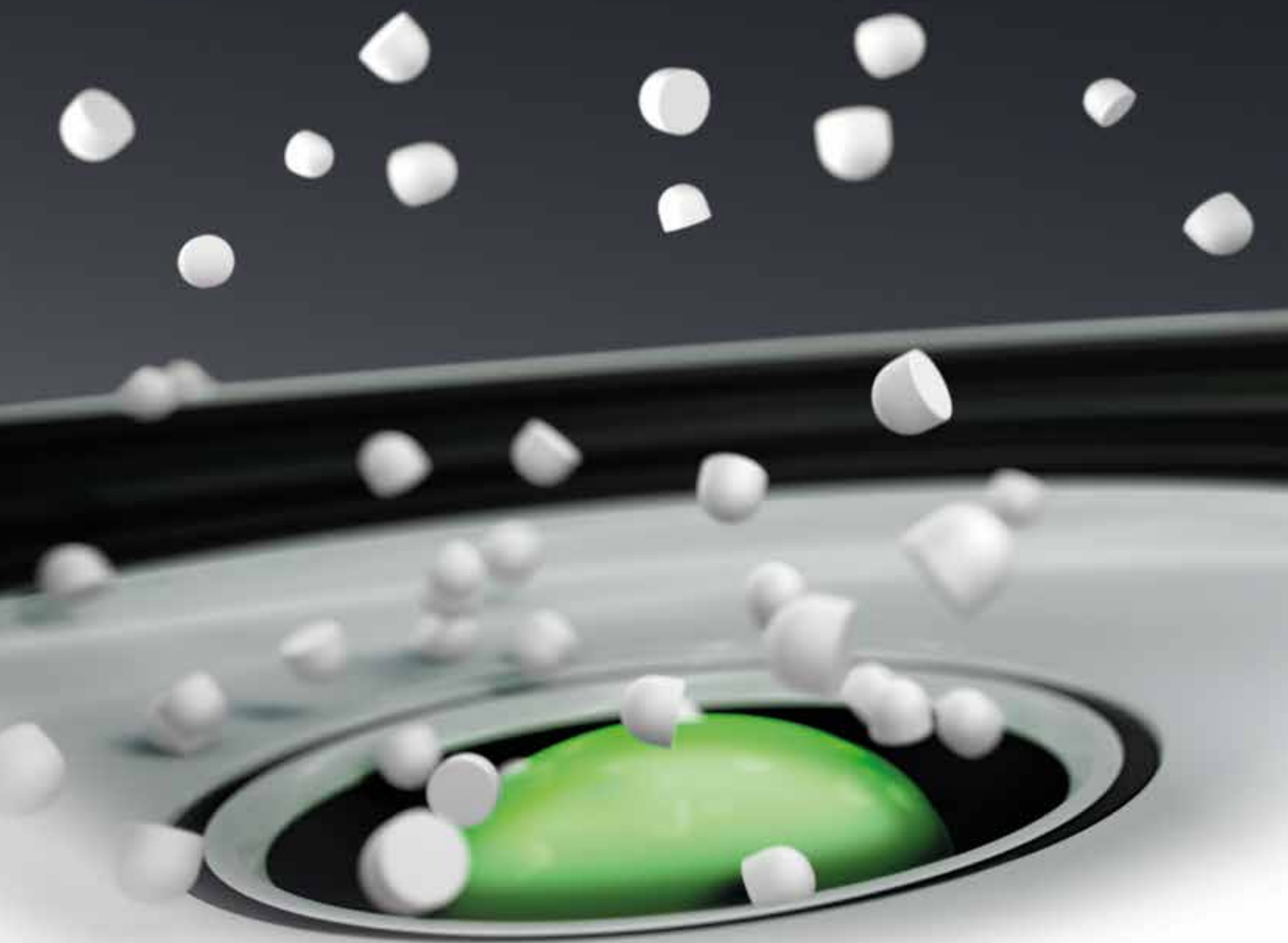


STIMULAN[®]

POWER TO TRANSFORM OUTCOMES[™]



