



# STIMULAN<sup>®</sup> Competitive Environment

In-person training for Distributor Sales Representatives

# Training objectives

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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

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



# Infection market

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## 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® Wright Medical®	InterSep® Exactech®	Syntheticure™ Austin Medical Ventures, Inc.	STIMULAN® Biocomposites®
Composition	CaSO <sub>4</sub> , Calcium stearate, Sterile saline	CaSO <sub>4</sub> , Unknown aqueous solution	CaSO <sub>4</sub> , Unknown aqueous solution	CaSO <sub>4</sub> , Sterile water
Ordering sizes	5cc (3, 4.8mm beads) 25cc (7mm beads)	5cc, 10cc, 20cc	5cc, 10cc, 20cc	Rapid Cure: 3cc, 5cc, 10cc, 20cc Kit: 5cc, 10cc
Formats	3 bead sizes, paste, injectable	3 bead sizes, paste, injectable	3 beads sizes, paste, injectable	3 bead sizes, 2 bullet sizes, paste, injectable
Bead mat included	Yes – Not universal	Yes – Double-sided bead mats included in each box	Yes – Not universal	Yes - Universal bead mats are included in every box. A combination bead and bullet mat is included in the 3cc box
Setting time	5 minutes (Fast Cure) 20 minutes (Standard Cure)	5 minutes	4 minutes	4 minutes (Rapid Cure) 8 minutes (Kit)
Impurities	Contains non-absorbable impurities	No	No	No. STIMULAN has controlled purity
Hydrophilic or Hydrophobic	Hydrophobic	Hydrophilic	Hydrophilic	Hydrophilic
pH	Acidic	Extremely acidic	Acidic	Physiologic
Claimed absorption rate	4-8 weeks	Not specified	4-8 weeks	4-8 weeks
Cleared for infected sites	Yes	Yes	Yes	Yes



# Products contraindicated for use in infected sites

Product Comparison	Calcigen® S Zimmer Biomet®	Cerament® Bonesupport® AB	OsteoBoost® OsteoRemedies®
Composition	CaSO <sub>4</sub> , Potassium citrate, Sodium phosphate	CaSO <sub>4</sub> , HA, Iohexol	CaSO <sub>4</sub> , β-TCP, HA, Sterile water
Ordering sizes	5g, 10g, 25g	5cc, 10cc, 18cc	5cc, 10cc
Formats	Moldable, injectable, beads, blocks, wedges	3 bead sizes, injectable, moldable	3 bead sizes, paste, injectable
Bead mat included	No – Bead tray available for order	No – Mold tray available for order	Yes – Not universal
Setting time	4-6 minutes (at room temperature)	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 infected sites	No - contraindicated	No – contraindicated	No - contraindicated

# Competitor differentiation summary

Product Name	Cleared for Infected Sites	Fully Absorbed	Claimed Absorption Rate	Bead Mat Included	Fast / Standard Set Option	Composition	Source of CaSO <sub>4</sub>	STIMULAN Key points of differentiation
STIMULAN® Biocomposites®	Yes	Yes	4-8 weeks	Yes	Yes / Yes	CaSO <sub>4</sub> , Sterile water	Pharmaceutical-grade reagents	N/A
OSTEOSET® Wright Medical®	Yes	May not fully absorb	4-8 weeks	Yes	Yes / Yes	CaSO <sub>4</sub> , Calcium stearate, Sterile saline	Mined	<ul style="list-style-type: none"> <li>Purity – no impurities</li> <li>No third body damage</li> <li>Bullet option</li> </ul>
InterSep® Exactech®	Yes	Yes	Not specified	Yes	Yes / No	CaSO <sub>4</sub> , Unknown aqueous solution	Medical-grade	<ul style="list-style-type: none"> <li>Physiologic pH</li> <li>Bullet option</li> <li>Peer-reviewed evidence</li> </ul>
Syntheticure™ Austin Medical Ventures	Yes	Yes	4-8 weeks	Yes	Yes / No	CaSO <sub>4</sub> , Unknown aqueous solution	Medical-grade	<ul style="list-style-type: none"> <li>Standard injectable option</li> <li>Bullet option</li> <li>Peer-reviewed evidence</li> </ul>
Calcigen® S Zimmer Biomet®	Contra-indicated	Unknown	8-12 weeks	No	No / Yes	CaSO <sub>4</sub> , Potassium citrate, Na <sub>3</sub> PO <sub>4</sub>	Unknown	<ul style="list-style-type: none"> <li>Cleared for infected sites</li> <li>Truly absorbable</li> <li>Bullet option</li> </ul>
Cerament® Bonesupport® AB	Contra-indicated	No	6-12 months	No	No / Yes	CaSO <sub>4</sub> , HA, Iohexol	Unknown	<ul style="list-style-type: none"> <li>Cleared for infected sites</li> <li>Truly absorbable</li> <li>Bullet option</li> </ul>
OsteoBoost® OsteoRemedies®	Contra-indicated	No	Not specified. Expected to be > 6 months	Yes	No / Yes	CaSO <sub>4</sub> , β-TCP, HA, Sterile water	Unknown	<ul style="list-style-type: none"> <li>Cleared for infected sites</li> <li>Truly absorbable</li> <li>Bullet option</li> </ul>

