. In the event packaging has been compromised, discard the product. Damaged packaging should be returned to the manufacturer.
- Do not use to support reduction of a defect site. Rigid fixation techniques are recommended as needed to assure stabilization of the defect in all planes. Screws must gain purchase in the host bone as opposed to the Accell Evo3 or Accell Evo3c.
- Do not use to repair bone defects where soft tissue coverage cannot be achieved as complete post-operative wound closure is necessary.
- Do not overfill the graft site.

### Accell Evo3c

Reference	Description	Size
02-6000-025	Putty (syringe)	2.5cc
02-6000-050	Putty (syringe)	5cc
02-6000-100	Putty (syringe)	10cc

### Precautions

- Accell Evo3 and Accell Evo3c are sterile for the duration of the product's shelf life, provided that the package is in its original sealed condition and that it is unopened and undamaged.
- As with all biological products, the tissue in Accell Evo3 and Accell Evo3c has the potential to transmit infectious agents despite processing treatments, extensive donor screening, tissue selection and laboratory testing. To date, there have been no reports of experimental or clinical viral seroconversion attributed to the use of demineralized bone.
- 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.
- Once the container seal has been compromised, the tissue product shall be either transplanted, if appropriate, or otherwise discarded.
- Use caution with filling a closed defect. Resistance during extrusion may be an indication of over pressurization. Excessive pressurization of the device could result in fat embolization and/or embolization of the material into the bloodstream.
- When introducing Accell Evo3 or Accell Evo3c, care must be taken to avoid excessive compaction.
- Appropriate placement and/or fixation are critical factors in the avoidance of potentially adverse effects.
- Overfilling the implantation site should be avoided to achieve a tension-free closure of the wound.

### References

1. Data on file.
2. Khaliq S, Lollis R, Bell D, Oliver R, Walsh WR, and Ingram R, Evaluation of a next-generation DBM putty in a posterolateral spinal fusion model, (2009) Integra LifeSciences Corporation.
3. Chnari, E; Javoroncov, M; Gertzman AA; Sunwoo MH; Dunn, MG, Bone Morphogenetic Protein 2 (BMP-2) Levels are Predictive of the Osteoinductive Potential of Demineralized Bone Matrix, 56th Annual Meeting of the Orthopaedic Research Society Poster No. 485



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