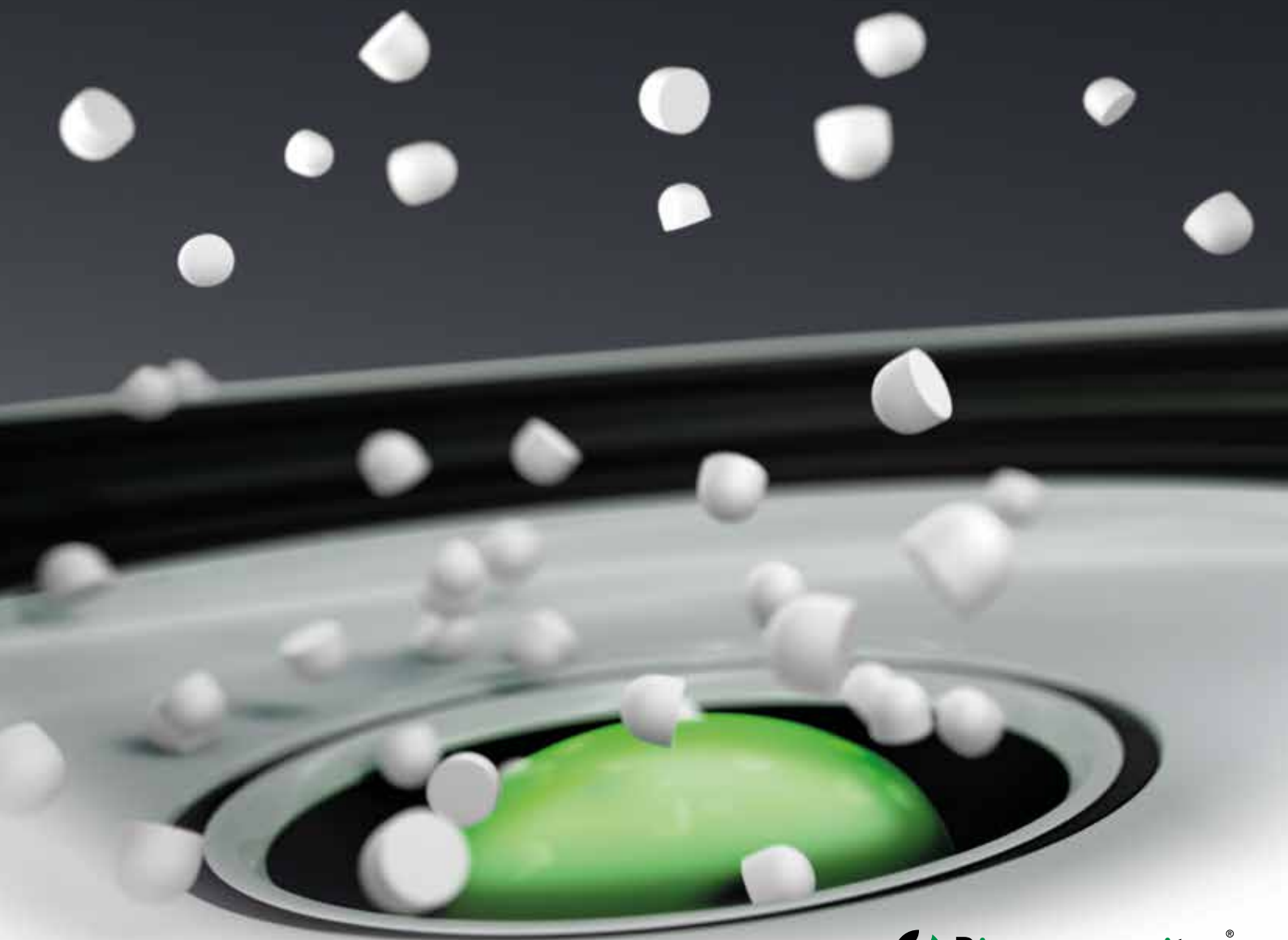


STIMULAN[®]