# Product profiles



# OSTEOSET - Wright Medical

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## Indication & absorption rate<sup>1,2</sup>

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

## Composition<sup>1,2</sup>

- 98.5% mined calcium sulfate
- 1.5% calcium stearate

## Formats, sizing and setting times<sup>1-4</sup>

- 3 bead sizes, paste, injectable
- 5cc kit: Bead mat produces 3 and 4.8mm beads
- 25cc kit: Two bead mats produce 7mm beads
- Fast-Cure (5 min set time) and Standard Cure (20 min set time) options are available



# OSTEOSET

## Manufacturing<sup>1,2,5</sup>

- 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

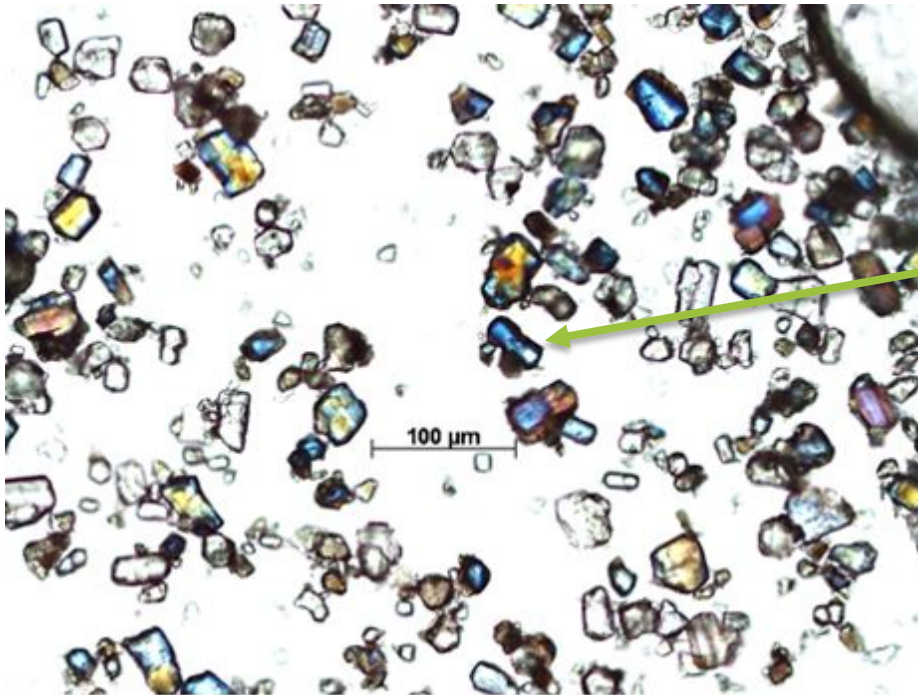


OSTEOSET	CaSO <sub>4</sub> (98.5%)	CaSO <sub>4</sub> · ½H <sub>2</sub> O (98%+) CaCO <sub>3</sub> · MgCO <sub>3</sub> (0.5%) CaCO <sub>3</sub> (0.3%) Aggregate (0.3%)
	Calcium Stearate (1.5%)	

