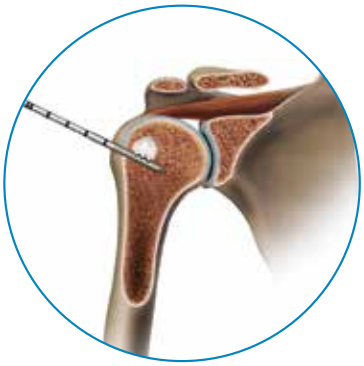
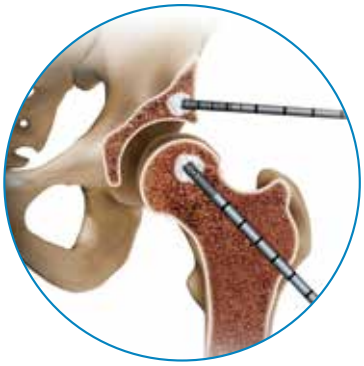
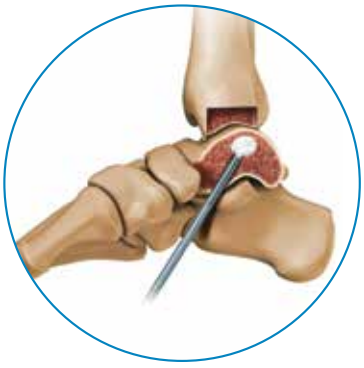
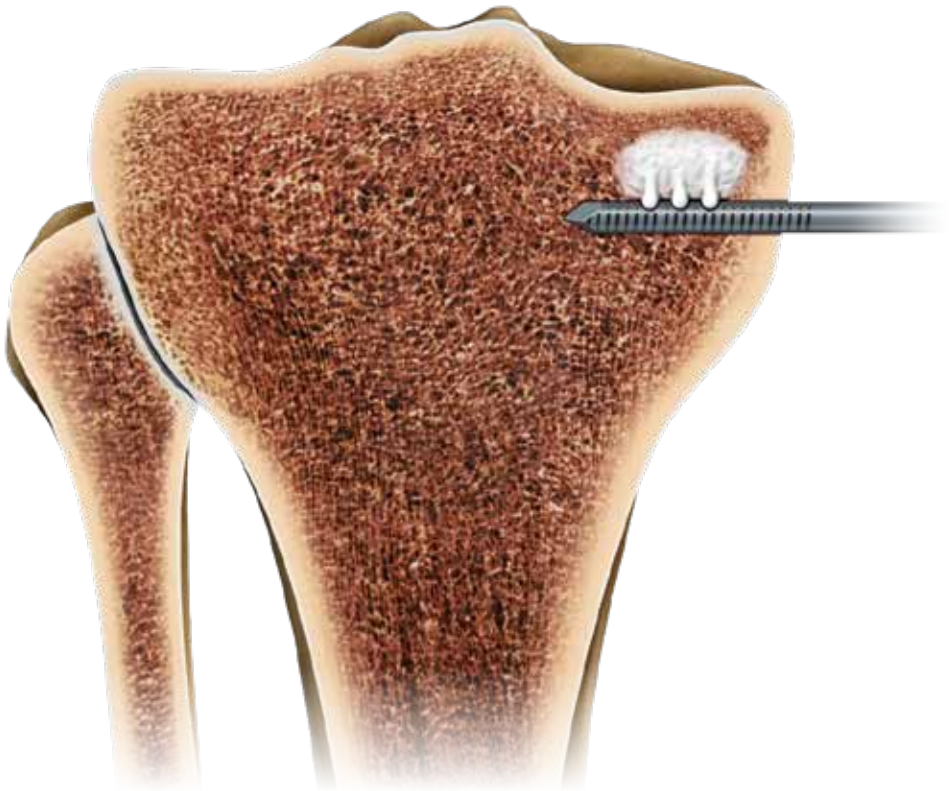
# AccuFill® Bone Substitute Material (BSM)