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

- ✓ minimising 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

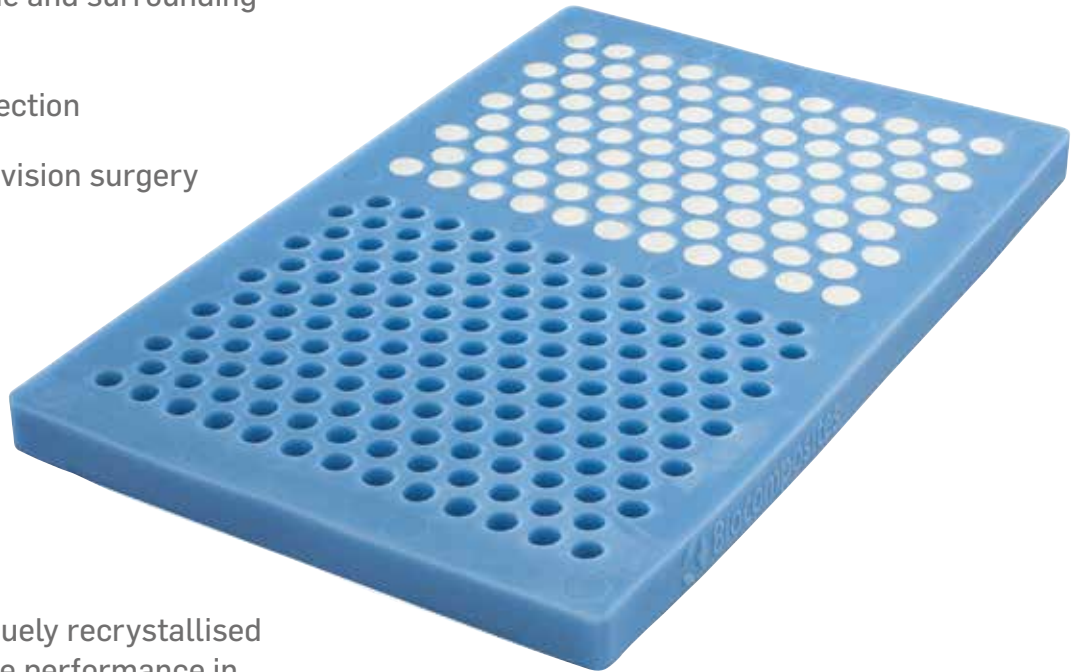


STIMULAN[®]

Perfect partner for resolving infection

STIMULAN is a truly absorbable, calcium sulfate antibiotic carrier – specifically designed to support the proactive management of dead space and assist in the treatment of infection, with unrivalled flexibility and the broadest surgical application.¹

- ✓ the only calcium matrix approved to deliver a combination of Gram-positive and Gram-negative antibiotics
- ✓ approved for use in bone and surrounding soft tissue
- ✓ approved to resolve infection
- ✓ reduces the need for revision surgery



STIMULAN is uniquely recrystallised for consistent and reliable performance in delivering antibiotics to resolve infection

Ideal properties of an antibiotic carrier

Choice of antibiotics

Therapeutic concentration

Effective duration

Implantation at site of infection

STIMULAN[®]

Bring the challenge of infection under your control

Placing antibiotics directly into bone voids and soft tissue with **STIMULAN** effectively and comprehensively targets a broad spectrum of infections 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**.

“It saves the hospital money as it decreases the hospital readmission rate”

Dr. Jorge Casas-Gánem

*Additional information and case studies are available on request.

STIMULAN[®]

Truly absorbable, antibiotic carrier recrystallised 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™ recrystallisation method that starts with pharmaceutical-grade reagents and results in its consistent and reliable performance – suitable for delivering 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

“It’s very reproducible... I get the same outcomes time and time again”

Dr. Herrick Siegel



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.