# OSTEOSET

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Microscopic analysis of purity<sup>6</sup>



Insoluble crystalline impurities

OSTEOSSET residue

# OSTEOSET

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## Take away points<sup>1-7</sup>

- Can be used at infected sites
- Calcium sulfate component is mined
- Contains 1.1% insoluble impurities
- May not fully absorb
- Contraindicated in articulating surfaces and may cause third body damage
- Acidic pH
- Hydrophobic
- Less product volume per cc
  - OSTEOSET 5cc box (5cc bead volume) closest to 3cc STIMULAN box (7cc bead volume)
  - OSTEOSET 25cc box (25cc bead volume) closest to 10cc STIMULAN box (25cc bead volume)
- No universal bead mat available



# InterSep – Exactech, Inc

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## Indication & absorption rate<sup>8,9</sup>

- Bone void filler that may be used at infected sites
- Claims to fully absorb

## Composition<sup>8,9</sup>

- Medical-grade calcium sulfate powder
- Unknown aqueous solution

## Formats, sizing and setting times<sup>8-10</sup>

- Injectable, paste, beads
- 5cc, 10cc and 20cc kits
- Double-sided round bead mat included to produce 3, 4.5, and 6mm beads
- Fast-Cure only (5 min set time)
- A standard setting option is not available



# InterSep

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## pH analysis<sup>6</sup>

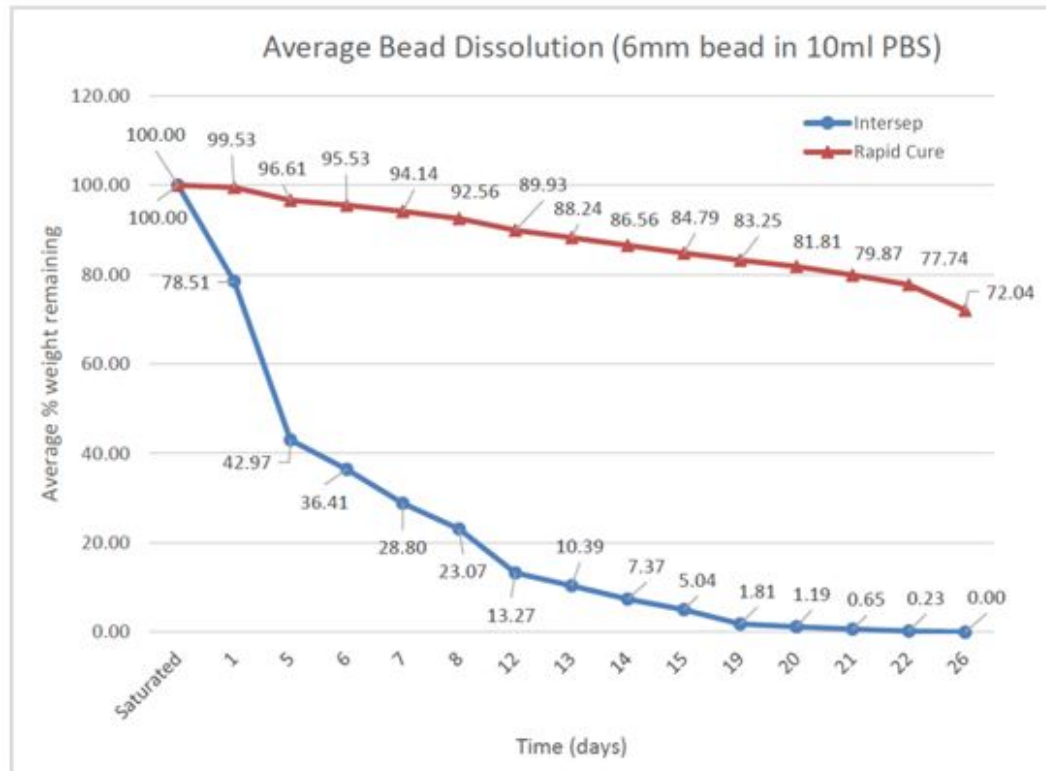
Sample Name	Ref	Lot Number	Appearance	pH
InterSep Sample	CS-05cc	016371	White powder, clear liquid	3.59
	CS-05cc	016371	White powder, clear liquid	3.81
STIMULAN Sample	620-005D	2018-03a	White powder, clear liquid	7.35
	620-005D	2017-12	White powder, clear liquid	7.25

