GranuLab (M) Sdn Bhd

**2006**

established in May

---

Your trusted partner in Synthetic Bone Graft

GranuLab (M) Sdn Bhd (GranuLab), a BioNexus Status Company (BNX 100217) established in May 2006, is a medical device manufacturer specializing in the production and commercialization of synthetic bone graft under the brand name GranuMaS®.

The company is a subsidiary of Sirim Tech Venture (STV), a company wholly owned by SIRIM Berhad. GranuLab is an ISO 13485:2016 accredited medical device manufacturing facility and the product “GranuMaS®” is European CE Mark certified by BSI, UK.

Its manufacturing facility located in Shah Alam, Selangor is an ISO 13485:2003 (MD579182) certified by BSI, UK and also has Manufacturing Licence (A017866) issued by Malaysian Industrial Development Authority (MIDA). The facility supports the technology to produce up to 350kg p.a of multiple types of synthetic bone grafts such as Hydroxyapatite (HA), Tricalcium Phosphate (TCP) and Biphasic that are available for various forms of sizes and shapes including paste (bone cement) to meet the specific needs of the industry.

Supported by the Ministry of Science, Technology and Innovation of Malaysia (MOSTI), GranuLab (M) Sdn Bhd has formed a smart partnership® with SIRIM Berhad by obtaining the exclusive rights to commercialise GranuMaS® as the sole licensed manufacturer via a vide Technical Licensing Agreement.
The Product: GranuMaS®

GranuMaS® is a synthetic calcium phosphate bioceramic-based substitute bone graft, developed through a collaborative R&D effort of Malaysian researchers from Advanced Material Research Centre (AMREC)-SIRIM Berhad, International Islamic University Malaysia (IIUM), Science University of Malaysia (USM), National University of Malaysia (UKM) & Malaysian Institute of Nuclear Technology (MINT).

With composition properties identical to human bones, GranuMaS® is the innovative alternative in surgical applications requiring bone grafting procedures for non-load bearing in Orthopaedics, ENT, Dental and Maxillofacial. The fabrication of Hydroxyapatite (HA) via the Solid State Reaction method, as invented by AMREC-SIRIM, shortens its production process with good reproducibility properties. This novel design conforms to all the required criteria for surgical implants as indicated by the American Society for Testing and Materials (ASTM) F1185-88 (1993) Standards: the “Standard Specification for Composition of Ceramic Hydroxyapatite for Surgical Implants”.

Prior to its commercialization, GranuMaS® had successfully passed all the necessary in vitro and in vivo biocompatibility tests for cytotoxicity, genotoxicity, serologic, and sterilization; including animals and humans clinical studies; for both dental and orthopaedic applications based on the required criteria as set by ISO 10993 and FDA matrices.

GranuMaS® is a CE mark medical Class 111 product (CE 586440 & CE 587328) certified by BSI, UK in 2013.
## GranuMaS® Hydroxyapatite - Product List
### Available in Granule

<table>
<thead>
<tr>
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<th>Items</th>
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<tr>
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<td>SM</td>
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<td>0.5 cc</td>
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<td>2 cc</td>
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<td>100134</td>
<td>SM</td>
<td>0.2-1.0</td>
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<td>100143</td>
<td>L</td>
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<td>2 cc</td>
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<tr>
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<td>2 cc</td>
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<td>100154</td>
<td>XL</td>
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## GranuMaS® Hydroxyapatite - Product List
### Available in Cube

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<td>100163</td>
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<tr>
<td>100164</td>
<td>Cube</td>
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## GranuMaS® Hydroxyapatite - Product List
### Available in Pin (Matchstick)

<table>
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<tr>
<td>100184</td>
<td>Pin (Matchstick)</td>
<td>3 x 3 x 30</td>
<td>5 cc</td>
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</table>

## GranuMaS® Hydroxyapatite - Product List
### Available in Chip

<table>
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<tr>
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<th>Items</th>
<th>Sizes (mm)</th>
<th>Volume</th>
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<td>100174</td>
<td>Chip</td>
<td>~1.0-2.5</td>
<td>5 cc</td>
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</table>
Committed to Quality

GranuMaS® bone graft substitute has been certified with full quality assurance for the design & manufacture of GranuMaS® Hydroxyapatite (HA) synthetic bone graft.