POWER TO TRANSFORM OUTCOMES[™]



Choosing an innovative device to work alongside your infection management strategy is key to:

- ✓ minimizing avoidable complications
- ✓ improving outcomes
- ✓ reducing costs

"The economic benefits are significant... the cost of a recurrent infection is in the hundreds of thousands relative to a product that is a few hundred"

Dr. John Xenos



STIMULAN[®]

Perfect partner for treating infection

STIMULAN is a truly absorbable, calcium sulfate antibiotic carrier – specifically designed to be mixed with antibiotics to treat bacterial infection and proactively manage dead space¹

- ✓ the only calcium matrix approved for mixing with antibiotics to treat bacterial infection
- ✓ approved for mixing with liquid and powder antibiotics
- ✓ can be placed directly into infected and non-infected sites



STIMULAN is uniquely recrystallized for mixing with antibiotics to treat bacterial infection and assist in wound healing

Ideal properties of an antibiotic carrier

Choice of antibiotics

Therapeutic concentration

Effective duration

Implantation at site of infection

STIMULAN[®]

Bring the challenge of treating infection under your control

Placing **STIMULAN** mixed with antibiotics directly into bone voids effectively targets a broad spectrum of infection risks and treats bacterial infection of the surrounding soft tissue across a variety of settings – at concentrations unachievable with systemic administration.



Transform osteomyelitis in diabetic foot^{2*}

Patient presented with: persistent osteomyelitis and interphalangeal joint destruction of left hallux. He was already receiving treatment for Charcot arthropathy to his right foot.

Outcome: 2 weeks' post-operatively, the toe reduced in size. At the 16 month x-ray the patient was infection free and amputation had been avoided. **STIMULAN** was seen to have completely absorbed at 4 months.



Transform trauma infected with *Staphylococcus aureus*^{3*}

Patient presented with: infected femoral nail and non-union of left femur with persistent discharging wounds proximally and distally.

Outcome: at 7 months' follow-up showed complete healing of the non-union and at 1 year patient remains infection free, walking with no pain.





Transform revision arthroplasty infected with group B *Streptococcus*^{4*}

Patient presented with: infected total knee replacement 2 years after primary procedure.

Outcome: at 1 year follow-up the patient remains infection free and is under regular follow-up.



Transform pilon fracture infected with group B *Streptococcus* and MRSA^{5*}

Patient presented with: drainage issues, 1 year after pilon fracture repair and then 2 weeks after hardware removal.

Outcome: 6 months after treatment the patient was fully weight-bearing and without restrictions on activity – with complete absorption of **STIMULAN**.

“I will put **STIMULAN** with the most appropriate antibiotic...to treat the dead space and assist in eradicating the infection”

Dr. Alastair Younger

*Additional information and case studies are available on request.

STIMULAN[®]

Truly absorbable, antibiotic carrier recrystallized for enhanced clinical performance

STIMULAN is a pharmaceutical-grade calcium sulfate with a unique crystal structure that has tightly controlled properties.¹

- ✓ controlled purity
- ✓ no hydroxyapatite
- ✓ easily mixed with liquid and powder antibiotics

Only STIMULAN undergoes a proprietary DRy26™ recrystallization method that starts with pharmaceutical-grade reagents and results in its consistent and reliable performance – suitable for carrying antibiotics to infected sites.^{1,6-11}

- ✓ completely absorbs at an optimal rate
- ✓ no third body damage
- ✓ predictable elution profile
- ✓ proven action against biofilms
- ✓ flexibility to tailor antibiotic to clinical need

“STIMULAN helps you add to your present-day treatment with an antibiotic regime that can improve your outcomes”

Dr. Ross Leighton



Completely absorbs at an optimal rate¹

No hydroxyapatite, insoluble impurities or PMMA debris – leaves no nidus for infection.¹²⁻¹⁷



Post-operative



1 month



11 weeks



6 months



15 months

No third body damage to articulating surfaces^{7,8}

Less scratching than competitor calcium sulfate.