## The Subchondroplasty® Procedure









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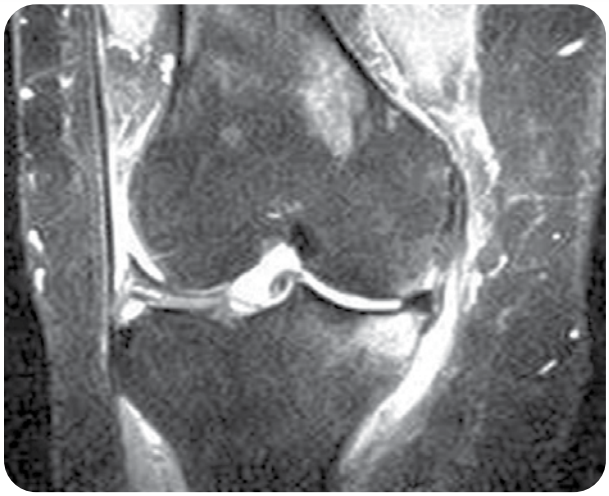
## AccuFill BSM

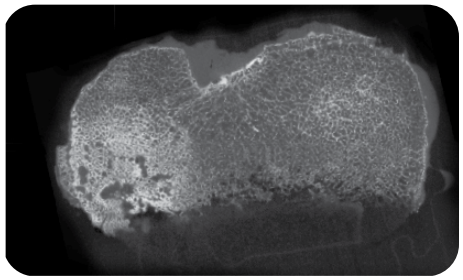


BML Bone Defect on T2 MRI

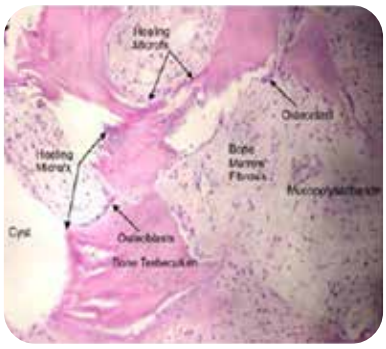
The Subchondroplasty Procedure is a minimally invasive, fluoroscopically-assisted procedure that targets and fills subchondral bone defects not intrinsic to the bony structure. These defects can be associated with bone marrow lesions (BML), insufficiency or microtrabecular fractures, repetitive stress injuries to the cancellous bone or cysts. Successfully filling osseous defects of the trabecular bone requires an injectable BSM with very specific characteristics.

**An optimal material for the Subchondroplasty Procedure:**

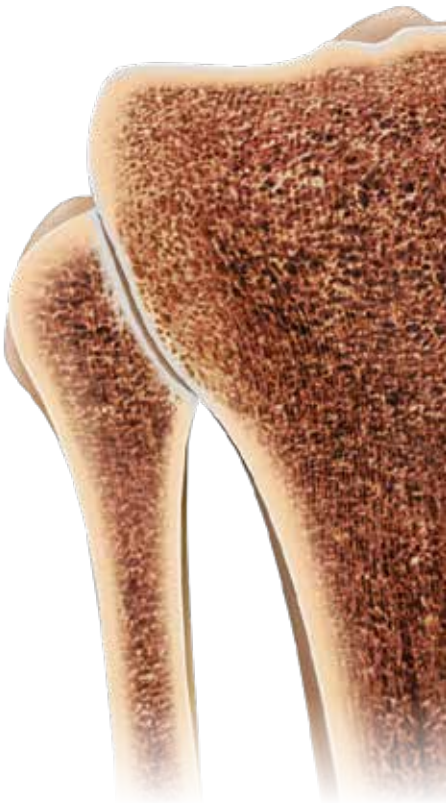
1. Flows readily into closed trabecular bone[1]
2. Sets hard upon implantation with properties comparable to healthy cancellous bone[2]
3. Undergoes cell-mediated remodeling as the bone heals[2]



