Regeneration TECHNOLOGIES, INC.

FACT SHEET

Next-Generation BioCleanse™ Tissue Sterilization Process:
Sterilizes tissue from single donors in separate chambers

As awareness of the benefits of human donor (allograft) tissue increases, more surgeons and patients elect to use it in surgery; allograft is used in more than 600,000 surgical procedures in the United States every year. Unless tissue is sterilized through an effective process, however, there is a risk of disease transmission.

Processed Aseptically *Processed through BioCleanse™*

Allograft safety can be improved by using validated, low temperature chemical sterilization technologies that kill the most resistant organisms (such as non-enveloped viruses and spores) but preserve the biomechanical integrity and function of allografts. The BioCleanse™ Tissue Sterilization Process addresses this through its sterilization and viral inactivation process that does not alter the beneficial properties of tissue, allowing for the more consistent processing of allografts.

The BioCleanse process sets a new standard for tissue safety. It has been validated to eliminate HIV, hepatitis, bacteria, fungi and spores, and remove 99.9% of blood, lipids and marrow.

Regeneration Technologies has spent months developing the next generation of the BioCleanse process, made possible largely because of the company's new state-of-the-art processing facility. This new BioCleanse system sterilizes tissue from a single donor in one of several individual units. No commingling of tissue or fluids occurs at any time.

What is the BioCleanse process?

The BioCleanse process is a revolutionary, validated, patent-pending ***tissue sterilization process*** that is designed to provide surgeons and patients with allografts that are free of viral and bacterial contaminants. It is a fully automated pharmaceutical grade process that offers an ***added*** measure of safety. The same strict donor screening and tissue testing, which has always been adhered to, is still performed.

What are the advantages of the BioCleanse process?

- **Tissue sterilization process:** The BioCleanse process is a sterilization process that eliminates bacteria, fungi and spores, as well as enveloped and non-enveloped viruses such as HIV and hepatitis. Under conventional processing methods, the chances of viral transmission are exceedingly low. The BioCleanse process reduces this risk even further, eliminating the risk of donor to patient disease transmission.

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Donor Screening

- Behavioral / Lifestyle Risk Assessment
- Family / Next-of-Kin Interview
- Medical Record Evaluation / Hospital Records

Donor Tissue Testing

- Syphilis
- Hepatitis B Surface Antigen
- Hepatitis B Core Antibody
- Hepatitis C Virus Antibody
- Human Immunodeficiency Virus 1 and 2 Antibody
- Human T-Lymphotropic Virus Antibody I /II
- HIV - 1 PCR (Polymerase Chain Reaction)

BioCleanse™ Process

- Thoroughly penetrates tissue
- Eliminates viral and bacterial contaminants
- Kills bacteria, fungi and spores
- Removes blood, fats and marrow
- Retains desirable tissue characteristics such as biomechanical strength
- Preserves biocompatibility

BIOCLEANSE™
TISSUE STERILIZATION PROCESS
FROM REGENERATION TECHNOLOGIES, INC.

- **Consistent quality:** The BioCleanse process allows for automation of critical steps in tissue processing to ensure reproducible sterilization of each allograft.
- **Regulatory compliance:** The BioCleanse process is an automated, validated process designed to meet or exceed current and future tissue regulations.
- **Tissue functionality:** The BioCleanse process sterilizes without altering the strength or biocompatibility of allograft.

Is the BioCleanse process used on all allografts?

The BioCleanse process is currently used on hard tissue and is being implemented with musculoskeletal soft tissue allografts.

How does BioCleanse raise the level of safety?

In addition to adhering to current donor screening and testing guidelines, RTI's BioCleanse process raises the level of tissue safety through reproducible sterilization.

Comprehensive validation studies have been performed. Several different studies were performed (in part by independent laboratories) to provide a high degree of confidence in the process. These studies collectively demonstrate the effectiveness of the BioCleanse process to eliminate contamination during processing. This effectiveness has been demonstrated on a broad range of viruses, including enveloped and non-enveloped, RNA and DNA viruses, and viruses of varying size. Additionally, the process was validated to be effective against relevant bacterial and fungal contaminants as well as bacterial spores, which are recognized to be more resistant than viruses or vegetative bacteria.

How does the BioCleanse process work?

Allografts from a single donor are placed in an individual unit and are put through an automated multi-step cleansing process using chemicals that have a well established history of safety in tissue processing. The system is unique in that it completely penetrates tissue, allowing the process to first remove blood and bone marrow, then sterilize the tissue. BioCleanse does not use excessive heat, irradiation or ethylene oxide (ETO) to achieve sterilization.

Tissue sterilized through the BioCleanse process appears consistently white due to the absence of blood and lipids.

How does the BioCleanse process assure biocompatibility?

Human musculoskeletal tissue for transplantation is an inherently biocompatible material and has a well established record of safety. Before the BioCleanse process was implemented it was tested to ensure it did not adversely affect this natural tissue attribute. FDA and ISO publish guidelines for Biocompatibility Safety Testing (based on ISO 10993 and FDA G95-1 guidelines). RTI follows these guidelines and has conducted a series of standard *in vitro* and *in vivo* tests with the goal of verifying the biocompatibility of tissues processed through the BioCleanse process. The following assays were performed:

- Intracutaneous Irritation
- Intramuscular Implantation
- Acute Systemic Toxicity
- Subchronic Toxicity
- Sensitization
- Genotoxicity

The results of these studies demonstrate that donor tissue processed through the BioCleanse process meets established criteria for biocompatibility.

How does the BioCleanse process compare to other industry methods of tissue cleansing?

Although the risk of disease transmission through allograft transplantation is low, the BioCleanse process essentially eliminates that risk. Tissue processed using the BioCleanse process has an unmatched level of safety. The BioCleanse process completely penetrates tissue and eliminates a broad range of contaminants. The BioCleanse process, unlike other processes, is able to inactivate the most resistant organisms such as non-enveloped viruses and spores.

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