Testing confirmed that InterSep samples each have an extremely acidic pH below 4



# InterSep

## Degradation analysis<sup>6</sup>



STIMULAN

InterSep

InterSep beads degrade at a much higher rate than STIMULAN Rapid Cure beads

# InterSep

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## Take away points<sup>6,8-10</sup>

- Can be used at infected sites
- Degrades at a rapid rate
- Extremely acidic pH (3.6-3.8)
- Contains less product per volume
  - InterSep 5cc box (7.7g powder) closest to 3cc STIMULAN box (6.3g powder)
- No standard set option
- No data or publications to support efficacy
- OEM product with separate companies cover R&D, manufacturing and sales/marketing



# Synthecure - Austin Medical Ventures, Inc.

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## Indication & absorption rate<sup>11,12</sup>

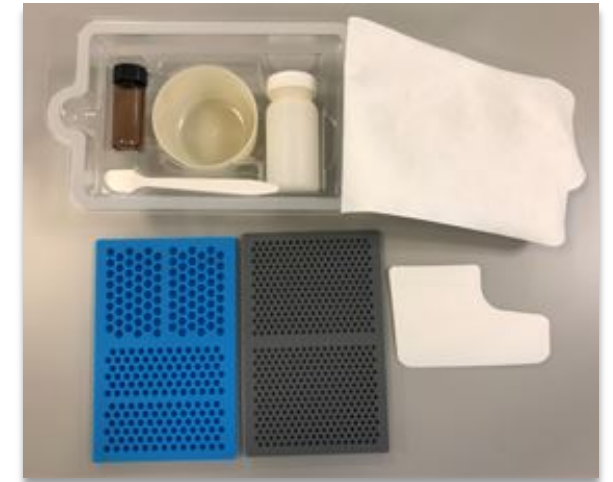
- Bone void filler that may be used at infected sites
- Claims to absorb within 4-8 weeks

## Composition<sup>11,12</sup>

- Medical grade calcium sulfate powder
- Unknown aqueous solution


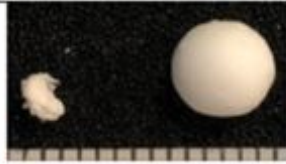



## Formats, sizing and setting times<sup>11-13</sup>

- 3 bead sizes, paste, injectable
- 5cc, 10cc and 20cc kits
- Two single-sided bead mats included to produce 3.0, 4.8 and 6.0mm beads
- Rapid curing option (4 min set)
- A standard setting option is not available



# Synthecure

## Porosity & degradation analysis<sup>6</sup>

<b>Day 4</b> Bead Loss Synthecure -18% Stimulan -1.8%		<b>Day 13</b> Bead Loss Synthecure - 70.23% Stimulan -11.76%	
<b>Day 5</b> Bead Loss Synthecure -31% Stimulan -3.39%			
<b>Day 6</b> Bead Loss Synthecure -41% Stimulan -4.47%			
<b>Day 7</b> Bead Loss Synthecure -49% Stimulan -6%			

The higher porosity of Synthecure (left) contributes to its increased rate of degradation

# Synthecure

## Clinical feedback<sup>6</sup>



Post-op



12 days post-op



Serous wound drainage

20cc of Synthecure was fully absorbed at 12 days post-op with reported drainage

\*Case images courtesy of Dr. Erik Schnaser

# Syntheticure

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## Take away points<sup>6,11-13</sup>

- Can be used at infected sites
- Claims to absorb within 4-8 weeks
  - Testing results show that Syntheticure is highly porous and degrades much faster than STIMULAN Rapid Cure
- Acidic pH (<7)
- Low compressive strength
- No standard set option available – difficulty with injection
- Limited data or publications to support efficacy
- Limited direct field support to customers and hospitals





# Calcigen S – Zimmer Biomet

## Indication and absorption rate<sup>14-16</sup>

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

## Composition<sup>14,15</sup>

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

## Formats, sizing and setting time<sup>14-16</sup>

- Moldable, injectable, beads, blocks, wedges
- Supplemental mold tray is available for order
- Available in 5g, 10g and 25g sizes
- Sets within 4-6 minutes



