

STIMULAN[®] Competitive Environment

In-person training for Distributor Sales Representatives

Training objectives

At the end of this 30 minute training session you will:

- Know who the key competitors are for STIMULAN® in the infection market
- Understand the key characteristics of their products and positioning
- Be aware of their strengths and weaknesses relative to STIMULAN
- Know which differentiating factors to focus on in conversations with your surgeons
- Have an action plan for protecting and increasing STIMULAN sales

Agenda

- Infection market
- Products indicated & contraindicated for use in infection
- Competitor differentiation summary
- Product profiles:
 - OSTEOSSET®
 - BonePlast®
 - Calcigen® S
 - Cerament®
 - OsteoBoost®
 - STIMULAN
- Protect and increase STIMULAN sales



Infection market

Medical device suppliers are now focusing on infection as a growth opportunity

- Hospitals are under increased scrutiny to provide high quality care, reduce patient readmissions and lower treatment costs
 - There is a growing willingness by surgeons to discuss their infection challenges
 - There is a greater sensitivity to the cost impact of managing infection in patients
- Surgeons are willing to consider calcium-based medical devices
- These calcium-based devices can be segmented into products that are:
 - Cleared for use at an infected site
 - Contraindicated for use at an infected site

Products indicated for use in infected sites

Product Comparison	OSTEOSET	BonePlast	STIMULAN
Composition	CaSO ₄ , Calcium stearate	CaSO ₄ , Accelerating saline solution	CaSO ₄ , Sterile water
Ordering sizes	5cc (3, 4.8mm beads) 25cc (7mm beads)	18cc	Rapid Cure: 5cc, 10cc, 20cc Kit: 5cc, 10cc
Bead mat included	Yes – Not universal	No - Sold separately	Yes - Universal bead mats are included in every box. Can be used to create 3, 4.8 or 6mm beads
Setting time	5 minutes (Fast Cure) 20 minutes (Standard Cure)	20 minutes	4 min (Rapid Cure) 8 min (Kit)
Impurities	Contains non-absorbable impurities	Unknown	No. STIMULAN has controlled purity
Hydrophilic or Hydrophobic	Hydrophobic	Hydrophilic	Hydrophilic
pH	Acidic	Unknown	Physiologic
Claimed absorption rate	4-8 weeks	4-8 weeks	4-8 weeks
Cleared for infection	Yes	Yes	Yes

Products contraindicated for use in infected sites

Product Comparison	Calcigen S	Cerament	OsteoBoost
Composition	CaSO ₄ , Potassium citrate, Sodium phosphate	CaSO ₄ , HA, Iohexol	CaSO ₄ , β-TCP, HA, Distilled water
Ordering sizes	5g, 10g, 25g	5cc, 10cc, 18cc	5cc, 10cc
Bead mat included	No	No – Sold separately	Yes – Not universal
Setting time	4-7 minutes	15 minutes	5+ minutes
Impurities	Unknown	Unknown	Unknown
Hydrophilic or Hydrophobic	Hydrophilic	Hydrophilic	Unknown
pH	Unknown	Slightly acidic	Neutral
Claimed absorption rate	8-12 weeks	6-12 months	Not specified. Expected to be > 6 months
Cleared for infection	No - contraindicated	No – contraindicated	No - contraindicated

Competitor differentiation summary

Product Name	Cleared for Infection	Fully Absorbed	Claimed Absorption Rate	Bead Mat Included	Fast Set Option	Cost Position	Source of CaSO ₄	STIMULAN Key points of differentiation
STIMULAN	Yes	Yes	4 - 8 weeks	Yes	Yes	Medium	Pharmaceutical-grade reagents	N/A
OSTEOSET	Yes	May not fully absorb	4 - 8 weeks	Yes	Yes	Low	Mined	<ul style="list-style-type: none"> Purity – no impurities as not mined gypsum No third body damage
BonePlast	Yes	Unknown	4 - 8 weeks	No	No	Low	Unknown	<ul style="list-style-type: none"> Truly absorbable Rapid Cure option
Calcigen S	Contra-indicated	Unknown	8 -12 weeks	No	No	Low	Unknown	<ul style="list-style-type: none"> Cleared for infected sites Truly absorbable
Cerament	Contra-indicated	No	6 -12 months	No	No	High	Unknown	<ul style="list-style-type: none"> Cleared for infected sites Truly absorbable
OsteoBoost	Contra-indicated	No	Not specified. Expected to be > 6 months	Yes	No	Medium	Unknown	<ul style="list-style-type: none"> Cleared for infected sites Truly absorbable

