



# Frequently Asked Questions for Distributors (USA)

April 2017

# FAQs

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## What is STIMULAN® indicated for?

STIMULAN is the perfect partner for cases with an infected site. It can be used in the presence of infection and is indicated for use to fill a bone void or defect of the skeletal system created by surgery, a cyst, a tumor, osteomyelitis or traumatic injury. STIMULAN is indicated only for bony voids or defects/gaps that are not intrinsic to the stability of the bony structure. STIMULAN paste can be digitally packed into the bone void to set in-situ, or molded into solid implants that are to be gently packed into the defect.

## Who is using STIMULAN and in which hospitals?

STIMULAN is used in over 20,000 cases a year in a wide range of different indications. Biocomposites would be happy to introduce you to an appropriate surgeon if you would like to have a peer to peer conversation.

## What supporting data do you have for STIMULAN?

Biocomposites has a variety of data ranging from pre-clinical laboratory testing, animal model data and clinical data. Biocomposites also has numerous case studies available that provide an overview of the use of STIMULAN in various clinical applications. Biocomposites would be happy to provide you with case studies for the clinical applications that you are most interested in.

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## What volume and size of beads can be prepared using the STIMULAN Rapid Cure bead mat?

The STIMULAN Rapid Cure bead mat can be used to prepare 3mm, 4.8mm or 6mm hemispherical beads. A 10cc pack of STIMULAN Rapid Cure will yield 25cc of bead volume.

## What are the working and setting times of STIMULAN?

- STIMULAN Rapid Cure has a 1-2 minute working time and will set ~4 minutes after mixing. Following mixing and application onto the bead mat, allow to set undisturbed for at least 8 minutes prior to release from bead mat.
- STIMULAN Kit (beads) has a working time of 1-2 minutes and will set in approximately 8 minutes after mixing. Following mixing and application onto the bead mat, allow to set undisturbed for at least 15 minutes prior to release from bead mat.
- STIMULAN Kit (injectable paste) has a 30 second working time prior to injection and begins to set 2-3 minutes after mixing. Following mixing and application, allow paste to set undisturbed for at least 15 minutes prior to closure.

## Can I substitute other mixing solutions or add additional solution when preparing STIMULAN Rapid Cure?

You should only use the mixing solution provided. Using alternative mixing solutions and/or adding other substances to the mixture may alter the setting time significantly. Some substance such as bone marrow and blood will prevent the paste from setting.

## Can I mix STIMULAN with antibiotics?

STIMULAN is not currently FDA cleared/approved to be mixed with antibiotics . Specific questions relating to off label/physician directed use should be sent to the Biocomposites' Compliance Unit via the unsolicited request process.

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## Can STIMULAN be applied to a wet field?

It is recommended that STIMULAN paste be applied to a dry and bloodless field. When implanted as a paste, do not irrigate site prior to material setting. Following bead placement do not irrigate site.

## What is the compressive strength of STIMULAN?

Stimulan Kit/Rapid Cure have been shown to have a 'wet' compressive strength (as set at implantation time) of 21 MPa. This helps maintain bead integrity immediately following bead placement. The compressive strength reduces rapidly as Stimulan is absorbed.

Product	Mean Compressive Strength (MPa)
STIMULAN Kit	21
STIMULAN Rapid Cure	21

## How long does STIMULAN take to absorb in bone?

STIMULAN is absorbed in approximately 4-8 weeks when used in accordance with the device labelling. Contributing factors are surgical site, quantity used and patient health.

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## What is STIMULAN contraindicated for?

Contraindications for STIMULAN can be found in the IFU. These include contraindications for filling defects which are intrinsic to the stability of the bony structure, renal compromised patients, hypercalcaemia, severe vascular or neurological disease, uncontrolled diabetes, pregnancy, severe degenerative bone disease and uncooperative patients who can't or won't follow post-operative instructions including individuals who abuse alcohol or drugs.