Micro CT from patient with bone marrow lesion




Histologic section of patient with bone marrow lesion showing evidence of microfracture non-union of the subchondral bone[3]

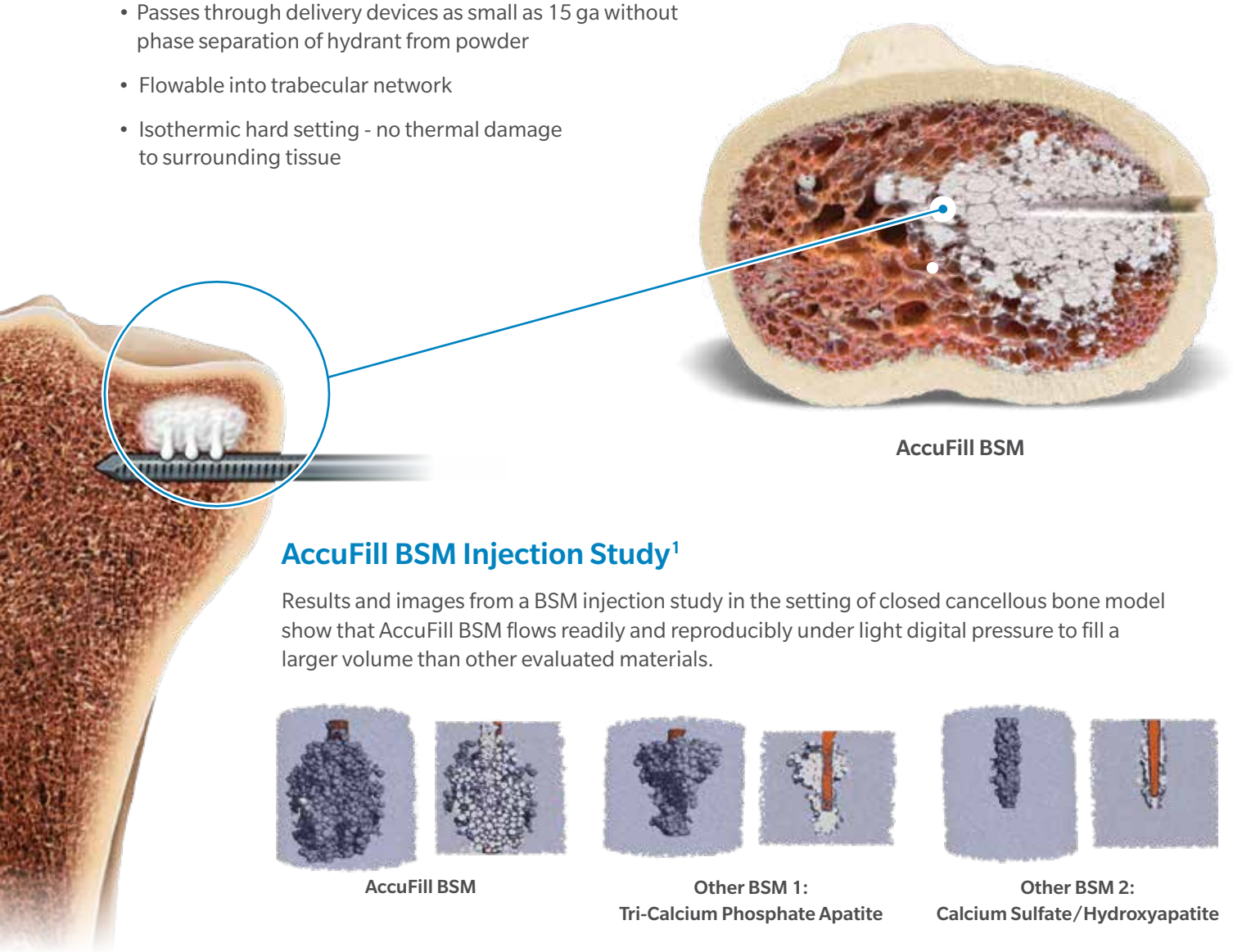


## AccuFill BSM:
## Performance Characteristics

AccuFill BSM is an engineered calcium phosphate compound. It flows readily to fill subchondral bone defects, then crystallizes and sets in an isothermic reaction at 37°C to form a nanocrystalline*, macroporous and osteoconductive scaffold in the bone. Inclusion of a binding agent (CMC [carboxymethylcellulose]) allows the material to remain bound in a paste form, and interdigitate into closed cancellous bone.