Product profiles

OSTEOSET - Wright Medical®

Indication & absorption rate ^{1,2}

- **Bone void filler that may be used at infected sites**
- Claims to absorb within 4-8 weeks

Composition ^{1,2}

- 98.5% surgical grade calcium sulfate
- 1.5% medical grade calcium stearate

Formats, sizing and setting times ¹⁻⁴

- Injectable, moldable paste, beads
- 5cc kit: Mini-bead kit with mat for 3 and 4.8mm beads
- 25cc kit: Bead kit with large bead mat for 7mm beads
- Fast-Cure (5 min set time) and Standard Cure (20 min set time) options are available



OSTEOSET

Manufacturing ^{1,2,5}

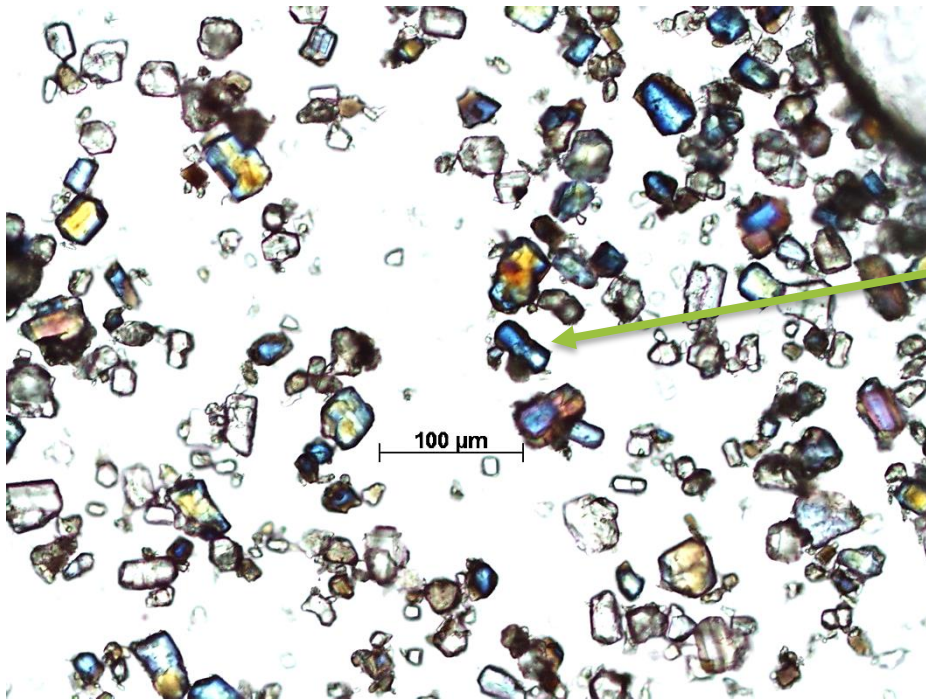


- OSTEOSET is manufactured from mined calcium sulfate
- The patents, technology, and process of producing OSTEOSET were acquired from the United States Gypsum Corporation
- Proprietary manufacturing methods are used to produce a consistent, high-quality material with **minimal lot-to-lot variation in chemical and material properties**
- OSTEOSET is composed of only 98.5% calcium sulfate