STIMULAN



Competitor calcium sulfate



Control

Microscope images (x6.5) of a cobalt chrome plate following damage simulation (360,000 cycles) with third body particles trapped between it and an articulating UHMWPE pin

STIMULAN does not damage total knee replacements when trapped between the articulating surfaces of the implant.

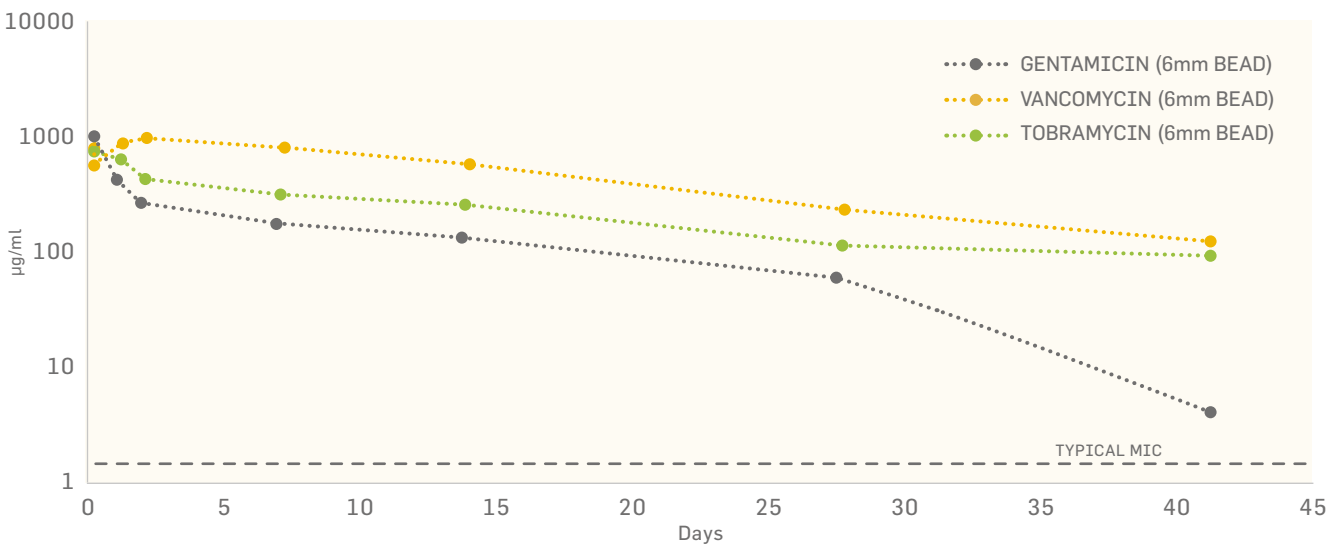
STIMULAN[®]

Uniquely engineered for the precision and control you demand every time

With the ability to mix substances according to the specific antimicrobial needs of each infection, **STIMULAN** combines flexibility with the predictability and consistency necessary to ensure sustained antibiotic cover.