## What potential adverse effects may be associated with the implantation of STIMULAN?

Adverse effects for STIMULAN can be found in the IFU. These may include but are not limited to: wound complications including hematoma, site drainage, bone fracture, infection and other complications that are possible with any surgery, fracture or extrusion of the bone void filler, with or without particulate debris generation, deformity of the bone at the site and incomplete or lack of osseous ingrowth into bone void as is possible with any bone void filler.

## What should I do if my surgeon requires technical or clinical information or peer-to-peer communication?

Information requested by the surgeon or their medical team should be directed to your Field Marketing Specialist (FMS) or Regional Manager (RM). Information may also be requested by contacting the Clinical Performance Department (CPD). The CPD is available to address all technical questions and discuss clinical concerns that cannot be addressed by the FMS or RM. The CPD can satisfy your surgeons' information requests by corresponding either by phone, email or in person to discuss and provide technical product data. The data is gathered from feedback and worldwide clinical research that is analyzed and organized into trends. The CPD is also available to present technical information to hospital boards. They can also coordinate peer-to-peer discussions with Key Opinion Leaders (KOLs).

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## What should I do if my surgeon experiences an adverse event?

In this case the event should be reported as per the hospital policy and/or reported to the Compliance Department, Biocomposites Inc.

## Can wound drainage occur with the use of STIMULAN?

Wound drainage is possible with any implanted material and may be attributed to several factors including patient health and surgical methods. To reduce the risk of drainage ensure complete soft tissue coverage and/or containment is achieved.

## Why is there so little drainage associated with STIMULAN?

STIMULAN is a pharmaceutical-grade, synthetic calcium sulfate. The physical and chemical properties are tightly controlled during manufacturing to ensure optimal purity, hydrophilicity and physiological pH. The absence of impurities in STIMULAN may be associated with reduced drainage rates when compared to naturally occurring mineral sources of calcium sulfate.

## Will STIMULAN grow bone in osteomyelitic or infected non-union cases?

We do have clinical evidence that STIMULAN is remodelled into bone when placed at an infected site following thorough debridement and removal of necrotic tissue. Biocomposites would be happy to provide you with the case studies that demonstrate this for the indication you are interested in.

## Will STIMULAN cause heterotopic ossification when implanted in or adjacent to soft tissue?

STIMULAN is an osteoconductive material and is not osteoinductive or osteogenic in nature. Biocomposites has published a range of clinical data indicating a minimal risk of heterotopic ossification when implanted in or adjacent to soft tissue.

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## Does STIMULAN damage articulating surfaces on joint prosthesis?

This is an area of ongoing research, but wear testing indicates that STIMULAN does not significantly scratch implant grade cobalt chrome and does not lead to increased wear of high density polyethylene components. Wear testing also shows that STIMULAN causes fewer scratches to cobalt chrome than PMMA and competitor calcium sulfates. Biocomposites has produced a white paper on the influence of third body damage to articulating surfaces with bone void fillers which can be viewed at:

<http://www.biocomposites.com/us/your-specialty/musculoskeletal-infections/case-studies-and-clinical-papers/>

## Can STIMULAN cause an adverse soft tissue response?

As part of a recent study by the University of New South Wales Australia, soft tissue inflammatory response to implanted STIMULAN was determined. The study describes a novel small animal model to investigate dead-space management in muscle tissue<sup>1</sup>. Results from histology and serological analysis indicated no significant unusual inflammatory response to the implanted materials.

### Reference:

1. Oliver, R.A., et al., Development of a Novel Model for the Assessment of Dead-Space Management in Soft Tissue. PLoS ONE, 2015. 10(8): p. e0136514.

## Can surgeons use STIMULAN when the patient has a known sulfonamide allergy?

The Instructions for Use does not contraindicate STIMULAN for sulfa allergies.

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## Is there an increased risk of hypercalcaemia when using large quantities of STIMULAN?

