REGENESORB Biocomposite Material
Criteria for the Ideal Bioabsorbable Implant

1. Provides adequate *initial fixation strength* to heal the soft tissues to bone

2. Maintains satisfactory *strength over time* while the healing tissues are regaining mechanical integrity

3. Made of materials that are *completely safe*: no toxicity, antigenicity, pyrogenicity, or carcinogenicity

4. Must *not bioabsorb too slowly* or it will behave like its metal counterpart with potential breakage and migration

5. Is *replaced by bone*

References:


REGENESORB: Innovation Through Material

- Smith & Nephew’s latest biocomposite material

- Replaced by bone within 24 months in pre-clinical studies\(^1\)

- Dual osteoconductive calcium components

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1. *In vivo* animal testing has demonstrated that the composite material is bioabsorbable and is replaced by bone. Implants (9x10 mm) were implanted in ovine cancellous bone and compared to an empty defect (9x10 mm) at 6, 12, 18, and 24 months (n=6). Micro-CT analysis demonstrated that by 24 months, bone in-growth into this material (289.5 mm\(^3\)) was significantly greater (p<0.05) than bone in-growth into an empty defect (170.2 mm\(^3\)) and reaches a bone volume not statistically different from intact bone (188.2 mm\(^3\)). Results of in vivo simulation have not been shown to quantitatively predict clinical performance. Data on file at Smith & Nephew in report 15000897.
REGENESORB Biocomposite Material

Benefits of the advanced biocomposite material

Reliable
- Unique formulation of proven materials, each with proven safety and biocompatibility over decades of clinical use\(^1\)
- REGENESORB safety has been demonstrated in a Japanese human clinical trial evaluating REGENESORB-based instability anchors for shoulder labral repair\(^2\)

Innovative
- Contains dual osteoconductive calcium components – \(\beta\)-TCP and calcium sulfate – which have been individually shown to act during different stages of bone healing

Replaced by bone within 24 months in pre-clinical studies\(^3\)

Durable
- Designed and engineered specifically to meet the demanding biomechanical specifications of the most advanced surgical implants

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2. Smith & Nephew Clinical Study Report for Protocol No. SNE-CL-1101
3. In vivo animal testing has demonstrated that the composite material is bioabsorbable and is replaced by bone. Implants (9x10 mm) were implanted in ovine cancellous bone and compared to an empty defect (9x10 mm) at 6, 12, 18, and 24 months (n=6). Micro-CT analysis demonstrated that by 24 months, bone in-growth into this material (289.5 mm\(^3\)) was significantly greater (p<0.05) than bone in-growth into an empty defect (170.2 mm\(^3\)) and reaches a bone volume not statistically different from intact bone (188.2 mm\(^3\)). Results of in vivo simulation have not been shown to quantitatively predict clinical performance. Data on file at Smith & Nephew in report 15000897.
REGENESORB: Description

A unique formulation of proven materials including an additional osteoconductive ingredient – calcium sulfate:

- Calcium Sulfate 20%
- β-TCP 15%
- Polymer 65%
- PLGA 20%
- Osteoconductive calcium materials

Designed and engineered to
- Be absorbed and replaced by bone
- Meet the demanding biomechanical specifications of the most advanced surgical implants
REGENESORB: Intelligent Design

Biocomposite material = Polymer + Osteoconductive Component(s)

<table>
<thead>
<tr>
<th>POLYMER</th>
<th>OSTEOCONDUCTIVE COMPONENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provides mechanical strength and dictates absorption rate</td>
<td>Aids in regeneration of new bone</td>
</tr>
</tbody>
</table>

REGENESORB components

Better aligned with body’s healing rate

PLLA
PLDLA
PDLA
PLGA
PDLGA
PGA

Degradation Rate

Slow
Fast

Regeneration Rate

HA
BCP
β-TCP
CS
CC

PLLA: Poly-L lactic acid; PLDLA: Poly-L-D-lactic acid; PDLA: Poly-D lactic acid; PLGA: Poly-L-lactic co-glycolic acid; PDLGA: Poly-L-D-lactic co-glycolic acid; PGA: polyglycolic acid
HA: Hydroxyapatite; BCP: biphasic calcium phosphate; β-TCP: Beta tricalcium phosphate; CS: Calcium sulfate; CC: Calcium carbonate
## REGENESORB: Benefits of Each Component