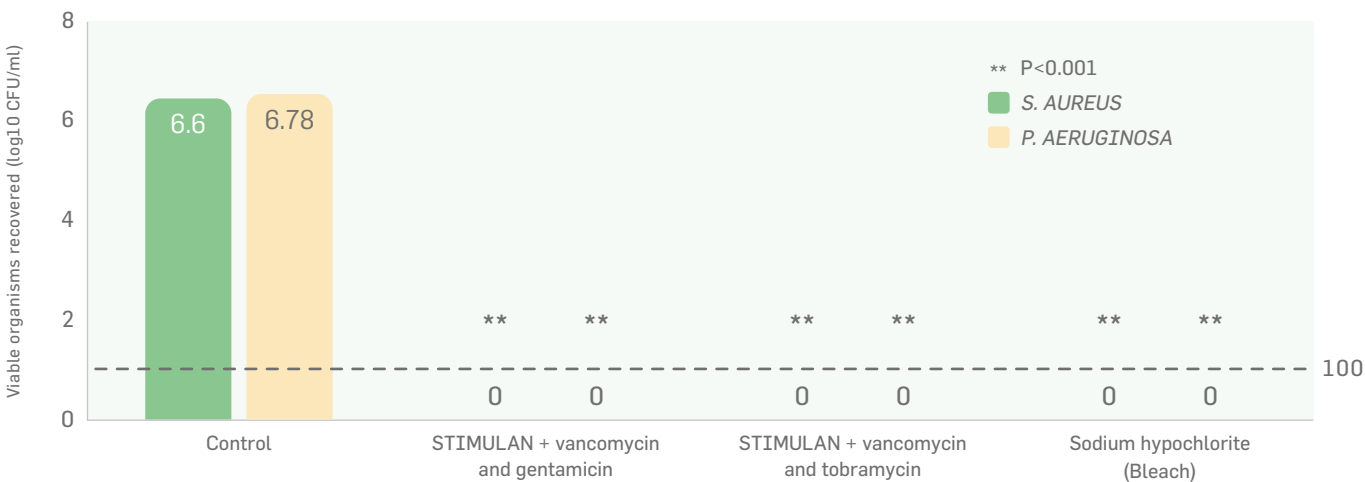
Predictable, supra-therapeutic elution profile⁹

Antibiotic levels sustained above MIC for over 40 days with **STIMULAN** Rapid Cure.

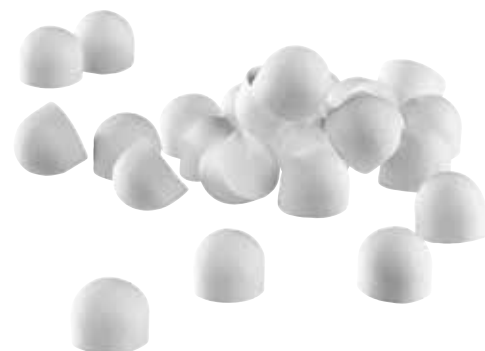


Proven action against biofilms¹⁰

No viable organisms were recovered from pre-formed biofilms.



In vitro study determining the efficacy of antibiotic-loaded **STIMULAN** beads against *Pseudomonas aeruginosa* and *Staphylococcus aureus* biofilms.



Flexibility to tailor antibiotic to clinical need¹¹

Effective against a broad spectrum of pathogens.

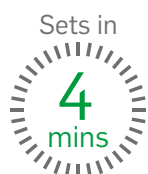
<i>Staphylococcus aureus</i>	<i>Staphylococcus epidermidis</i>
 Vancomycin	 Gentamicin
 Tobramycin	 Tobramycin

Zone of inhibition (ZOI) testing using a modified Kirby–Bauer disk diffusion method. 6mm bead after 24 hours.

STIMULAN[®]

Flexibility at your fingertips

Every part of STIMULAN is optimized to work around you according to the clinical and surgical demands of the individual patient. Whatever the time, shape, accessibility or size constraints, STIMULAN gives you a way to adapt to each case.



STIMULAN Rapid Cure¹

For faster setting times

+ antibiotic



Vancomycin
(1000mg powder)



Gentamicin
(240mg in 6ml solution)



Tobramycin
(240mg in 6ml solution)



STIMULAN Kit¹

More time to sculpt or inject

+ antibiotic



Vancomycin
(1000mg powder)



Gentamicin
(240mg in 6ml solution)



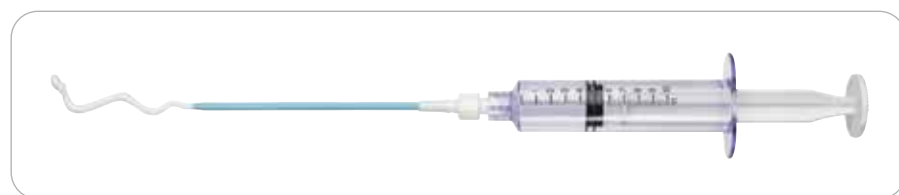
Tobramycin
(240mg in 6ml solution)

STIMULAN includes a range of pack sizes which enable you to mix and match to any size of void.

