

# STIMULAN<sup>®</sup> 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®
  - Synthesure™
  - 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® Wright Medical®	BonePlast® Zimmer Biomet®	Syntheticure™ Austin Medical Ventures, Inc.	STIMULAN® Biocomposites®
Composition	CaSO <sub>4</sub> , Calcium stearate	CaSO <sub>4</sub> , Accelerating saline solution	CaSO <sub>4</sub> , Mixing solution	CaSO <sub>4</sub> , Sterile water
Ordering sizes	5cc (3, 4.8mm beads) 25cc (7mm beads)	18cc	5cc, 10cc, 20cc	Rapid Cure: 5cc, 10cc, 20cc Kit: 5cc, 10cc
Formats	3 bead sizes, paste, injectable	Pellets, injectable	3 beads sizes, paste	3 bead sizes, 2 bullet sizes, paste, injectable
Bead mat included	Yes – Not universal	No - Sold separately	Yes – Not universal	Yes - Universal bead mats are included in every box.
Setting time	5 minutes (Fast Cure) 20 minutes (Standard Cure)	20 minutes	5 minutes	4 minutes (Rapid Cure) 8 minutes (Kit)
Impurities	Contains non-absorbable impurities	Unknown	No	No. STIMULAN has controlled purity
Hydrophilic or Hydrophobic	Hydrophobic	Hydrophilic	Hydrophilic	Hydrophilic
pH	Acidic	Unknown	Acidic	Physiologic
Claimed absorption rate	4-8 weeks	4-8 weeks	4-8 weeks	Approx. 30-60 days (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, Distilled water
Ordering sizes	5g, 10g, 25g	5cc, 10cc, 18cc	5cc, 10cc
Formats	Granules, paste, injectable	Injectable	Beads, paste, injectable
Bead mat included	No	No	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 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	Approx. 30-60 days (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	Mined	<ul style="list-style-type: none"> <li>Purity – no impurities</li> <li>No third body damage</li> <li>Bullet option</li> </ul>
BonePlast® Zimmer Biomet®	Yes	Unknown	4-8 weeks	No	No / Yes	CaSO <sub>4</sub> , Accelerating saline solution	Unknown	<ul style="list-style-type: none"> <li>Truly absorbable</li> <li>Rapid Cure option</li> <li>Bullet option</li> </ul>
Syntheticure™ Austin Medical Ventures	Yes	Yes	4-8 weeks	Yes	Yes / No	CaSO <sub>4</sub> , Mixing solution	Unknown	<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, Distilled 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

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

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

- Injectable, moldable paste, beads
- 5cc kit: Mini-bead kit with mat for 3 and 4.8mm cylindrical 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<sup>1,2,5</sup>

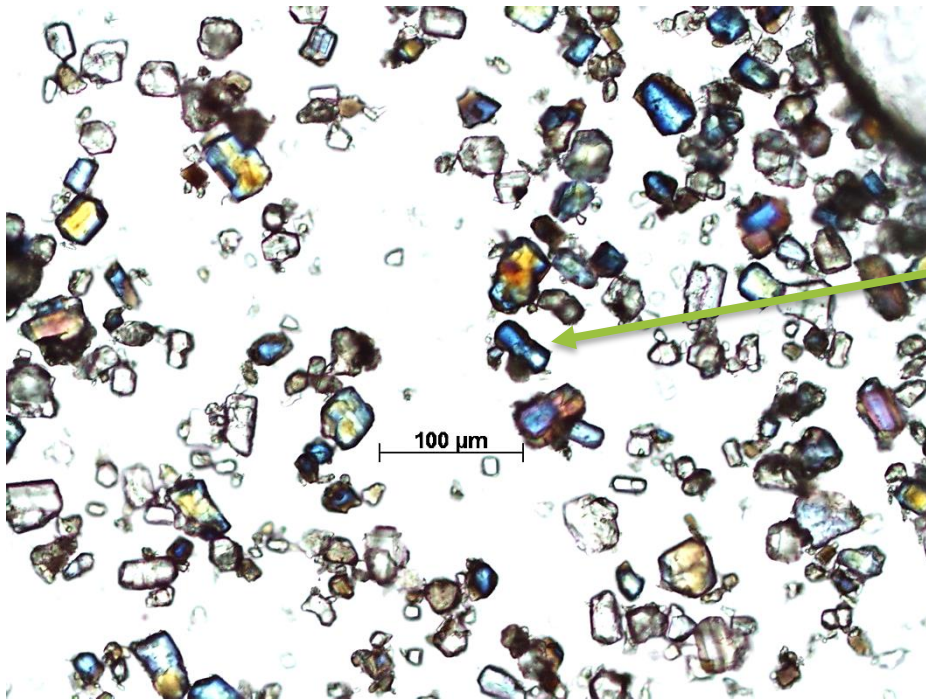
- OSTEOSET is manufactured from mined calcium sulfate
- The patents, technology, and process of producing OSTEOSET were acquired from the United States Gypsum Corporation
- Proprietary manufacturing methods are used to produce a consistent, high-quality material with **minimal lot-to-lot variation in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