Standard Injectable BSM

- Passes through delivery devices as small as 15 ga without phase separation of hydrant from powder
- Flowable into trabecular network
- Isothermic hard setting - no thermal damage to surrounding tissue



AccuFill BSM

## AccuFill BSM Injection Study[1]

Results and images from a BSM injection study in the setting of closed cancellous bone model show that AccuFill BSM flows readily and reproducibly under light digital pressure to fill a larger volume than other evaluated materials.



AccuFill BSM

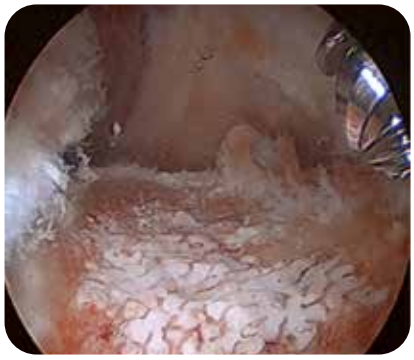
Other BSM 1:
Tri-Calcium Phosphate Apatite

Other BSM 2:
Calcium Sulfate/Hydroxyapatite

**Important Safety Information:** The use of AccuFill BSM is not intended to be intrinsic to the stability of the bony structure. Radiographic studies should be used to confirm that the adjacent cortical bone is intact. AccuFill BSM is not intended for use in vertebroplasty or similar load-bearing indications. AccuFill BSM is not intended for the treatment of cartilage defects or injury. AccuFill BSM is not intended to support articular cartilage or cortical bone.

## AccuFill BSM: Performance Characteristics

**Intra-operative Images of AccuFill BSM Interdigitation**



**Proximal Femur**

**Distal Tibia**

## AccuFill BSM: Properties[2]

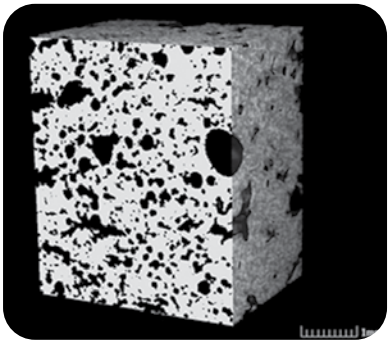
- Mimics chemical composition and crystalline structure of natural human bone mineral
- Incorporation of metal ions (M) keeps the crystal domain of AccuFill BSM to a size similar to those formed by bone apatite
- Reactive material, undergoes cell-mediated remodeling

AccuFill BSM is composed of two distinct forms of calcium phosphate - amorphous calcium phosphate (ACP) and dicalcium phosphate dihydrate (DCPD). Due to rapid hydrolysis of the ACP into apatite, the final product is a calcium deficient, nanocrystalline* material that has the crystal structure and chemical formulation to undergo cell-mediated remodeling.