Choice of formats



Bead mat available with **STIMULAN** Rapid Cure and **STIMULAN** Kit



Syringe available with **STIMULAN** Kit

Quickly and easily fill medullary canals

STIMULAN Bullet Mat and Introducer

Streamlined, flexible design that simplifies the delivery of **STIMULAN**, into the medullary canal – more efficiently and cost-effectively than using paste.



(See page 18 for further details and ordering codes)

STIMULAN[®]

Unrivalled evidence and expertise bring confidence

With our industry-leading knowledge, dedication and experience, you can be sure that the high level of consistency you demand in your cases will be met.

Peer-reviewed papers, presentations and posters



With over 30 years of clinical experience and use in 150,000 new cases each year, **STIMULAN** continues to expand the possibilities for surgeons and patients through a commitment to innovation and consistently high levels of satisfaction.

"... happier with this product than anything I've used in the last 30 years"

Dr. Richard Biama

Case study

Courtesy of Dr. Amit Atrey

Orthopaedic Surgeon, Toronto, ON, Canada

Clinical particulars

77-year-old female with a prior left total hip replacement presented with chronically draining sinuses in the groin crease and at the greater trochanter. The patient suffered from extreme hip pain for 14 months but avoided orthopaedic consultation due to fear of surgery. An acute injury occurred warranting immediate surgical intervention. Irrigation and debridement were performed and culture swabs from both sinuses revealed infection to be *Staphylococcus aureus*. A two-stage revision was planned due to the presence of the two chronic sinuses and virulent bacteria.

Treatment - Stage 1

All implants were removed. The well-bonded femoral implant was explanted with difficulty through an extended trochanteric osteotomy. A temporary intramedullary (IM) nail covered with vancomycin paste was placed to maintain the lumen of the fractured shaft. A thorough debridement and splaying/excision of the sinuses was performed. 20cc **STIMULAN** beads mixed with antibiotic was used to treat the bacterial infection at the acetabulum, along the tract of the groin crease sinus and along the entire tract length of the lateral thigh sinus. I.V. antibiotics were administered for 6 weeks after surgery, followed by a 2 week antibiotic-free time period. The CRP returned to normal limits within 4 weeks and remained low after the antibiotic holiday.

Treatment - Stage 2

At 10 weeks, revision surgery was performed with removal of the temporary IM nail and placement of a diaphyseal fitting modular femoral stem and multi-hole titanium cup.

Outcome

3 weeks after stage 1 treatment, both sinuses had healed. At 8 weeks, CRP levels returned to normal and infection was eradicated with complete absorption of **STIMULAN**. At 24 months, the patient lives independently, ambulates without gait aids and remains pain and infection free.



Presentation



Stage 1 – Post-operative



Stage 1 – 8 weeks



Stage 2 – Post-operative



Stage 2 – 6 weeks



Stage 2 – 12 months

Case study

Courtesy of Mr. Hemant K. Sharma

Consultant Orthopaedic Surgeon, Hull, UK

Clinical particulars

35-year-old male involved in a road traffic accident suffered multiple injuries and subtrochanteric fracture of left femur. This was nailed but subsequently, he developed infection and drainage from both proximal and distal locking screw areas. He went to theatre multiple times and developed wound approx. 15cm on the proximal lateral thigh, which was treated with VAC.

He presented a year later with discharging wound proximally and distally.

Treatment

The femoral nail was removed followed by reaming of the femoral canal and wash-out procedure. 40cc of **STIMULAN** was used to carry the antibiotic, fill resulting dead space in the intramedullary canal and treat the bacterial infection. Cultures revealed infection to be *Staphylococcus aureus*. Antibiotics were administered to treat the infection.