OSTEOSET	CaSO ₄ (98.5%)	CaSO ₄ · ½H ₂ O (98%+) CaCO ₃ · MgCO ₃ (0.5%) CaCO ₃ (0.3%) Aggregate (0.3%)
	Calcium Stearate (1.5%)	

OSTEOSET

Microscopic analysis of purity ⁶



Insoluble crystalline impurities

OSTEOSET residue

OSTEOSET

Take away points ¹⁻⁷

- **Can be used at infected sites**
- Calcium sulfate component is mined
- **Contains non-absorbable impurities and may not fully absorb**
- Contraindicated in articulating surfaces and may cause third body damage
- Acidic pH
- Hydrophobic
- Less product per volume
- No universal bead mat available
- Positioned as a low cost “me too” competitor
- Non-focus product but marketed on the Wright Medical website



BonePlast– Zimmer Biomet®

Indication and absorption rate ^{8,9}

- **Bone void filler that may be used at infected sites**
- Claims to absorb within 4-8 weeks

Composition ^{8,9}

- 27.6g calcium sulfate powder
- 8.28cc accelerating saline solution

Formats, sizing and setting time ^{8,9}

- Available as an injectable or individual pelletizing kit
- Known size: 18cc
- Large bore syringe is included
- Flexible mold is sold separately
- Sets in 20 minutes



BonePlast

Take away points ^{8,9}

- **Can be used at infected sites**
- No rapid cure option is available
- No bead mat is provided. Flexible mold must be purchased separately
- Positioned as a low cost competitor
- Future of product is unknown – no product information on Zimmer Biomet website



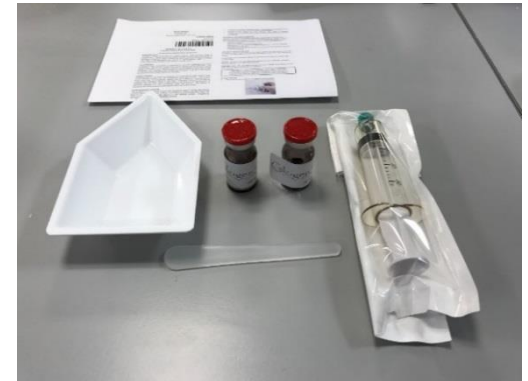
Calcigen S – Zimmer Biomet®

Indication and absorption rate ^{10,11}

- Indicated to fill bony voids or gaps of the skeletal system
- **Contraindicated for infected sites**
- Claims to absorb within 8-12 weeks

Composition ^{10,11}

- Calcium sulfate dihydrate powder
- Potassium citrate (setting time additive) and sodium phosphate solution
- When mixed, calcium ions from the calcium sulfate dihydrate react with the phosphate ions in the solution and forms a calcium phosphate



Formats, sizing and setting time ^{10,11}

- Available as a moldable or injectable paste and in pre-formed granules
- Available in 5g, 10g and 25g sizes
- Sets within 4-7 minutes

Calcigen S

Take away points ^{10,11}

- **Contraindicated for infected sites**
- Precaution for treating patients with impaired potassium metabolism
- Additional substances (e.g. antibiotics, blood, etc.) cannot be added to the filler material
- Will not set without the liquid supplied
- Becomes a calcium phosphate when fully set - can cause a long-term nidus for infection
- Should only be used in a dry surgical field
- No bead mat or fast setting option available
- Less product per volume
- Positioned as a low cost competitor
- Future of product is unknown – no product information on Zimmer Biomet website



Cerament - Zimmer Biomet

Indication and absorption rate ^{12,13}

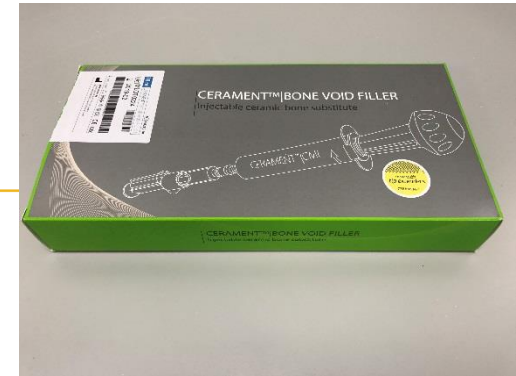
- A ceramic bone void filler for orthopaedic applications
- **Contraindicated for local infection at the site of implantation**
- Claims to remodel to bone within 6-12 months