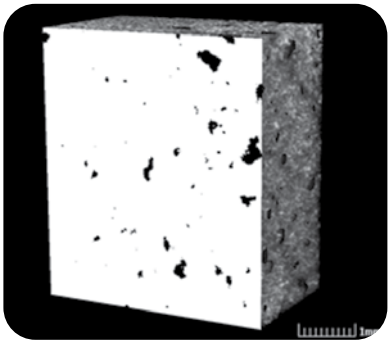
### Chemical Formula/Crystalline Structure

| Material | Chemical Composition | Average Nano Crystal Length (nm) | Average Nano Crystal Width (nm) | Average Nano Crystal Height (nm) | Total Volume ($nm^3$) |
|---|---|---|---|---|---|
| Human Bone Mineral | $Ca_{10-x}(M)_x(PO4)_{6-x}(HPO_4, CO_3)_x(OH)_{2-x}$ | 23 - 32 | 6.7 - 8.0 | 6.7 - 8.0 | 1,485 |
| AccuFill BSM | $Ca_{10-x}(M)_x(PO_4)_{6-x}(HPO_4, CO_3)_x(OH)_{2-x}$ | 26 | 8 | 8 | 1,664 |
| Standard Calcium Phosphate | $Ca_{10-x}(PO4)_{6-x}(HPO_4, CO_3)_x(OH)_{2-x}$ | 22 | 26 | 26 | 14,872 |

AccuFill BSM is 55% porous, with micropores and macropores up to 300µm. Greater surface area allows for revascularization and remodeling.[5,6] The inclusion of an effervescent agent (sodium bicarbonate) releases carbon dioxide during the setting process and forms pores within the material.



**AccuFill BSM Porosity[4]**



**Standard CaP Porosity[4]**

* The grain size of the hydroxyapatite (HA) crystals that form as part of the amorphous and crystalline mixture of calcium phosphate sets are on the nanometer scale. The size of the crystalline structures were measured by X-ray diffraction to be less than 100 nanometers.

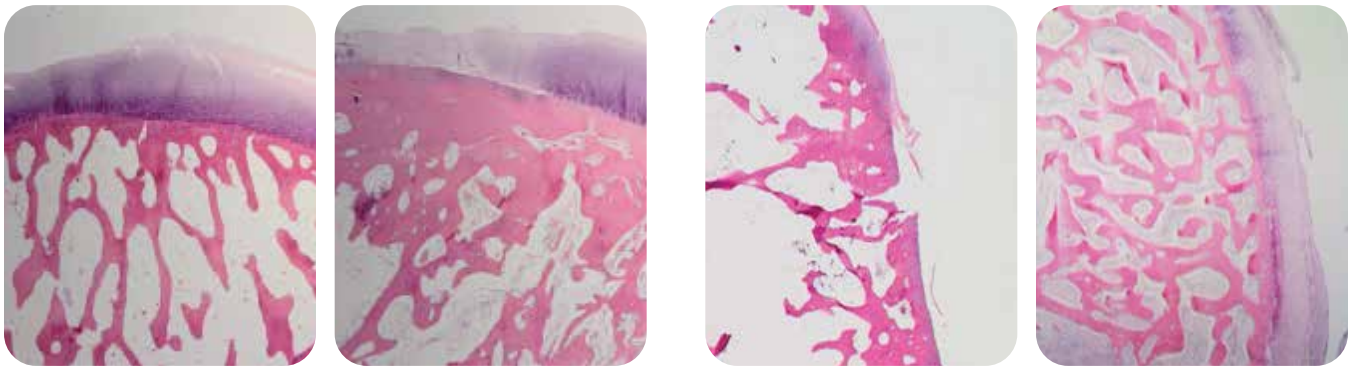
## AccuFill BSM: Properties

**AccuFill BSM in a Femoral Condyle Preclinical Canine Model[8]**

Subchondroplasty Canine Impact Model Study 1 Year Report**
James L. Cook, DVM, PhD
Comparative Orthopaedic Laboratory
Missouri Orthopaedic Institute