# Calcigen S

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## Take away points<sup>14-16</sup>

- 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
- Setting time is temperature dependent
- Becomes a calcium phosphate when fully set – potential to be a nidus for infection
- No fast setting option available
- Supplemental mold tray is available for order
- Contains 1/2 less product per volume
  - Calcigen S 5g box (2.5cc powder) closest to 3cc STIMULAN box (6.3g powder)
  - Calcigen S 10g box (5cc powder) closest to 5cc STIMULAN box (9.5g powder)



# Cerament - Bonesupport

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## Indication and absorption rate<sup>17-20</sup>

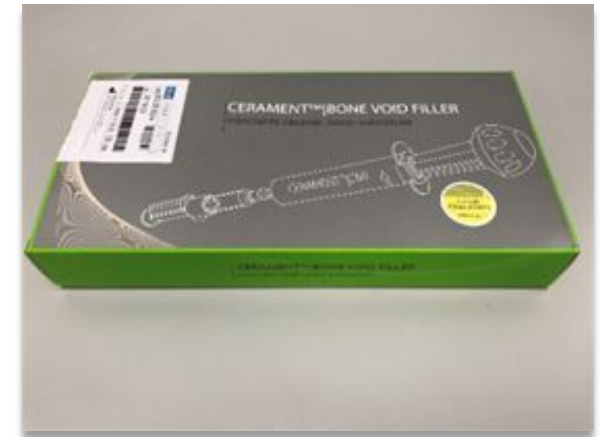
- A ceramic bone void filler for orthopaedic applications
- Contraindicated for local infection at the site of implantation
- Claims to remodel to bone within 6-12 months

## Composition<sup>17-20</sup>

- 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<sup>17-20</sup>

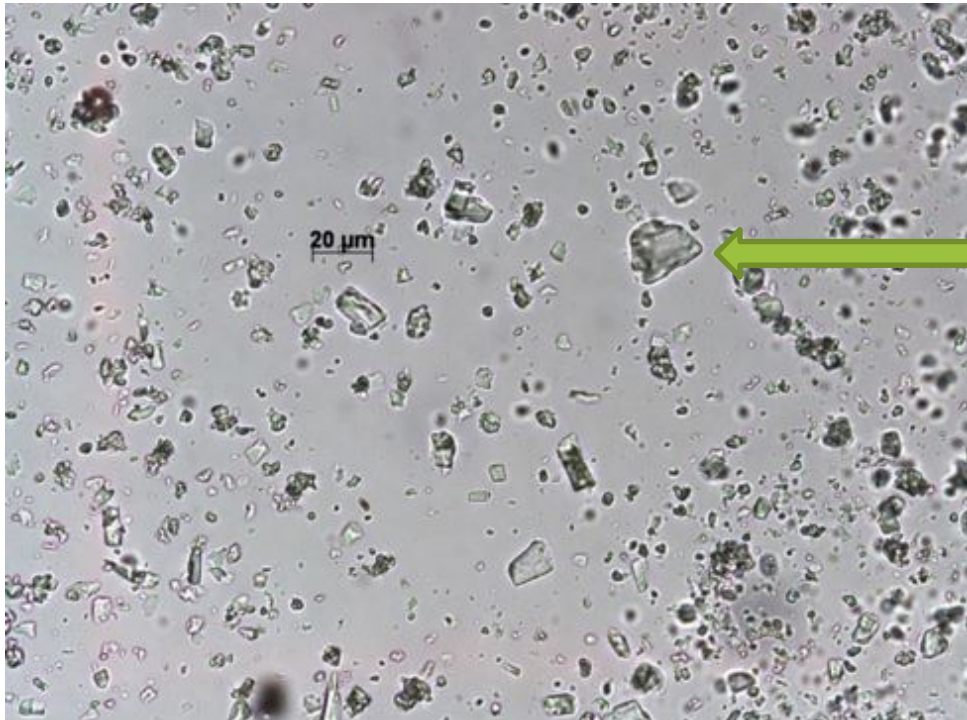
- 3 bead sizes, injectable, moldable
- Bead tray is available for order
- Available in 5cc, 10cc, 18cc sizes
- Sets in 15 minutes