Composition ^{12,13}

- 40% hydroxyapatite and 60% calcium sulfate
- Water soluble radiocontrast agent (Iohexol 180mg iodine/ml)
 - Iohexol is contraindicated for significant bacterial infection

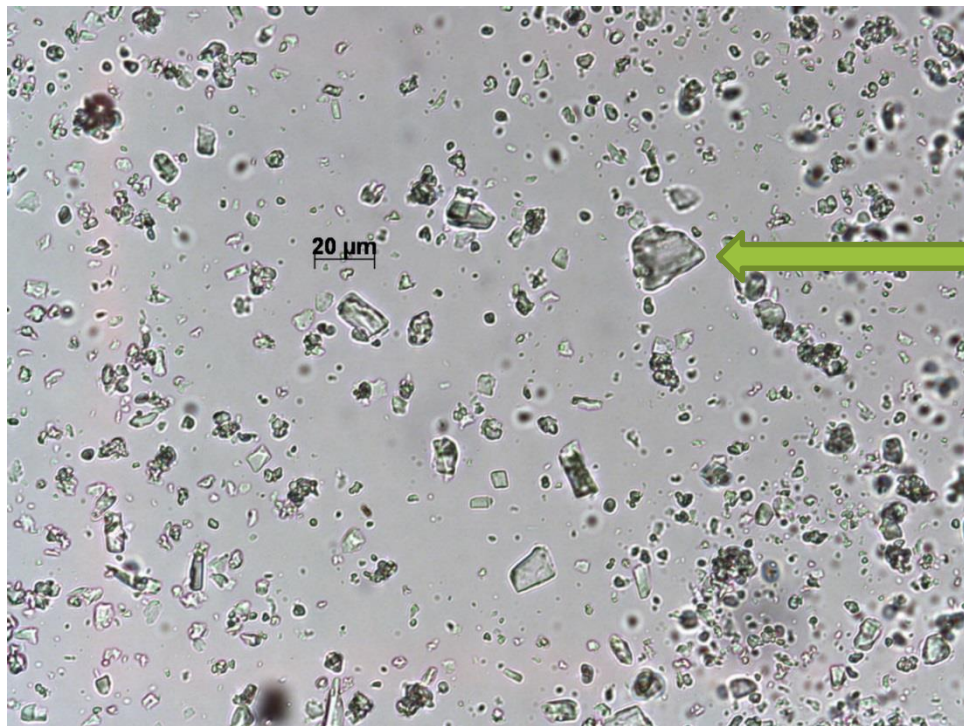
Formats, sizing and setting time ^{12,13}

- Marketed as an injectable product
- Optional bead mat is available
- Available in 5cc, 10cc, 18cc sizes
- Sets in 15 minutes



Cerament

Microscopic analysis of purity ⁶



← Insoluble HA

Microscopic analysis showing the 40% of HA remaining after calcium sulfate is dissolved

Cerament

Take away points ^{6,12-13}

- **Contraindicated for infected sites**
- Contraindicated for patients with a history of serious reaction to iodine based radio contrast agents
- Precaution to avoid intra-articular use
- **HA has a slow/incomplete absorption rate**
- HA can cause a long-term nidus for infection
- Slightly acidic pH
- No bead mat provided in box
- Positioned as a high cost competitor (list price)
- Focus product and fully marketed on the Zimmer Biomet website



OsteoBoost - OsteoRemedies®

Indication and absorption rate ¹⁴

- Osteoconductive bone void filler
- Manufactured by Berkeley Advanced Biomaterials
- **Contraindicated for use at infected sites**
- Slow absorption rate (>6 months)