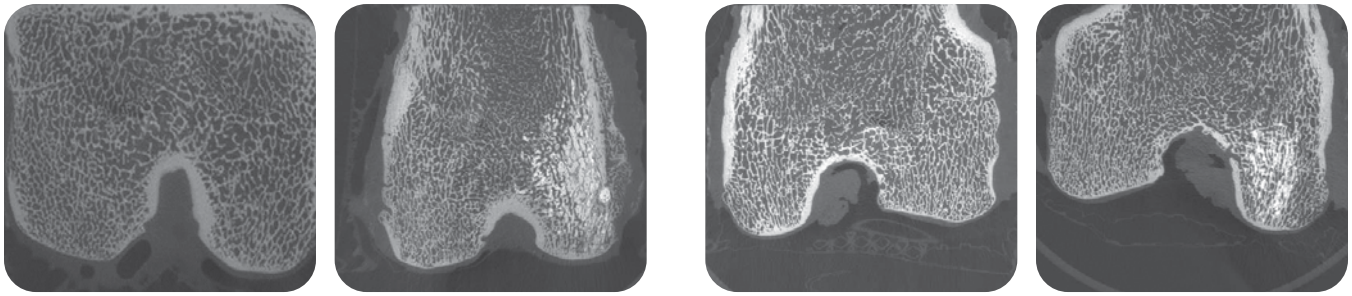
Study tested healing response in canine subjects to an artificially created bone defect treated with SCP vs control group with no treatment. The bone defects were created using a validated impact model, replicating the pathology of a chronic BML.[9]

Histology



3 Month Control | 3 Month Post SCP Injection | 12 Month Control | 12 Month Post SCP Injection

Micro CT

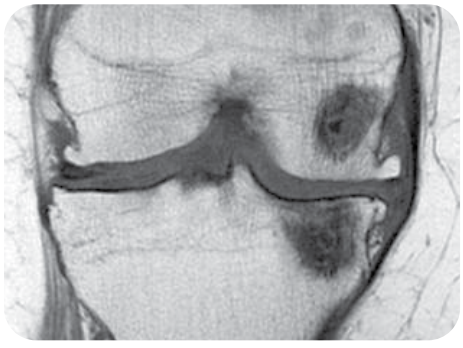


3 Month Control | 3 Month Post SCP Injection | 12 Month Control | 12 Month Post SCP Injection

**Note, the incorporation of the AccuFill BSM in the SCP samples vs. the loss of trabeculae and unresolved subchondral insufficiency fractures in the control samples.**

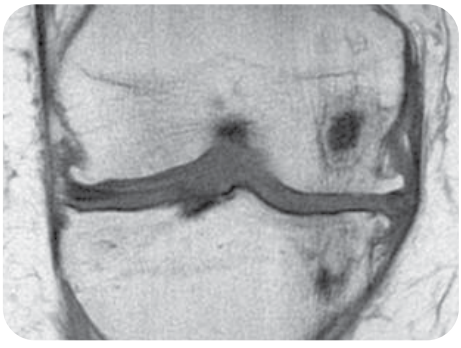
Canine models may not be predictive of human clinical results.

## MRI Evidence of AccuFill BSM Undergoing Cell-Mediated Remodeling



AccuFill BSM 1 Month Post-Operative

Post-operative MRI evaluation following SCP Procedure shows gradual remodeling of AccuFill BSM into natural cancellous bone.



AccuFill BSM 14 Months Post-Operative

## AccuFill BSM: Handling Properties

- May be mixed with saline
- 15-minute working time - easy, closed syringe mixing
- Inject with 1cc syringes - digital injection pressure

## AccuFill BSM: Summary

| Criteria | Feature | Benefit |
|---|---|---|
| **Performance** | • Truly injectable and flowable through cancellous bone<br>• Remains cohesive<br>• Isothermically sets in 10 minutes at 37º C | • Interdigitates easily into trabecular network – no need to create a void<br>• No phase separation from injection pressure<br>• Sets hard, no thermal necrosis |
| **Properties** | • Proprietary engineered apatite similar to apatite of bone<br>• Osteoconductive<br>• Nanocrystalline* structure, macroporous scaffold<br>• 55% total porosity; 1-300µm pore size<br>• ~7-9 MPa compressive strength[2] | • Undergoes cell-mediated remodeling into natural bone<br>• Porosity and pore size give it greater surface area for cellular activity[7]<br>• Physical properties comparable to cancellous bone |
| **Handling** | • 15-minute of working time<br>• May be mixed with saline<br>• Injectable under digital pressure | • Long window for implantation; intra-operative flexibility<br>• Tactile feedback during injection |