There have been a small number of reported cases of hypercalcemia in patients where STIMULAN has been used. Vancomycin and aminoglycoside antibiotics are known to be nephrotoxic. Implantation of Stimulan beads with locally administered vancomycin or aminoglycoside antibiotics may result in elevated serum calcium levels. These levels may be increased further in the absence of adequate kidney function and/or dehydration which may result in an increased risk of hypercalcemia.

In laboratory *in-vitro* trials, Biocomposites has found that large amounts of vancomycin (hydrochloride) with STIMULAN may cause the beads to dissolve faster. This increased rate of dissolution of STIMULAN beads may potentially elevate serum calcium levels which may lead to an increased risk of hypercalcaemia. This would be more likely with patients who are dehydrated or have impaired kidney function.

## Uncontrolled diabetes and renal compromised patients.

The kidneys regulate the amount of fluid and various salts in the body, helping to control blood pressure. Kidney disease or nephropathy can happen to anyone but is more common in patients with diabetes and develops very slowly, over many years. It is most common in people who have had the condition for over 20 years. About 1 in 3 people with diabetes may go on to develop nephropathy, although as treatment improves fewer people are affected.

<https://www.diabetes.org.uk/kidneys>



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## Why should I choose STIMULAN over other lower priced calcium sulfates?

- STIMULAN is a truly absorbable calcium sulfate that is uniquely recrystallized for consistent and reliable performance in the presence of infection.
- STIMULAN has the following differentiating features:
  - Controlled Purity - STIMULAN is manufactured in a state of the art clean room environment. The properties of STIMULAN are tightly controlled during manufacturing to ensure that it contains no traces of potentially toxic impurities. The absence of impurities in STIMULAN may be associated with reduced drainage rates when compared to naturally occurring calcium sulfates.
  - Hydrophilicity - STIMULAN is hydrophilic and mixes easily and quickly with liquid, and does not require pre-soaking. Competitor calcium sulfates may contain stearic acid, which functions as a molding agent. The addition of stearic acid causes other calcium sulfates to be hydrophobic and require pre-soaking for up to 1 minute prior to use.
  - Physiologic pH level - STIMULAN has a controlled physiologic pH for improved biocompatibility.
  - Truly absorbable & absorbs at an optimal rate - STIMULAN absorbs in 4-8 weeks and is replaced by bone during the natural healing process, leaving no nidus for infection.
  - No third body damage – STIMULAN causes no third body damage to articulating surfaces.
  - Versatility – STIMULAN can be mixed to form beads, a paste or for injection to meet surgical demands.

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## How does STIMULAN compare to Cerament?

STIMULAN is indicated for infected sites and is fully absorbable. Cerement is contraindicated for infected sites and does not fully absorb. Cerement does not have a fast set product and does not provide a mat for molding beads.

The most appropriate Biocomposites product to compare to Cerement is genex – our bone void filler for trauma and non-unions.

## How does STIMULAN compare to Calcigen S?

STIMULAN is indicated for infected sites and is fully absorbable. Calcigen S is contraindicated for active infection and does not fully absorb. Calcigen S does not have a fast set product and does not provide a mat for molding beads.

The most appropriate Biocomposites product to compare to Calcigen S is genex – our bone void filler for trauma and non-unions.

## How does STIMULAN compare to Osteoblast?

STIMULAN is indicated for infected sites and is fully absorbable. Osteoblast is contraindicated for infected sites and does not fully absorb. Osteoblast does not have a fast set product.

The most appropriate Biocomposites product to compare to Osteoblast is genex – our bone void filler for trauma and non-unions.

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What is the powder weight of STIMULAN Rapid Cure per cc of paste volume?

The powder weight of STIMULAN Rapid Cure per cc of paste volume is:

STIMULAN PRODUCT	PASTE VOLUME	BEAD VOLUME	POWDER WEIGHT
Rapid Cure	5cc	12cc	9.5g
	10cc	25cc	19.0g
	20cc	50cc	38.0g

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For any other questions please contact your Biocomposites Regional Sales Manager.

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.

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