Outcome

2.5 months' post-operative x-rays showed almost complete absorption of the **STIMULAN** beads and at 7 months there was complete healing of the non-union.

At 1 year follow-up the patient remains infection free, walking with no pain.



Pre-operative x-ray showing non-union



X-ray – 2 months



CT – 2 months



2.5 months



1 year

Case study

Courtesy of Mr. Ramasubramanian Dharmarajan

Consultant Orthopaedic Surgeon, Cumbria, UK

Clinical particulars

59-year-old female patient presented with infected well fixed total knee replacement two years after primary total knee replacement surgery. This was an acute presentation with all clinical features of infection with samples testing positive for Group B *Streptococcus*.

Treatment - Stage 1

Radical debridement, implant removal and insertion of antibiotic-loaded cement spacer and **STIMULAN** mixed with vancomycin was used to fill the dead space and treat the infection.

Treatment - Stage 2

At 10 weeks, clinically soft tissues were healthy and intra-operative specimens were clear for organisms. Rotating hinge prosthesis was re-implanted.

Outcome

At 1 year follow-up the patient remains infection free and is under regular follow-up.



Presentation



First stage – Post-operative



Second stage – Post-operative



Second stage – Post-operative

Case study

Courtesy of Dr. Daniel Schlatterer

Orthopaedic Surgeon, Atlanta, GA, USA

Clinical particulars

73-year-old female with osteomyelitis caused by Group B *Streptococcus* and MRSA infection. Presented with exposed hardware and post-operative drainage issues, 1 year after pilon fracture repair and subsequently 2 weeks after removal of all hardware.

Treatment

Hardware removal and repeat debridement on the medial side of the ankle resulted in a large dead space which was managed using **STIMULAN** paste mixed with antibiotic to treat the bacterial infection.

Outcome

6 months after treatment the patient was free from infection, fully weight bearing and without restrictions on activity – with complete absorption of **STIMULAN** paste.



Presentation



Post-operative



1 month



11 weeks



6 months



15 months

Case study

Courtesy of Dr. Ross Leighton

Orthopaedic Surgeon, Halifax, NS, Canada

Clinical particulars

60-year-old male involved in a motor vehicle accident presented with an isolated left open plafond fracture (Gustilo IIIA), ankle under compression and extensive soft tissue damage. CT scans indicated severe fracture of the distal tibia plafond and fracture lines with extensive comminution. External fixation was applied for 10 days.

Treatment - Stage 1

A large partially dysvascular segmental piece on the medial side of the tibia was fixed with anterolateral plating and medial malleolar screw, and a lateral plate was applied to the fibula. At 3 months, the hardware construct loosened due to infection. Irrigation and debridement (I&D) was performed and screws were tightened. At 6 months, the patient underwent another I&D due to infection. 3 months later, the bone fracture appeared to be healing but culture samples tested positive for *Staphylococcus aureus*.

Treatment - Stage 2

1 year after index surgery, initial fixation was removed and a tibiototalcanal (TTC) nail was inserted to fuse the subtalar and ankle joints. I.V. and oral antibiotics were administered for infection control. 4 months later, another I&D was carried out for infection and proximal screws were removed due to backout from the construct.

Treatment - Stage 3

At 1 year following stage 2 surgery, the fracture healed but infection persisted as osteomyelitis. The TTC nail was removed and 10cc **STIMULAN** bullets mixed with 240mg liquid tobramycin and 10cc **STIMULAN** bullets mixed with 1g vancomycin powder were inserted through the heel into the intramedullary canal to fill dead space and treat bacterial infection. I.V. antibiotics were administered for infection control.

Outcome

1 year following stage 3 treatment, the subtalar joint and ankle joint were well-aligned and fused. Sed rate and C-reactive protein levels returned to normal and infection was eradicated with complete absorption of **STIMULAN** bullets. The patient remains pain and infection free and is walking and weight-bearing as tolerated.