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



Insoluble crystalline impurities

OSTEOSSET residue

# OSTEOSET

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

- 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



# BonePlast– Zimmer Biomet

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

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

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

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

## Formats, sizing and setting time<sup>8,9</sup>

- 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<sup>8,9</sup>

- 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



# Synthecure - Austin Medical Ventures, Inc.

## Indication & absorption rate<sup>10,11</sup>

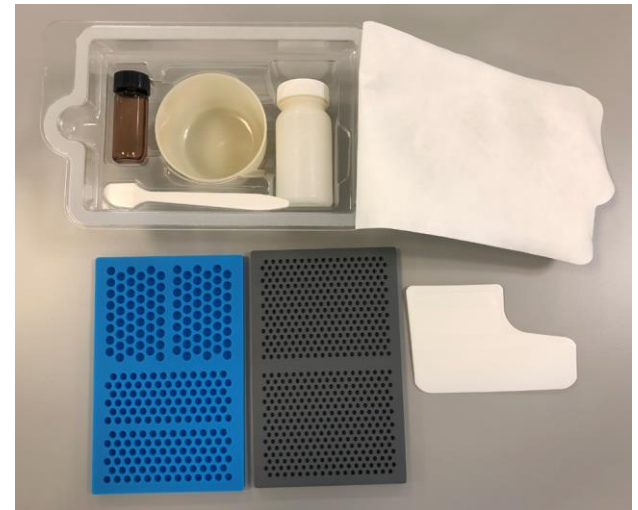
- Bone void filler that may be used at infected sites
- Claims to absorb within 4-8 weeks

## Composition<sup>10,11</sup>

- Medical grade calcium sulfate powder
- Pre-measured mixing solution

## Formats, sizing and setting times<sup>10,11,12</sup>

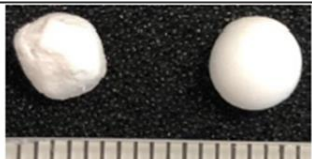
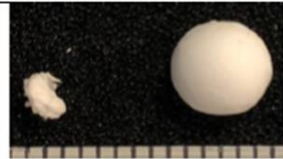
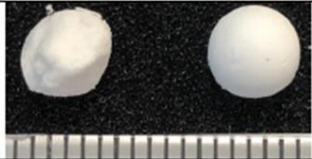
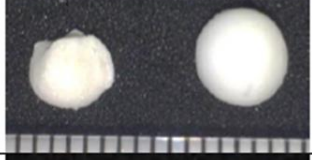

- Moldable paste, beads
- 5cc, 10cc and 20cc kits
- Single-sided bead mats included to produce 3, 4.8 and 6mm beads
- Rapid curing option (5 min set)
- No slow curing option





# Syntheticure

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

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

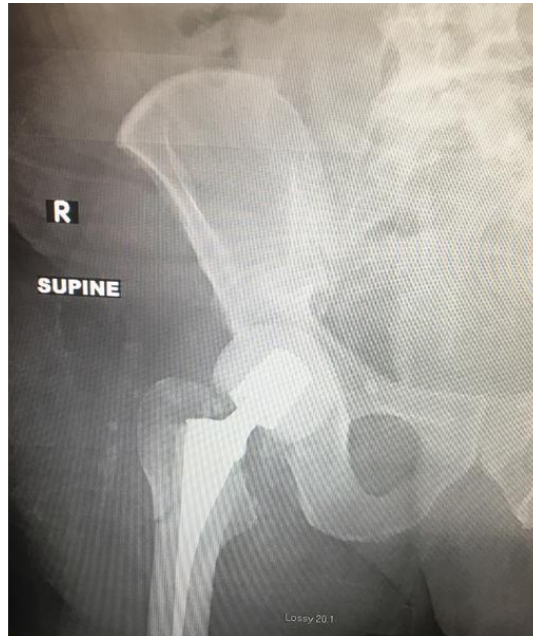
The higher porosity of Syntheticure (left) contributes to its increased rate of degradation

# 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

# Synthecure

## Take away points<sup>6,10-12</sup>

- Can be used at infected sites
- Claims to absorb within 4-8 weeks
  - Testing results show that Synthecure has higher porosity and degrades much faster than STIMULAN Rapid Cure
- Acidic pH
- No standard set option available – difficulty with injection
- Positioned as a low cost “me too” competitor
- No *in-vitro*, *in-vivo*, pre-clinical, clinical or animal data exists on PubMed (MEDLINE database) search engine