# Cerament

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## Microscopic analysis of purity<sup>6</sup>



← Insoluble HA

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

# Cerament

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## Take away points<sup>6,17-20</sup>

- 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
- Contains HA, which has a slow and incomplete absorption rate
- HA can cause a long-term nidus for infection
- Slightly acidic pH
- Bead tray must be ordered separately (18cc pack requires two trays)
  - Bead tray requires creation of all three bead sizes if using a 10cc pack or greater



# OsteoBoost - OsteoRemedies

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## Indication and absorption rate<sup>21</sup>

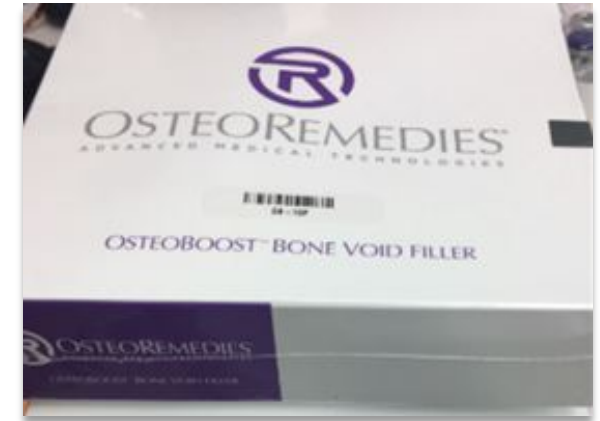
- Osteoconductive bone void filler
- Manufactured by Berkeley Advanced Biomaterials
- Contraindicated for use at infected sites
- Slow absorption rate (>6 months)

## Composition<sup>21</sup>

- Calcium sulfate,  $\beta$ -tricalcium phosphate, hydroxyapatite
- Sterile water

## Formats, sizing and setting time<sup>21</sup>

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



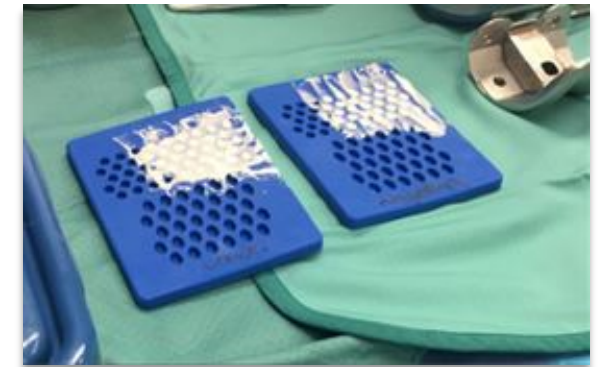


# OsteoBoost

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## Take away points<sup>6, 21</sup>

- Contraindicated for use at infected sites
- Contraindicated for inflammatory bone disease (osteomyelitis)
- Contains HA, which has a slow and incomplete absorption rate
- HA can cause a long-term nidus for infection
- Available in limited sizes
- No universal bead mat available
  - Mold for small and medium beads included in 5cc box
  - Mold for medium and large beads included in 10cc box
- Contains 1/2 less product volume per cc
  - OsteoBoost 5cc box (5g powder) closest to 3cc STIMULAN box (6.3g powder)
  - OsteoBoost 10cc box (10g powder) closest to 5cc STIMULAN box (9.5g powder)



# STIMULAN - Biocomposites

## Indication and absorption rate<sup>6,22-24</sup>

- 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 in 4-8 weeks

## Composition<sup>6,22-24</sup>

- 100% pharmaceutical-grade calcium sulfate
- Sterile water

## Formats, sizing and setting times<sup>6,22-25</sup>

- 3 bead sizes, 2 bullet sizes, paste, injectable
- STIMULAN Rapid Cure: 3cc, 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
- A combination bead and bullet mat is included in the 3cc box
- Bullet mat available to create 7 and 9mm bullets



# What makes STIMULAN different?

DRy26<sup>®</sup> recrystallization method<sup>22</sup>



# STIMULAN

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## Take away points<sup>6,22-24</sup>