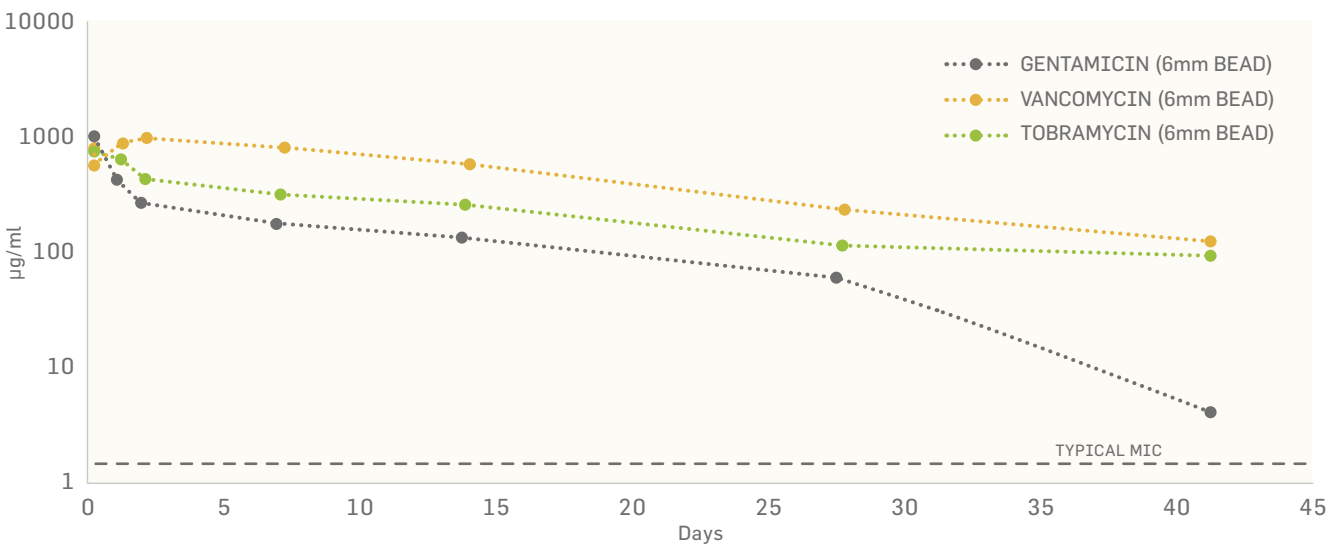
STIMULAN[®]

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.

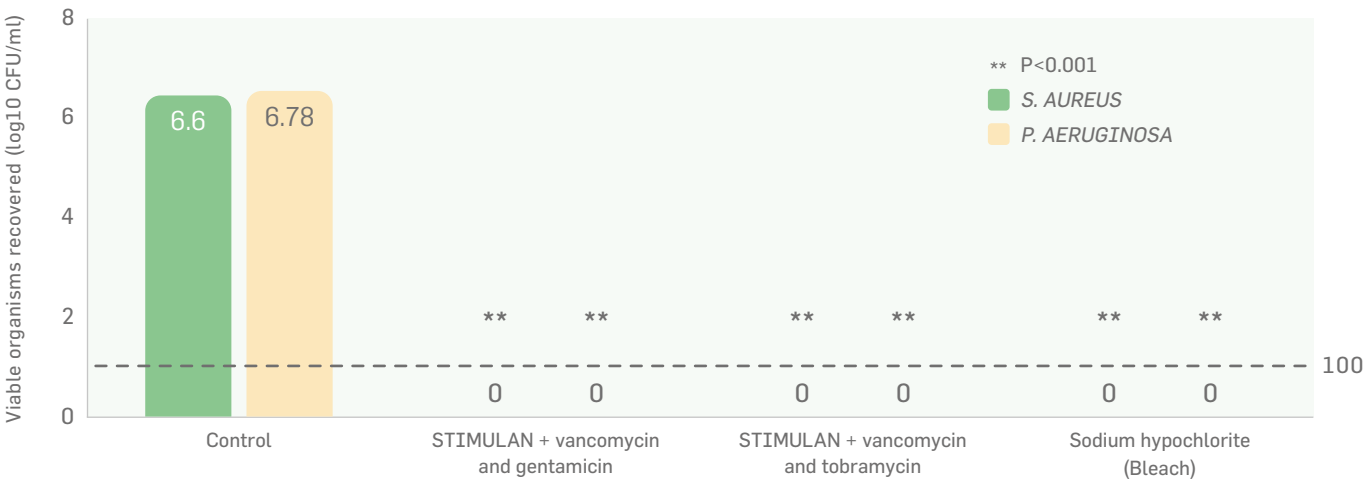
Predictable, supra-therapeutic elution profile⁹

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 Gram-positive and Gram-negative pathogens.