# Calcigen S – Zimmer Biomet

## Indication and absorption rate<sup>13,14</sup>

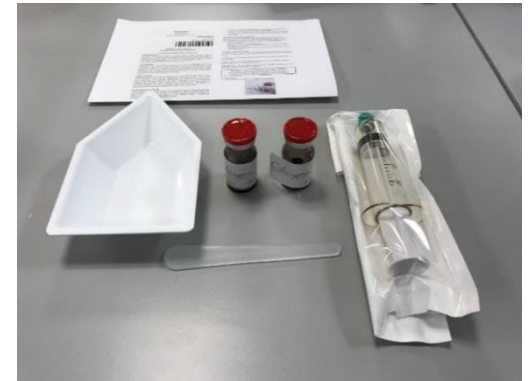
- Indicated to fill bony voids or gaps of the skeletal system
- Contraindicated for infected sites
- Claims to absorb within 8-12 weeks

## Composition<sup>13,14</sup>

- 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<sup>13,14</sup>

- 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<sup>13,14</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
- Will not set without the liquid supplied
- Becomes a calcium phosphate when fully set – potential to be a 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



# Cerament - Bonesupport

## Indication and absorption rate<sup>15,16</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>15,16</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>15,16</sup>

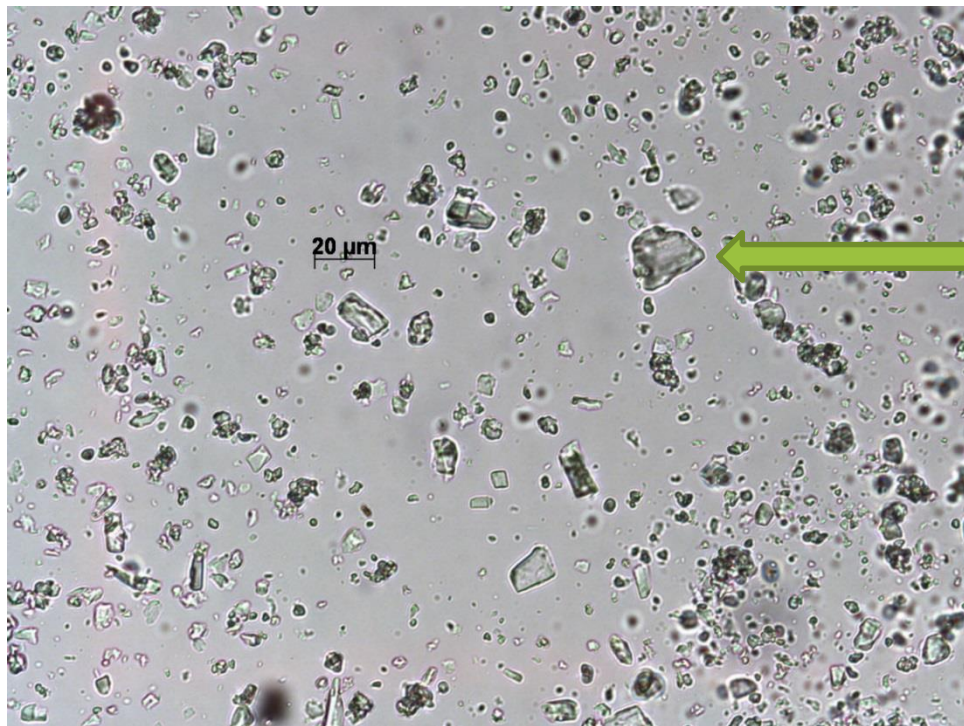
- Marketed as an injectable product
- Optional bead mat is available
- Available in 5cc, 10cc, 18cc sizes
- Sets in 15 minutes





# Cerament

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



Insoluble HA

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



# Cerament

## Take away points<sup>6,15-16</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
- HA has a slow/incomplete absorption rate
- HA has a potential to be a nidus for infection
- Slightly acidic pH
- No bead mat provided in box
- Positioned as a high cost competitor (list price)



# OsteoBoost - OsteoRemedies

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

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



## Composition<sup>17</sup>

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

## Formats, sizing and setting time<sup>17</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

## Take away points<sup>17</sup>

- Contraindicated for use at infected sites
- Contraindicated for inflammatory bone disease (osteomyelitis)
- HA has a slow/incomplete absorption rate
- HA has a potential to be a 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



