

Regena*afil*[®]
ALLOGRAFT PASTE

Regena*form*[®]
MOLDABLE ALLOGRAFT PASTE

Testing Summary

Regenafil® and Regenaform® Allograft Paste Products are single donor allograft products that were shown in a human clinical study to induce bone formation. Each lot of product is tested using the athymic nude rat model to verify osteoinductive potential. Regenafil and Regenaform are processed by RTI Biologics, Inc. (RTI) and distributed by Exactech.

OVERVIEW

RTI's innovations continuously raise the bar of science and safety for biologics: RTI was the first company to offer grafts designed to maximize each gift of donation and invent fully validated sterilization processes that include viral inactivation steps.

RTI has developed standards based on scientific analysis. For example, RTI studies have shown that qualities such as allograft osteoinductive capacity are donor-dependent; every donor must be individually assessed. For this reason, RTI does not use arbitrary criteria such as donor age limits to screen donors. If you have additional questions, please contact RTI's customer service department at 800-624-7238.

PATIENT SAFETY

The safety of tissue is contingent on three stages: donor screening, laboratory testing and tissue preparation validated to eliminate potential disease transmission. In the event that any one of these stages is challenged, RTI's tissue processing system includes built-in redundancies to ensure patient safety.

STAGE 1: SCREENING

After consent for donation is obtained, potential donors are screened for risk factors associated with infectious diseases and medical conditions that would rule out donation. This screening includes: family/next-of-kin interview, medical/hospital record evaluation and physical assessment of the donor. Once this preliminary screening is satisfactorily completed, recovery may begin.

The medical/social history evaluation for every donor includes:

- Cause of death: Donors are only accepted if cause of death is established.
- Medical / Social history:

*Potential donors with any of the following conditions are excluded from donation:**

- AIDS
- High risk of AIDS
- Abdominal disorders such as peritonitis, bowel necrosis without removal, bowel perforation with peritonitis and large or multiple intra-abdominal abscesses
- Alzheimer's or Dementia of unknown cause
- Hepatitis B or C, or unexplained jaundice
- Autoimmune diseases such as rheumatoid arthritis, myasthenia gravis or lupus
- Neurological and/or demyelinating diseases such as amyotrophic lateral sclerosis or multiple sclerosis

- Disease of bone and connective tissues
- Use of human derived pituitary growth hormone
- Positive tests for infectious diseases including: HCV, HBV, HIV I & II, syphilis, HTLV I/II
- High risk sexual activity
- Incarcerated in jail or correctional facility for 72 consecutive hours or longer in the past 12 months
- Tattoos, ear or other body piercing or acupuncture in the past 12 months where shared instruments or inks are known to have been used
- Chagas disease
- Cushing's Syndrome
- Creutzfeldt-Jakob disease (CJD or vCJD)
- Active infection such as meningitis, encephalitis, tuberculosis, Epstein Barr, West Nile Virus, cardiomyopathy, fungal infections, syphilis and mononucleosis
- Active or unexplained immune disorders
- Active systemic infection
- Intravenous drug abuse within the past five years

**This is an overview, not a comprehensive list. Contact RTI for a complete list of donor eligibility criteria.*

Donated tissues must be recovered within a specified time frame established by the American Association of Tissue Banks (AATB) to reduce the potential for microbial contamination. After recovery is completed, the donated tissue is carefully packaged and sent to RTI's state-of-the-art processing facility in Alachua, Fla. Upon receipt, the tissues are inspected to ensure proper packaging, labeling and transport temperature before being placed in quarantine pending laboratory testing and determination of donor eligibility. The final determination of donor eligibility is made by a licensed physician utilizing all available, relevant information.

STAGE 2: TESTING

Beyond donor screening, RTI performs an extensive panel of serological and microbiological tests. These results are subject to stringent criteria in order to release the donor tissue to the processing stage.

Serological testing:

- HCV Antibody
- HBV Surface Antigen
- HIV 1 & 2 Antibody
- HBV Total Core
- HTLV I & II Antibody
- RPR for Syphilis
- HIV-1/NAT
- HCV/NAT

In addition to serological testing, microbiological testing is used throughout the process to screen for potential contamination and to provide confirmation of tissue suitability for transplant.

Microbiological testing:

- Pre-processing culturing: Performed before processing begins, removes potentially unsuitable tissue from process.
- Environmental controls: Monitors cleanliness of processing environment.