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

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

STIMULAN[®]

Flexibility at your fingertips

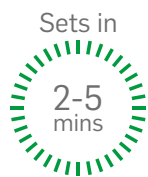
Every part of **STIMULAN** is optimised to work around you according to the clinical and surgical demands of the individual patient. Whatever the time, shape, accessibility or size constraints, **STIMULAN** gives you a way to adapt to each case.



STIMULAN Rapid Cure¹

For faster setting times

+ antibiotic



Vancomycin
(1000mg powder)



Gentamicin
(240mg in 6ml solution)



Tobramycin
(240mg in 6ml)



Tobramycin
(1000mg powder)

+ combination antibiotics



Vancomycin
(1000mg powder)
+
Gentamicin
(240mg in 6ml solution)



Vancomycin
(1000mg powder)
+
Tobramycin
(240mg in 6ml solution)

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

STIMULAN Rapid Cure 10cc.

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.



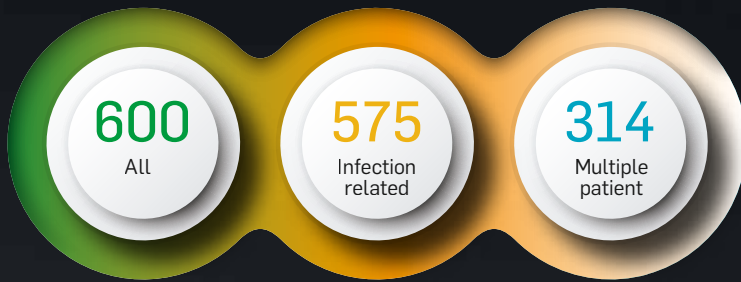
(See the inside back cover for further details and ordering codes)

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 30 years of 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 Mr. Rajesh Jogia

Consultant Podiatric Surgeon, Leicester, UK

Clinical history

67-year-old male with type 2 diabetes and BMI of 37 presented with osteomyelitis and interphalangeal joint destruction to his left hallux. This failed to resolve with conservative treatment regime of oral antibiotics and off-loading. Surgical management was to amputate the left hallux, however there was a risk of re-ulceration as he was already receiving treatment for Charcot arthropathy to his right foot.

Treatment

As a last effort to prevent amputation, surgical debridement was carried out, the bone was fenestrated and **STIMULAN** mixed with vancomycin and gentamicin was used to fill the cavities and treat the infection. Surgery was carried out as a day case under local anaesthetic.

Outcome

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



Presentation



Post-operative



2 weeks



16 months

Case study

Courtesy of Mr. Hemant K. Sharma

Consultant Orthopaedic Surgeon, Senior Clinical Tutor, Hull, UK

Clinical history

35-year-old male involved in a road traffic accident, suffered multiple injuries and subtrochanteric fracture of left femur. This was nailed, however, subsequently he developed infection and drainage from both at 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 **STIMULAN** was used to deliver the antibiotic to the intramedullary canal. Cultures revealed infection to be *Staphylococcus aureus* which was treated with vancomycin and tobramycin.

Outcome

2.5 months' post-operatively 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



Post-operative x-ray – 2 months



Post-operative CT – 2 months



Post-operative – 2.5 months



Post-operative – 1 year

Case study

Courtesy of Mr. Ramasubramanian Dharmarajan

Consultant Orthopaedic Surgeon, Cumbria, UK

Clinical history

59-year-old female patient presented with infected well fixed total knee replacement 2 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

First stage – radical debridement, implant removal and insertion of antibiotic-loaded cement spacer and **STIMULAN** combined with vancomycin and formed into beads was used to fill the dead space.

Second stage – 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 history

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 vancomycin and tobramycin to treat the 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. Daniel Schlatterer

Orthopaedic Surgeon, Atlanta, GA, USA

Clinical history

40-year-old male sustained an open calcaneus fracture after a 20 foot fall. Initial surgery was an irrigation and debridement with definitive fixation 10 days after injury. 6 months later patient presented with an infected non-union and hardware failure. Cultures were positive for MRSA.