Presentation x-ray



Presentation CT



Stage 1 - Post-operative



Stage 2 - Post-operative



Stage 3 - Intra-operative



Stage 3 - 1 year

STIMULAN®

Overview

STIMULAN Rapid Cure

Paste volume	Bead volume	In the pack	Order code
5cc	12cc	• Powder and solution • Spatula	620-005
10cc	25cc	• Paste applicator • Bead mat	620-010
20cc	50cc	• Powder and solution • Mixing bowl • Spatula • Paste applicator • 2 x bead mats	620-020

STIMULAN Kit

Paste volume	Bead volume	In the pack	Order code
5cc	10cc	• Powder and solution • Spatula	600-005
10cc	20cc	• Paste applicator • Bead mat • Syringe and extension tube	600-010

STIMULAN Bullet Mat and Introducer

Bullet dimensions	Reamed diameter	In the pack	Order code
7mm x 20mm	10mm reamed diameter (minimum)	• Bullet mat • 7mm (black) inserter	660-001
9mm x 20mm	12mm reamed diameter (minimum)	• 9mm (silver) inserter • Obturator	

References: **1.** Biocomposites, STIMULAN Instructions for Use. **2.** Data on file, Mr. Rajesh Joggia. **3.** Data on file, Mr. Hemant K. Sharma. **4.** Data on file, Mr. Ramasubramanian Dharmarajan. **5.** Data on file, Dr. Daniel Schlatterer. **6.** Cooper, J.J., Method of producing surgical grade calcium sulphate; Patent. 1999. **7.** Analysis of the Wear Effect 3rd Body Particulate (Bone Cement) has on UHMWPE, Accutek Testing Laboratory, Fairfield OH, K13107732-1, 2014. **8.** Cowie, R.M. et al., The influence of a calcium sulphate bone void filler on the third-body damage and polyethylene wear of total knee arthroplasty. Bone Joint Res, 2019. 8(2): p. 65-72. **9.** Cooper, J.J. et al., Antibiotic stability in a synthetic calcium sulphate carrier for local delivery. Poster presented at European Bone and Joint Infection Society Annual Meeting, Prague, Czech Republic, 2013. **10.** Delury, C. et al., Determining the Efficacy of Antibiotic-loaded Calcium Sulfate Beads against Pre-Formed Biofilms: An In Vitro Study. Poster presented at ASM Microbe 2019, 20-24 June 2019, Moscone Center, San Francisco, CA, USA. **11.** Laycock, P. et al., In Vitro Efficacy of Antibiotics Released from Calcium Sulfate Bone Void Filler Beads. Materials, 2018. 11(11): p. 2265. **12.** Somasundaram, K. et al., Proximal humeral fractures: the role of calcium sulphate augmentation and extended deltoid splitting approach in internal fixation using locking plates. Injury, 2013. 44(4): p. 481-7. **13.** Lei D., Zhanzhong, et al., Treatment of Distal Radius Bone Defects with Injectable Calcium Sulphate Cement. In: Bone Grafting, A., Zorzi, Editor. 2012, InTech. p. 125-134. **14.** Lei, D., Jing, L., Yang-yong, S., Calcium sulfate versus calcium phosphate in treating traumatic fractures. Journal of Clinical Rehabilitative Tissue Engineering Research, 2008. 12. **15.** Lei, D., Ma, Z., Jing, X., Treatment of bone defect with injectable calcium sulfate powder in distal fractures of radius. Chinese Journal of Bone Tumor and Bone Disease, 2007. **16.** Aiken, S.S., Cooper, J.J., Zhou, S., Osseointegration of a calcium sulphate bone substitute in a large animal model, in The 5th International Congress of Chinese Orthopaedic Association. 2010: Chengdu, China. **17.** Lazarou, S.A. et al., Correction of alveolar cleft with calcium-based bone substitutes. J Craniofac Surg, 2011. 22(3): p. 854-7.