<table>
<thead>
<tr>
<th>PLGA</th>
<th>β-TCP</th>
<th>Calcium Sulfate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poly-L-lactic co-glycolic acid</td>
<td>Beta tricalcium phosphate</td>
<td></td>
</tr>
<tr>
<td>• Has a long history of clinical use&lt;sup&gt;1&lt;/sup&gt;</td>
<td>• Longer-term (18 months) absorption profile for sustained bone formation&lt;sup&gt;3&lt;/sup&gt;</td>
<td>• Shorter-term (4-12 weeks) absorption profile for enhanced early bone formation&lt;sup&gt;3&lt;/sup&gt; and calcium release&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td>• Degradation rate faster than PLLA&lt;sup&gt;2&lt;/sup&gt; and better aligned with the body’s healing rate</td>
<td>• Osteoconductive (&lt;em&gt;physical&lt;/em&gt;)</td>
<td>• Osteoconductive (&lt;em&gt;biochemical&lt;/em&gt;)</td>
</tr>
<tr>
<td>• Comprised of natural products – lactic acid and glycolic acid</td>
<td>➢ Serves as a scaffold to allow for bone ingrowth&lt;sup&gt;4&lt;/sup&gt;</td>
<td>➢ Associated with increased levels of local growth factors&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

# Competitive Biocomposite Materials

<table>
<thead>
<tr>
<th>Company</th>
<th>Material/Product Name</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>S&amp;N</td>
<td>REGENESORB</td>
<td><strong>65% PLGA, 20% CS, 15% β-TCP</strong></td>
</tr>
<tr>
<td></td>
<td>HA</td>
<td>75% PLLA, 25% HA</td>
</tr>
<tr>
<td>Mitek</td>
<td>Biocryl™ Rapide™</td>
<td>70% PLGA, 30% β-TCP</td>
</tr>
<tr>
<td>Arthrex</td>
<td>BioComposite™</td>
<td>Anchors: 85% PLLA, 15% β-TCP</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Screws: 70% PLDLA, 30% BCP</td>
</tr>
<tr>
<td>Linvatec</td>
<td>Genesys™</td>
<td>75% PLDLA, 25% β-TCP</td>
</tr>
<tr>
<td>Biomet</td>
<td>ComposiTCP™</td>
<td>40% PLDLA, 60% β-TCP</td>
</tr>
<tr>
<td>Arthrocare</td>
<td>Bilok™</td>
<td>70% PLLA, 30% β-TCP</td>
</tr>
<tr>
<td>Stryker</td>
<td>Biosteon™</td>
<td>75% PLLA, 25% HA</td>
</tr>
</tbody>
</table>

**PLGA:** Poly-L-lactic co-glycolic acid; **PLLA:** Poly-L lactic acid; **PLDLA:** Poly-L-D-lactic acid  
**CS:** Calcium sulfate; **β-TCP:** Beta tricalcium phosphate; **HA:** Hydroxyapatite; **BCP:** biphasic calcium phosphate

2. Biocryl and Rapide are trademarks of Johnson & Johnson; BioComposite is a trademark of Arthrex; Genesys is a trademark of Conmed Linvatec; ComposiTCP is a trademark of Biomet; Bilok is a trademark of Arthrocare; Biosteon is a trademark of Stryker
The REGENESORB Advantage

- Competitive materials rely solely on the osteoconductive properties of $\beta$-TCP
  - Provides **sustained bone formation** over 18 months\(^1\)
  - Acts primarily **as a scaffold** for enhancing new bone formation\(^2\)

- REGENESORB material also includes a second osteoconductive material, **Calcium sulfate**
  - Works in **early stages (4-12 weeks) of bone healing**\(^1\)
  - Associated with **increased levels of local growth factors**\(^3\)

- Therefore, **REGENESORB material contains dual osteoconductive components**, which have been individually shown to act during different stages in the bone healing process and through different mechanisms of action – physical and biochemical.