Treatment - Stage 1

Hardware removal, debridement of grossly infected bone and soft tissues. **STIMULAN** combined with vancomycin and tobramycin and formed into beads was used to fill the resulting dead space. I.V. antibiotics for 8 weeks.

Outcome - Stage 1

Infection eradicated, soft tissues healed, infectious lab studies normal (1 month after I.V. antibiotics completed). Foot suitable for correction of proximal migration of calcaneus (soft tissue releases) and subtalar fusion.

Treatment - Stage 2

Subtalar fusion procedure performed. **STIMULAN** was used again to fill the remaining dead space in and around the talus and calcaneus (image with **STIMULAN** at the fusion stage not included). I.V. antibiotics restarted as prophylaxis. 2 months later hardware removed again due to positive blood cultures. Calcaneus cultures were negative however the PICC line catheter tip was culture positive. A new PICC line was placed followed by another 8 weeks of I.V. antibiotics.

Outcome - Stage 2

This patient is now weight bearing as tolerated and clinically no signs of infection.

Infection in open calcaneus fractures is common and in some series amputation rates exceed 50%. For this patient a 2 stage approach was utilised to treat the infected non-union. Removal of hardware and aggressive debridement of the bone. The dead space was managed with **STIMULAN**.



Presentation



Post-operative - Stage 1



Stage 1 complete



13 months after subtalar fusion, 11 months after hardware removal

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 (EU). **2.** Data on file, Mr. Rajesh Jogia. **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., Aiken, S., Thomas, H., 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., Huber, C.P., Babu, V., 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, M., Huaikuo, Y., 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., Contodimos, G.B., Gkegkes, I.D., 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. Concurrent use of locally administered antibiotics may affect setting time, absorption characteristics and/or bone formation. It is the surgeon/healthcare professional's responsibility to give due consideration to the details in the medicinal product marketing authorisation in deciding whether it is appropriate for the patient under his/her care. The relevant Summary of Product Characteristics (SmPC) must be consulted. The type and dose of medicinal substance should also be assessed according to the individual patient's clinical circumstance. 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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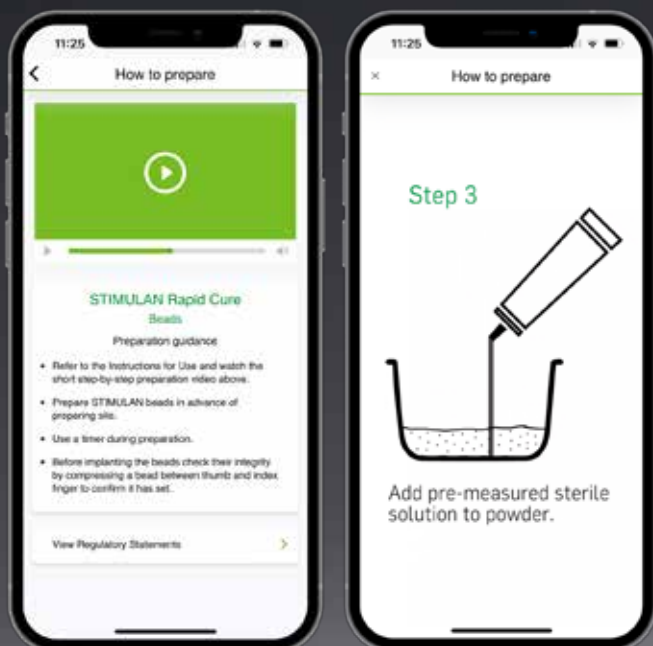
Patents granted: GB2367552, EP 1204599 B1, US 6780391, EP 2594231 B1, US 8883063, CN ZL2012101466117X, GB2496710, EP 3058899 B1, US 10390954, US 10,588,748, CN ZL201610089710.5
Patents pending: GB1502655.2, GB1704688.9, EP 18275044.8, US 15/933936, CN 108619579A

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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[™]

- ✓ Resolves infection and reduces the need for revision surgery
- ✓ Freedom to select and source your preferred antibiotics
- ✓ Only calcium matrix approved for use in bone and surrounding soft tissue¹
- ✓ Unique DRy26[™] recrystallisation method for consistent and reliable performance⁶



All Biocomposites' products are engineered, manufactured and shipped from our facilities in Keele, UK.

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