- Cleared for placement directly at the site of infection
- Uniquely engineered through our DRy26<sup>®</sup> recrystallization method
- Contains no HA or insoluble impurities
- Fully absorbs in 4-8 weeks
- Physiologic pH
- Bullet format available
- Causes no third body damage
- Featured in 382 peer reviewed papers, presentations and posters
- Used in over 50,000 cases per year
  - Biocomposites offers a comprehensive network of specialists, sales representatives and surgeons to support our customers and hospitals



# Protect & Increase STIMULAN sales

## Strategies and resources

# How do we protect our accounts?

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## 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

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## Useful resources

- Comprehensive marketing materials & website
- Distributor Hub & training information
- Distributor Hub app
- Large surgeon following
- Surgeon testimonials
- Peer-reviewed evidence to support the use of STIMULAN
- Clinical experience - STIMULAN is used in over 50,000 cases each year
- Comprehensive support network for our customers in hospitals
- Unsolicited Request process



# STIMULAN competitive environment

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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 88883063, CN ZL201210466117.X, GB2496710, EP 3058899 B1, US 10390954

Patents pending: GB1502655.2, US 15/040075, CN 201610089710.5, GB1704688.9, EP 18275044.8, US 15/933936, CN 108619579A

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# STIMULAN competitive environment

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1. Wright Medical OSTEOSET® Bone Graft Product IFU. October 2013.
2. Wright Medical Technology OSTEOSET® BVF Kit 510(K) Summary of Safety and Effectiveness. K010532. 2001.
3. Wright Medical Technology OSTEOSET® Resorbable Mini-Bead Kit brochure. 008901A 09-Nov-2013.
4. Wright Medical Technology OSTEOSET® Resorbable Bead Kit brochure. 009269A 16-Dec-2013.
5. Wright Medical Technology OSTEOSET® Bone Graft Substitute Technical Monograph. SK404-511.
6. Biocomposites Ltd, Data on File.
7. Wright Medical OSTEOSET® Resorbable Mini-Bead Kit for Bone Voids Secondary to Osteomyelitis in Diabetic Feet brochure. SK 677-102. Rev. 0806.
8. Exactech®, Inc. InterSep™ Calcium Sulfate Bone Void Filler Instructions for Use. 41272 Rev. A.
9. Exactech®, Inc. InterSep™ Calcium Sulfate Product Sheet. 715-08-10 0119.7. 2019.
10. Exactech®, Inc. CEMENT Handling Technique. InterSep® Calcium Sulfate Bone Void Filler. 00-0000440 0719. 2019.
11. Austin Medical Ventures, Synthecure Instructions for Use, Rev. February 21, 2018.
12. Austin Medical Ventures, Synthecure product brochure.
13. <https://www.synthecure.com/products>.
14. Biomet Orthopedics Calcigen™ – S Bone Void Filler Summary of Safety and Effectiveness and 510(k) K013790 March 12, 2002.
15. Biomet Calcigen™ S calcium sulfate bone void filler Instructions for Use. 01-50-1090. Rev. C 2011-06.
16. Zimmer Biomet Calcigen® S Calcium Sulfate Bone Void Filler Fact Sheet. 1940.1-US-en-0718.
17. Bonesupport™ CERAMENT™ Bone Void Filler Product Fact Sheet. PR 0649-01 en EU/US.
18. Bonesupport™ CERAMENT® Bone Void Filler Rapid and complete bone remodeling brochure. PR 0346-03 en US.
19. Bonesupport™ CERAMENT™ Bone Void Filler Instructions for Use. Document No. IFU 0007-08 en 2014-06.
20. Bonesupport™ CERAMENT™ Bone Void Filler Mixing Guide. PR 0647-01 en EU/US.
21. OsteoRemedies OSTEOBOOST™ IFU. Spec 50688 Rev. A. Jul 2016.
22. Cooper, J.J., Method of producing surgical grade calcium sulphate, patent 1999.
23. Biocomposites Ltd, STIMULAN - Instructions for Use (USA).
24. Biocomposites Ltd, STIMULAN - Brochure (USA). MA0123R3 2016.
25. Biocomposites Ltd, STIMULAN - Bullet mat and Introducer flyer (USA). MA0149R2 2018.