**References**


1. Colon DA, Yoon BJ, Russell TA, Cammisa FP, Abjornson C, Assessment of the injection behavior of commercially available bone BSMs for Subchondroplasty procedures, The Knee, Vol. 22, Issue 6, Pages 597-603, Copyright 2015, with permission from Elsevier.
   *Benchtop data is not necessarily indicative of clinical outcomes.*
2. Tofi ghi et al. Setting Reactions Involved in Injectable Cements Based on Amorphous Calcium Phosphate, Key Engineering Materials Vols. Pages 192-195 (2001).
   *Benchtop and animal data is not necessarily indicative of clinical outcomes.*
3. Zanetti et al. Bone Marrow Edema Pattern in Osteoarthritic Knee: Correlation Between MR Imaging and Histologic Findings, Radiol 2000; 215:835-840.
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   *Animal data is not necessarily indicative of clinical outcomes.*
5. Lee, D. Duke, et al. "[alpha]-BSM (R): A Biomimetic Bone Substitute and Drug Delivery Vehicle. Clinical orthopaedics and related research 367 (1999): S396-S405.
6. Wang W., Yeung K.W.K, Bone grafts and biomaterials substitutes for bone defect repair: a review, Bioactive Materials 2 (2017)224-227.
7. Murphy, Ciara M., et al. "Understanding the effect of mean pore size on cell activity in collagen-glycosaminoglycan scaffolds." Cell Adhesion & Migration 4:3, 377-381; July/August/September 2010; © 2010 Landes Bioscience.
8. Cook, J. Subchondroplasty Canine Impact Model Study 1 year report, Comparative Orthopaedic Labratory, Missouri Orthopaedic Institute.
   *Animal data is not necessarily indicative of clinical outcomes.*
9. Brimmo et al. Development of a Novel Canine Model for Posttraumatic Osteoarthritis of the Knee, The Journal of Knee Surgery, 2015.
   *Animal data is not necessarily indicative of clinical outcomes.*


AccuFill Bone Substitute Material is an injectable, self-setting, macroporous, osteoconductive, calcium phosphate bone graft substitute material that is intended for use to fill bony voids or gaps of the skeletal system of the extremities, spine (i.e., posterolateral spine), and the pelvis that are not intrinsic to the stability of the bony structure. These defects may be surgically created osseous defects or osseous defects created from traumatic injury to the bone. AccuFill Bone Substitute Material is a bone graft substitute that resorbs and is replaced with new bone during the healing process.

OUS Indications for Use:
AccuFill Porous Bone Substitute is an injectable, self-setting, macro-porous, osteo-conductive, calcium phosphate bone graft substitute material that is intended for use to fill bony voids or gaps of the lower extremities (pelvis through foot) that are not intrinsic to the stability of the bony structure. These defects may be surgically created osseous defects or osseous defects created from traumatic injury to the bone including bone marrow lesions. AccuFill is a bone graft substitute that resorbs and is replaced with new bone during the healing process.

* The grain size of the hydroxyapatite (HA) crystals that form as part of the amorphous and crystalline mixture of calcium phosphate sets are on the nanometer scale. The size of the crystalline structures were measured by X-ray diffraction to be less than 100 nanometers.

**Animal models may not be predictive of clinical results.



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zimmerbiomet.com
1-800-253-6190

**AccuFill BSM**
**MANUFACTURED BY:**
Etex Corporation
55 Messina Drive
Braintree, MA 02184

**AccuFill BSM**
**DISTRIBUTED BY:**
Zimmer Knee Creations, Inc.
841 Springdale Dr.
Exton, PA 19341