STAGE 3: PROCESSING

RTI-processed bone pastes are sterilized through the demineralization process. This process has been validated to achieve viral inactivation, and combined with terminal sterilization, allows RTI to provide sterile DBM paste products.

“The demineralization process inactivated infectious retrovirus in infected cortical bone, thereby preventing disease transmission.”

- *Journal of Bone and Joint Surgery (February 2003)*

The demineralization process is validated to inactivate relevant and model viruses:

- Human Immunodeficiency Virus (HIV)
- HCV Model (BVDV)
- Parvovirus (PPV)
- Herpes Virus Model (PrV)

Final safety assurance step:

Following processing, RTI bone pastes undergo low-temperature, low-dose gamma sterilization before final release. Grafts sterilized in the final package are validated to achieve 10^{-6} sterility level.

DELIVERING PATIENT SAFETY

RTI's primary goal is to ensure patient safety. To fulfill this goal, RTI employs stringent tissue testing combined with processes validated to eliminate potential disease transmission. These redundant safeguards provide the highest level of confidence that patients will receive safe, high quality tissue.

ACCREDITATIONS, REGISTRATIONS, LICENSES AND CERTIFICATIONS

As a tissue processor and medical device manufacturer, RTI maintains a Quality Management System in compliance with the following federal and state licensure/regulations and voluntary standards:

- FDA Current Good Tissue Practices, 21 CFR Part 1271
- FDA Current Good Manufacturing Practices, 21 CFR Part 820
- State of Florida Statutes (other state licenses as applicable)
- AATB Standards for Tissue Banking
- ISO 13485, Medical Devices Quality Management Systems

RTI is registered with the U.S. Food and Drug Administration (FDA), which conducts periodic inspections. Quality inspections are also performed by

applicable state regulatory agencies, as well as accreditation and certification organizations, such as the American Association of Tissue Banks (AATB) and Notified Bodies for ISO certification.

RTI's Biomedical Laboratory holds the following registrations, certifications or licenses:

- FDA Registration
- CLIA Certificate of Compliance (Federal)
- State of Florida (other state licenses as applicable)

PASTE HANDLING:

Storage

Regenafil and Regenaform Frozen Allograft Paste should be stored frozen. It may be stored for six months at -20 to -40° C (conventional freezer)* or up to five years if stored at -40° C or colder (see expiration date on label).

**Product stored in a conventional freezer requires a manual change of expiration date. Regenafil and Regenaform Room Temperature must be stored at room temperature.*

Warming

Regenafil and Regenaform Frozen Allograft Paste must be warmed prior to use. Detailed instructions for warming the graft are included in the package insert that accompanies each graft. Each package of Regenafil and Regenaform Frozen Allograft Paste has a temperature indicator strip for convenience.

Hydration

Regenafil and Regenaform Room Temperature Allograft Paste may be hydrated with sterile saline, sterile water or patient's blood prior to use. Detailed instructions for hydrating the graft are included in the package insert that accompanies each graft. Each package of Regenafil and Regenaform Room Temperature Allograft Paste contains a premarked fluid syringe for convenience.

Indications

These products are intended to be packed into bony voids or gaps to fill and/or augment dental intraosseous, oral and cranio-/ maxillofacial defects. These defects may be surgically created osseous defects or osseous defects created from traumatic injury to the bone, including:

- Periodontal defects
- Alveolar ridge augmentation
- Extraction sockets
(ridge preservation, implant preparation/ placement)
- Maxillary sinus floor elevation
- Craniofacial augmentation
- Root resection, apicoectomy and cystectomy
- Tumor resection

One or more of the product formulations, depending upon specific anatomical location and dentist preference, can be placed in the dental intraosseous defect site.

These products were evaluated in a human clinical study and were shown to induce bone formation. Each lot of product is tested using the athymic nude rat assay to verify osteoinductive potential.

ORDERING

Please call our dedicated dental customer service representative to order Regenafil and Regenaform Allograft Paste Products.

Regenafil Frozen	Regenaform Frozen
0.2cc Syringe	0.5cc
0.5cc Syringe	1cc
1.0cc Syringe	2cc

Regenafil Room Temperature	Regenaform Room Temperature
0.5cc Syringe	1cc Jar
	2cc Jar

SHIPPING

Regenafil and Regenaform Frozen Allograft Pastes are shipped frozen in insulated shipping containers with dry ice via standard overnight services, unless a designated carrier or method is requested.

Regenafil and Regenaform Room Temperature Allograft Pastes may be shipped via two-day delivery or overnight service.