- CE Mark Certification for the Current Product (CE 586440 & CE 587328)
Product Awards Won

GranuMaS® is an award winning product, receiving numerous recognitions both domestically and internationally. The following is the list of awards won:

1. **ISESCO Science Award 2006**
   - State of Kuwait
   - Gold Medal for category “Technology”

   - Geneva, Switzerland
   - Gold Medal for category of Health/Medicine

   - Kuala Lumpur, Malaysia
   - Silver Medal

4. **SIRIM Best Innovation Award 2004**
   - Malaysia
   - Category - Product: GranuMaS®

5. **SIRIM Best Innovation Award 2004**
   - Malaysia
   - Category - Technology

6. **Prime Minister Award for Malaysian Innovation (2007)**

“The Malaysian-based company GranuLab produces Synthetic bone graft material to avoid using animal bone,”

*May 2009*
Manufacturing Plant at Kota Kemuning, Shah Alam, Malaysia.

Granulab’s manufacturing plant is certified & in compliance with ISO 13485-2003 standards; complete with a control room facility (5200 sqf) and a clean room with class 10K (800 sqf).

Granulab facility highlight

1. All production areas are inclusive of 6 control rooms and one clean room class 10K
2. ISO13485-2003 certified production facility
3. Well trained and highly qualified production personnel
4. More than 10,000 sqf production floor area
Well trained and highly qualified production personnel

All production areas are inclusive of 6 control rooms and one clean room class 10K
Case No. 1

The use of GranuMaS® for the treatment of fracture non-union, one of the complications of long bone fracture.

A 33 year old woman who previously had multiple fractures following a road traffic accident developed hypertrophic non-union of her supracondylar right femur fracture.

She underwent open reduction and internal fixation of the non-union with a femoral locking plate. GranuMaS® was used as the bone graft substitute to promote bone formation.

Patient was followed up as an out-patient in the Orthopaedic Clinic and showed good healing and union of the fracture at 11 weeks. At 15 months there was partial resorption of the GranuMaS® granules and the space between the granules was filled up with bone.

Courtesy of
Assoc. Prof. Dr. Kamarul Aniffin Khalid, Department of Orthopaedics, Traumatology & Rehabilitation, Kulliyyah (Faculty) of Medicine, International Islamic University Malaysia
Case No.2

The use of GranuMaS® for the treatment of a closed volar Barton’s fracture of the left radius.

A 39 year old man was involved in a road traffic accident. The patient sustained a close comminuted intra-articular fracture of his left distal radius (volar Barton’s fracture).

The distal radius fracture was treated surgically with open reduction and internal fixation using a volar plate system. GranuMaS® was used as the bone graft substitute to fill in the gap in the metaphyseal region.

At 54 weeks follow-up there is evidence of partial resorption of the GranuMaS® with no loss of the reduction achieved intra-operatively.
Clinical Studies

Case No.3

The use of GranuMaS® for the treatment of a comminuted intra-articular fracture of the distal right radius with distal radioulnar joint (DRUJ) disruption.

A 26 year old man who was involved in a road traffic accident and sustained a closed comminuted intra-articular fracture of the right distal radius (AO 23-C2) associated with disruption of the DRUJ and ulna styloid process fracture.

The right radius was treated surgically with open reduction and internal fixation using variable angle fragment specific plates dorsally. GranuMaS® was used as the bone graft substitute for the defect in the metaphyseal region after reduction of the fracture. The ulna styloid and DRUJ was treated conservatively.

The fracture healed very well with no loss of reduction or instability of the DRUJ. At 66 weeks there was evidence of some resorption of the GranuMaS® granules.

Courtesy of
Assoc. Prof. Dr. Kamarul Ariffin Khalid, Department of Orthopaedics, Traumatology & Rehabilitation, Kulliyyah (Faculty) of Medicine, International Islamic University Malaysia
Case No.4

The use of GranuMaS® for the treatment of a Grade 1 open fracture of the femur supracondylar region.

A 25 year old man involved in a road traffic accident and sustained a Grade 1 open comminuted supracondylar fracture of his left femur with inter-condylar extension.

