AccuFill® Bone Substitute Material (BSM)

The Subchondroplasty® Procedure
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 bone¹
2. Sets hard upon implantation, with properties comparable to healthy cancellous bone²
3. Undergoes cell-mediated remodeling as the bone heals²

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¹ Micro CT from patient with bone marrow lesion.

² BML Bone Defect on T2 MRI

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

- 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

* 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.

AccuFill BSM Injection Study

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.

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 to support articular cartilage or cortical bone.

AccuFill BSM

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Other BSM 1:
Tri-Calcium Phosphate Apatite

Other BSM 2:
Calcium Sulfate/Hydroxyapatite

* 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: Performance Characteristics

Intraoperative Images of AccuFill BSM Interdigitation

![Proximal Femur](image1)

![Distal Tibia](image2)

**AccuFill BSM: Properties**

- 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 which has the crystal structure and chemical formulation to undergo cell-mediated remodeling.

### Chemical Formula/Crystalline Structure

<table>
<thead>
<tr>
<th>Material</th>
<th>Chemical Composition</th>
<th>Average Nano Crystal</th>
<th>Total Volume (nm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Length (nm)</td>
<td>Width (nm)</td>
</tr>
<tr>
<td>Human Bone Mineral</td>
<td>Ca₁₀₋ₓ(M)ₓ(PO₄)₆₋ₓ(HPO₄, CO₃)ₓ(OH)₂ₓ</td>
<td>23 - 32</td>
<td>6.7 - 8.0</td>
</tr>
<tr>
<td>AccuFill BSM</td>
<td>Ca₁₀₋ₓ(M)ₓ(PO₄)₆₋ₓ(HPO₄, CO₃)ₓ(OH)₂ₓ</td>
<td>26</td>
<td>8</td>
</tr>
<tr>
<td>Standard Calcium Phosphate</td>
<td>Ca₁₀₋ₓ(PO₄)₆₋ₓ(HPO₄, CO₃)ₓ(OH)₂ₓ</td>
<td>22</td>
<td>26</td>
</tr>
</tbody>
</table>

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

* 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: Handling Properties

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

AccuFill BSM: Summary

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

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.

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4. 3D CT reconstructions of BSM materials from CT Study #5163 – Numira Biosciences Etex DHF 060130. Animal data is not necessarily indicative of clinical outcomes.

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AccuFill BSM: Properties

AccuFill BSM in a Femoral Condyle Preclinical Canine Model

Subchondroplasty Canine Impact Model Study 1 year report
James L. Cook, DVM, PhD
Comparative Orthopaedic Laboratory
Missouri Orthopaedic Institute

Study tested canine subjects’ healing response 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.

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

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