For indications, contraindications, warnings and precautions see Instructions for Use. The treating physician is responsible for deciding the type and quantity of antibiotic used. Concurrent use of locally administered antibiotics may affect setting time. The mixing of antibiotics with the STIMULAN Kit/ STIMULAN Rapid Cure device is considered off-label usage of the medicinal product. To do so is at the professional risk of the surgeon / healthcare professional. 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.

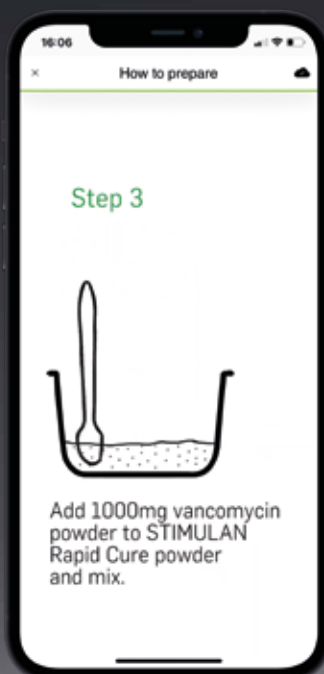
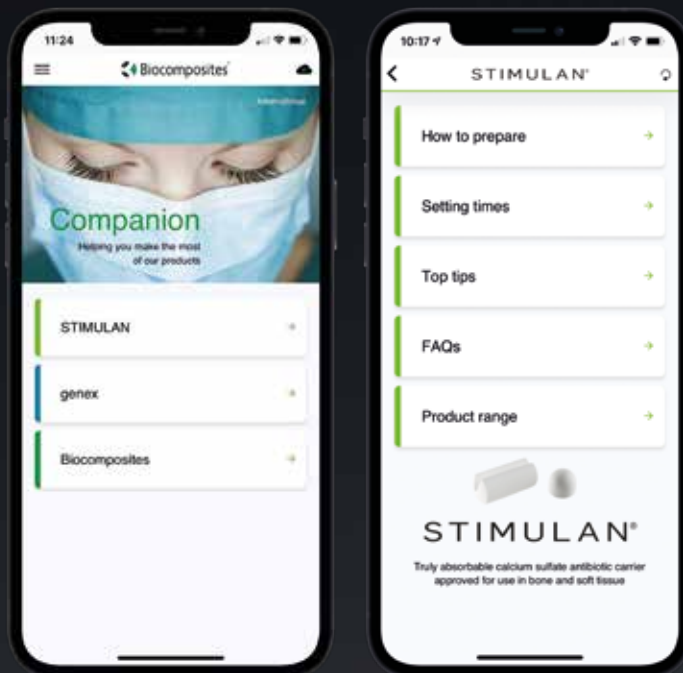
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Patents pending: GB1502655.2, GB1704688.9, EP 18275044.8, US 15/933936, CN 108619579A.

The Biocomposites Companion

Your essential guide to making the most of **STIMULAN** – all in one straightforward app.

Our accessible app provides all the information you need to meet different clinical demands when using **STIMULAN**. From surgeons' tips to how-to videos, this is the expert support tool you need, right at your fingertips.



- ✓ How to prepare: step-by-step videos
- ✓ Setting times: simple overview
- ✓ Top tips: tried and tested advice for surgeons
- ✓ FAQs: common questions answered
- ✓ Product range: what's available

To download your Biocomposites Companion, simply scan the QR code.



STIMULAN[®]

POWER TO TRANSFORM OUTCOMES[™]

- ✓ Perfect partner for treating infection
- ✓ Only STIMULAN is approved for mixing with antibiotics to treat bacterial infection¹
- ✓ Unique DRy26[™] recrystallization method for consistent and reliable performance⁶
- ✓ Provides case-by-case flexibility



We operate to the highest international standards from research through manufacture to distribution.

Innovation is at the heart of what we do

Biocomposites' innovative calcium compound and polymer products range from bone grafts to implants that aid in the treatment of infection. Possessing unique characteristics for regenerating bone and managing infected sites, our products are opening new possibilities for surgeons around the world.

Find out more at biocomposites.com