The patient underwent debridement and open reduction and internal fixation using a long supracondylar locking plate. GranuMaS® was used as the bone graft substitute in the gap formed by the bone loss.

At 18 weeks follow up there was good bone formation with the area of bone loss almost completely filled up, including the space between the GranuMaS® granules. At 67 weeks there is evidence of resorption of GranuMaS® occurring.

Courtesy of
Assoc. Prof. Dr. Kamarul Ariffin Khalid, Department of Orthopaedics, Traumatology & RehabilitationKulliyyah (Faculty) of Medicine, International Islamic University Malaysia
Collaborating Partners

10 main partners & supporting agencies

Medically Approved Products

Since the initial development phase, our company and our R&D partners have been collaborating in close partnership. All our R&D partners are known for their pionerity, quality & advanced research expertise; which is the key in spearheading Malaysia to be technologically advanced in the global platform primarily in biotechnology. GranuLab develops, produces and markets products that have been reviewed & approved by clinically literate body of organizations in Malaysia.

Being thoroughly tested & evaluated as well as receiving various certifications from standard upholding bodies both domestically & internationally, our product guarantees a confidence of usage for all our customers worldwide.
We are member of

R&D Partners

Government Supporting Agencies

Our company receives strong support from the Malaysian government agencies for our product research, development & marketing by providing us with all the research facilities, human resources & financial support and by ensuring a competitive commercial viability in the market.
GranuMaS® In Dental Surgery & Bone Substitutes

Alveolar Bone Resorption A Challenge To Dentist

The simple extraction of a tooth leaves in its wake a hole that is surrounded by a shell of alveolar bone (tooth supporting bone). This bone’s only purpose in the human body is to support a tooth. As a result, when the tooth is lost the body quickly begins to resorb the bone, unless it is immediately replaced with either another tooth, implant or in this case a “ridge preservation graft” (socket graft).

Natural And Artificial Teeth Must Be Supported By Bone

Most of the times it is impossible to place an implant immediately at the time of the extraction. Mainly it is cause by the presence of a dental infection, size discrepancy between the tooth extracted and any possibility of an immediate implant replacement. By placing a “ridge preservation graft” to fill the void left by the extracted tooth, it will give the opportunity of the natural bone to proliferate and fill the space with quality live bone. Depending on the size of the extracted tooth, the ridge graft requires between three to six months before an implant can be placed.

Phase I: Clinical Trial

- Hospital USM with 70 Dental Patients

Objective of Study

- To compare post-operative complications in treatment group and control group
- To compare the amount of alveolar bone resorption in both groups

Methodology

1. Study design
   - Comparative cross sectional study

2. Population
   - Patients undergoing dental extraction in Hospital Universiti Sains Malaysia (USM) dental clinic

3. Inclusion Criteria
   - Age 18-48 years
   - Mandibular molar & premolar teeth

4. Exclusion criteria
   - Systemic diseases
   - Smokers
   - Poor oral hygiene

5. Sampling method
   - Systematic random sampling 2 groups:
     1 – Treatment group (HA -Granumas)
     2 - Control Group (left empty)

6. Informed written consent

Statistic on the clinical study

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Follow up after week</th>
<th>Follow up after 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test material</td>
<td>32</td>
<td>32</td>
<td>28</td>
</tr>
<tr>
<td>Control</td>
<td>38</td>
<td>38</td>
<td>34</td>
</tr>
</tbody>
</table>
1. Tooth extraction under local anaesthesia, without complications
2. The size of the Granumas was handled very easily
3. Diagramatic representation of a tooth socket following extraction of teeth
4. End of healing period

**Radiological Evaluation of Alveolar Crest Level 6 Months Postoperative**

Measuring the level of alveolar bone from crest of ridget to mental foramen. Results showed an increase in the crest level above the original level.