Composition ¹⁴

- Calcium sulfate, β -tricalcium phosphate, hydroxyapatite
- Distilled water

Formats, sizing and setting time ¹⁴

- 5cc putty with single mat for small & medium beads
- 10cc putty with two mats for medium & large beads
- Sets in “at least 5 minutes”

OsteoBoost

Take away points ¹⁴

- **Contraindicated for use at infected sites**
- **Contraindicated for inflammatory bone disease (osteomyelitis)**
- **HA has a slow/incomplete absorption rate**
- HA can cause a long-term nidus for infection
- Available in limited sizes – 5g and 10g (5cc and 10cc implant volume)
- No universal bead mat available
- Positioned as a medium cost competitor
- Future of product is unknown - no product information available on OsteoRemedies website



STIMULAN - Biocomposites

Indication and absorption rate ^{6,15-17}

- Indicated to fill bony voids or gaps of the skeletal system
- **Cleared for placement directly at site of infection in bone voids and defects**
- Fully absorbs within 4-8 weeks

Composition ^{6,15-17}

- 100% pharmaceutical-grade calcium sulfate
- Sterile water

Formats, sizing and setting times ^{6,15-17}

- Injectable, paste, beads
- STIMULAN Rapid Cure: 5cc, 10cc & 20cc sizes; Sets in approximately 4 minutes
- STIMULAN Kit: 5cc & 10cc sizes; Sets in approximately 8 minutes
- Included universal bead mat can be used to create 3, 4.8 and 6mm beads



STIMULAN

What makes STIMULAN different? 6,15-17

- STIMULAN is manufactured from pharmaceutical-grade reagents in a state-of-the-art clean room
 - The calcium sulfate component of STIMULAN is synthetically manufactured in a laboratory setting. It is not derived from mined materials
- STIMULAN is the only calcium sulfate to undergo a patented recrystallization process that:
 - Imparts STIMULAN with a unique crystal structure and controlled properties
 - Results in STIMULAN's consistent & reliable performance
- STIMULAN has controlled purity; it is biocompatible and contains no traces of non-absorbable impurities
- STIMULAN fully absorbs at an optimal rate and therefore can be used at infected sites



STIMULAN

Take away points ^{6,15-17}

- **Cleared for placement directly at the site of infection**
- **Controlled purity (contains no impurities)**
- **Fully absorbs within 4-8 weeks**
- Physiologic pH
- Hydrophilic
- Universal bead mat included
- Causes no third body damage
- Positioned as a medium cost competitor
- Focus product: STIMULAN is fully marketed on the Biocomposites website
 - Biocomposites is focused only on the development of innovative calcium technologies



Protect & Increase STIMULAN sales

Strategies and resources

How do we protect our accounts?

Key strategies to protect accounts

- Understand what makes STIMULAN different
- Establish STIMULAN as a benchmark product
- Educate surgeons that competitor products are not equal substitutes
- Emphasize the importance of results over low prices
- Negative results will cost hospitals additional money
- React quickly
- Perform in-services
- Know what resources to draw on to help you sell STIMULAN



Resources to help you sell STIMULAN

Useful resources

- Comprehensive marketing materials & website
- Distributor Hub & training information
- Distributor Hub app
- Large surgeon following
- Surgeon testimonials
- Evidence-based medicine
- Company dedication to innovation, research & resources
- Unsolicited Request process



STIMULAN competitive environment

Find out more at biocomposites.com

For indications, contraindications, warnings and precautions see Instructions for Use. Concurrent use of locally administered antibiotics may affect setting time.

This brochure may include the use of STIMULAN or techniques that go beyond the current clearance / approval granted by the relevant regulatory authority. Please contact your local representative for further information.

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Patents granted: GB2367552, EP 1204599 B1, US 6780391, EP 2594231 B1, US 8883063, CN ZL201210466117.X, GB2496710

Patents pending: GB1502655.2, EP 16154210.5, US 15/040075, CN 201610089710.5, US 15/288328, GB1704688.9.

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