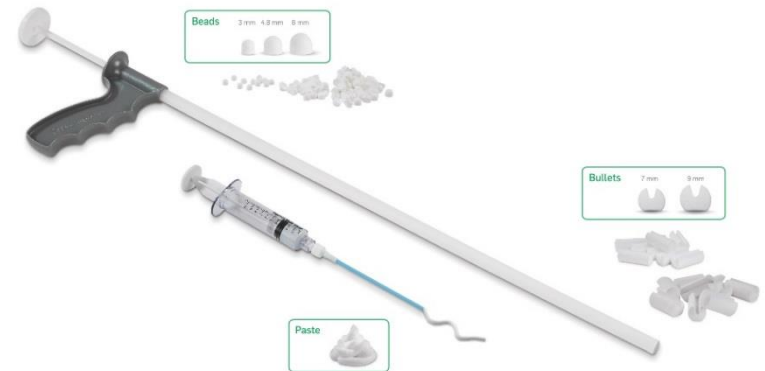
# STIMULAN - Biocomposites

## Indication and absorption rate<sup>6,18-20</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 approx. 30-60 days (4-8 weeks)
- **Composition**<sup>6,18-20</sup>
- 100% pharmaceutical-grade calcium sulfate
- Sterile water

## Formats, sizing and setting times<sup>6,18-21</sup>

- Injectable, paste, beads, bullets
- 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
- Bullet mat available to create 7 and 9mm bullets



# What makes STIMULAN different?

DRy26<sup>®</sup> recrystallization method<sup>18</sup>



# STIMULAN

---

## Take away points<sup>6,18-20</sup>

- Cleared for placement directly at the site of infection
- Uniquely engineered through our DRy26<sup>®</sup> recrystallization method
- Fully absorbs in approx. 30-60 days (4-8 weeks)
- Physiologic pH
- Hydrophilic
- Universal bead mat included
- Causes no third body damage
- Positioned as a medium cost competitor
- Used in over 30,000 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?

---

## 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.

©2019, Biocomposites, STIMULAN, Bringing Calcium to Life, Power to Transform and DRy26 are trademarks/registered trademarks of Biocomposites Ltd. All rights reserved. No unauthorized copying, reproduction, distributing or republication is allowed unless prior written permission is granted by the owner, Biocomposites Ltd.

Patents granted: GB2367552, EP 1204599 B1, US 6780391, EP 2594231 B1, US 8883063, CN ZL201210466117.X, GB2496710, EP 3058899 B1

Patents pending: GB1502655.2, US 15/040075, CN 201610089710.5, US 15/288328, GB1704688.9, EP 18275044.8, US 15/933936, CN 108619579A

Image on slides 3,10,30 – Used under license from Shutterstock.com

MA0162R4

PRIVATE & CONFIDENTIAL.



# STIMULAN competitive environment

---

## References:

1. Wright Medical OSTEASET® Bone Graft Product IFU. October 2013.
2. Wright Medical Technology OSTEASET® BVF Kit 510(K) Summary of Safety and Effectiveness. K010532. 2001.
3. Wright Medical Technology OSTEASET® Resorbable Mini-Bead Kit brochure. 008901A 09-Nov-2013.
4. Wright Medical Technology OSTEASET® Resorbable Bead Kit brochure. 009269A 16-Dec-2013.
5. Wright Medical Technology OSTEASET® Bone Graft Substitute Technical Monograph. SK404-511.
6. Biocomposites Ltd, Data on File.
7. Wright Medical OSTEASET® Resorbable Mini-Bead Kit for Bone Voids Secondary to Osteomyelitis in Diabetic Feet brochure. SK 677-102. Rev. 0806.
8. Interpore Cross Osteoplast Bone Void Filler 510(k) K991854 May 28, 1999.
9. Biomet Osteobiologics Calcium Sulfate (BonePlast) Bone Void Filler Instructions for Use. LD30-1000. Rev. A 5/07.
10. Austin Medical Ventures, Synthecure Instructions for Use, Rev. February 21, 2018.
11. Austin Medical Ventures, Synthecure product brochure.
12. <https://www.synthecure.com/products>.
13. Biomet Orthopedics Calcigen™ – S Bone Void Filler Summary of Safety and Effectiveness and 510(k) K013790 March 12, 2002.
14. Biomet Calcigen™ S calcium sulfate bone void filler Instructions for Use. 01-50-1090. Rev. C 2011-06.
15. CERAMENT™ Bone Void Filler Bone Healing Technical Monograph PR 0278-02 en EU/US.
16. CERAMENT™ Bone Void Filler Rapid and complete bone remodelling PR 0346-03 en US.
17. OsteoRemedies OSTEOBOOST™ IFU. Spec 50688 Rev. A. Jul 2016.
18. Cooper, J.J., Method of producing surgical grade calcium sulphate, patent 1999.
19. Biocomposites Ltd, STIMULAN - Instructions for Use (USA).
20. Biocomposites Ltd, STIMULAN - Brochure (USA). MA0123R3 2016.
21. Biocomposites Ltd, STIMULAN - Bullet mat and Introducer flyer (USA). MA0149R2 2018.