## REGENESORB Safety and Performance:
*Demonstrated in multiple animal studies*

- **Four total implantation studies** (two long-term and two shorter-term)
- **Total 82 animals** implanted with **no adverse events observed**
- **Key results**: Replacement by bone within 24 months and comparable strength to PLLA/HA

### Description | Design/Time Points | N | Key Results
--- | --- | --- | ---
**Long-term absorption**
9x10mm solid REGENESORB interference screw
- Sheep
- Direct-in-bone
- 6, 12, 18, 24 months
- Replaced by bone within 24 months
- No adverse events

2.3mm REGENESORB instability anchor
- Sheep
- Direct-in-bone
- 12, 18 months
- Faster absorbing than PLLA/HA
- No adverse events

ACL reconstruction
Solid REGENESORB interference screws
- Sheep
- ACL
- 6, 12 weeks
- Comparable strength to PLLA/HA screws
- No adverse events

Tendon re-attachment
2.3mm REGENESORB instability anchor
- Sheep
- Patellar tendon
- 6, 12 weeks
- Comparable strength to PLLA/HA anchors
- No adverse events

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1. Data on file at Smith & Nephew in reports 15000897, 15001194, 15000921, 15000919. Results of in vivo simulation have not been shown to quantitatively predict clinical performance.
REGENESORB Safety and Performance: 
*Demonstrated in human clinical study*

**OSTEORAPTOR® REGENESORB Japanese Clinical Study Summary**

<table>
<thead>
<tr>
<th>Study Design Overview</th>
<th>Key Results from 6-Month Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objective</strong></td>
<td>Safety and efficacy of OSTEORAPTOR REGENESORB Suture Anchors following arthroscopic shoulder labral repair</td>
</tr>
<tr>
<td><strong>Scale</strong></td>
<td>62 patients enrolled; 61 patients evaluated</td>
</tr>
<tr>
<td>7 Japanese medical institutions</td>
<td></td>
</tr>
<tr>
<td><strong>Implants</strong></td>
<td>273 total suture anchors (average of 4+ anchors per patient)</td>
</tr>
<tr>
<td><strong>Study phases</strong></td>
<td>6 months (complete)</td>
</tr>
<tr>
<td>24 months (in progress)</td>
<td></td>
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<tr>
<td><strong>Outcome measures</strong></td>
<td>6 months</td>
</tr>
<tr>
<td>Clinical assessment (JSS-SIS/Rowe scores)</td>
<td></td>
</tr>
<tr>
<td>Diagnostic imaging (MRI, CT)</td>
<td></td>
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<tr>
<td>Adverse events and device failures</td>
<td></td>
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<tr>
<td>24 months</td>
<td></td>
</tr>
<tr>
<td>Bone replacement of device (CT)</td>
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</tbody>
</table>

**Safety**
- No severe adverse events related to device
- Low rate of anchor hole enlargement observed (lower than published literature\(^2\))
  - Not associated with any clinical outcome differences

**Efficacy**
- 100% anchors in place at 6 months
- No failures caused by device
- JSS-SIS/Rowe scores improved with specific improvements in stability, pain, and function
- 89% patients able to return to sport at 6 months (in line with published literature\(^3\))

**Study Conclusion**
Investigators concluded that the OSTEORAPTOR REGENESORB Suture Anchor is safe when used for endoscopic shoulder labral repair.

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1. Smith & Nephew Clinical Study Report for Protocol No. SNE-CL-1101
## Additional Resources

<table>
<thead>
<tr>
<th>Reference #</th>
<th>Description</th>
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| 10601161    | **REGENESORB Material White Paper**  
*Provides further details on the REGENESORB’s individual components and pre-clinical studies conducted to date* |
| 00613       | **HEALICOIL® REGENESORB Suture Anchor Brochure**  
*Highlights benefits of the innovative, open-architecture HEALICOIL design now available in the advanced REGENESORB biocomposite material* |
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