**Result Table: The mean alveolar bone resorption before extraction and 6 months Post extraction**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Height before (mm)</th>
<th>Height after (mm)</th>
<th>mean diff. (95% CI)</th>
<th>T-statistic (df)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GRANUMAS</td>
<td>33.32 (4.80)</td>
<td>34.64 (4.32)</td>
<td>1.32 (0.78, 1.89)</td>
<td>4.95 (31)</td>
</tr>
<tr>
<td>Control</td>
<td>32.77 (3.8)</td>
<td>29.79 (3.83)</td>
<td>-2.97 (-3.47, -2.48)</td>
<td>-12.2 (31)</td>
</tr>
</tbody>
</table>

**Result Table: Mean alveolar bone resorption in both groups Anova Test**

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>Bone Ht. changes (mm)</th>
<th>F-statistics</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GRANUMAS</td>
<td>32</td>
<td>0.38 (0.88)</td>
<td>15.09 (2.92)</td>
<td>(&lt;0.001)</td>
</tr>
<tr>
<td>Control</td>
<td>38</td>
<td>-2.98 (1.37)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

There was a significant difference in the mean alveolar bone height 6 months after implantation with GranuMaS®

**Result Table: Comparison of the mean difference in alveolar bone height between the study groups (post – hoc comparison)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean difference (mm) (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GRANUMAS vs Control</td>
<td>-4.84 (-7.50, -2.22)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
Clinical Studies

GranuMaS® in dental surgery

• Biocompatible
• User friendly
• Builds Jaw Bone
• Intelligent Tissue Engineering material

Soluble Molecules in Craniofacial growth

• Stimulate regeneration of bone
• Influence growth and resorption
• Growth factors, cytokines, BMP
• Affect other tissue and cell types
• To develop site specific effects

Bone Tissue Reconstruction Acquired Deformity – Tumour & Trauma
Core Decompression With Reverse Bone Graft Technique and Hydroxyapatite Granules in Avascular Necrosis of the Femoral Head

Abstract

Introduction Core decompression is used in precollapse lesions to forestall disease progression in avascular necrosis (AVN) of femoral head (FH). The author reports a new technique using reverse bone graft technique to effectuate core decompression.

Aim To prevent precollapse in Ficat Type 1&2 and revascularization using synthetic bone graft material.

Methods A 18 year female police trainee with Magnetic Resonance Imaging (MRI) confirming AVN Stage 2 Ficat, clinically painful hip not evident in x-rays consented to undergo this new technique. Reverse bone graft technique with a Coring reamer – Patent 5423823. A minimally invasive technique with lateral 2 cm incision introducing 8.5 mm core reamer to remove a core of bone up to the subchondral bone. The subchondral cyst decompressed and curetted under video recorded Image Intensifier (II). Demarcated avascular bone segment excised and bone graft reversed and inserted with cortical bone acting as a support to prevent collapse and the distal segment augmented using 5 grams of osteoconductive granular synthetic bone graft material based on calcium phosphate hydroxyapatite (HA 2500–5000 µm). Avascular segment histopathologically confirmed AVN. The metaphyseal entry was extrapoliated at the lateral cortex using the combined necrotic angle described by Kerboul in the anteroposterior and lateral views under II. Protected weight bearing for 2 months to prevent stress riser.

Biomaterials HA granules named as GranuMas® developed under Intensified Research in Priority Areas (IRPA) Research Project (No. 03-01-03-0000-PR0026/05) and invented by the Advance Materials Research Centre (AMREC) and manufactured by GranuLab – Patent P1 20040748 fulfilling the criteria for American Society for Testing and Materials (ASTM) F1185-88(1993) Standards which is ‘Standard Specification for Composition of Ceramic Hydroxyapatite for Surgical Implants’. Derived from Malaysian limestone, ranging from 200–5000 µm gamma sterilized.

Results After 6 months, there was no collapse of subchondral bone and the FH showed revascularization along bone grafted site with viable graft and increased radiotracer activity using 99-Tc MDP Bone Planar Scintigraphy. Clinical analysis follow up at 2 years was descriptive rather than statistical with a x-ray evident incorporated graft and with pain free full range of movement.

Discussion Reduction in intraosseous pressure is achieved by using large bore 8.5 mm coupled with HA granules promoting revascularization. The core tract entering through the metaphyseal region reduces risk of subtrochanteric fracture a potential complication of vascularized fibular grafts and with less morbidity with other treatment methods for osteonecrosis of the femoral head. The concept can be extended in introducing stem cell and biologic material to treat AVN.

Conclusion This technique is minimally invasive and effective in young patients with early stage of FH AVN and has shown revascularization along the bone grafted site.
GranuLab (M) Sdn. Bhd.

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