PUROS® DEMINERALIZED BONE MATRIX

PATIENT SAFETY THROUGH REDUNDANT SAFEGUARDS

Introduction

The safety of tissue is contingent on three stages – donor history 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 for Patient Safety

Medical/social history evaluations are performed for every donor. This screening includes: family/next-of-kin interview, medical record evaluation/hospital record review, behavioral/lifestyle risk assessment, medical examiner/coroner's report (autopsy report, when available), and laboratory, pathology and radiology reports. RTI's medical director – a licensed physician – must approve each donor record.

Stage 2: Testing for Patient Safety

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 Antibody
- HTLV-I & HTLV-II Antibody
- RPR for Syphilis
- HIV-I/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 for Patient Safety

Demineralized Bone Products

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

Sterilized Through Demineralization Process

The demineralization process is validated to inactivate relevant human viruses using "model" viruses, closely related viruses having similar physical and chemical properties, in accordance with FDA guidance.** The validation study also includes "challenge" viruses which test the ability of the demineralization process to inactivate the most resistant viruses as a measure of its overall viral inactivation capability. The demineralization process is validated to inactivate the following model, relevant and challenge viruses:

- Bovine Viral Diarrhea Virus (BVDV) Model
  - Human Immunodeficiency Virus (HIV)
  - Hepatitis C Virus (HCV)
  - Human T-lymphotropic Virus (HTLV)
- Pseudorabies Virus (PrV) Model
  - Hepatitis B Virus (HBV)
- Human Poliovirus (Polio-1) Challenge
- Porcine Parvovirus (PPV) Challenge

Final Safety Assurance Step

- Low-temperature, low-dose gamma sterilization: Grafts are sterilized in final packaging to achieve a validated 10^{-6} sterility assurance 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 a high level of confidence that patients will receive safe, high-quality tissue.

* Cheryl L. Swenson and Steven P. Arnoczky: *Demineralization for Inactivation of Infectious Retrovirus in Systemically Infected Cortical Bone: In Vitro and in Vivo Experimental Studies*; J. Bone Joint Surg. Am., Feb 2003; 85: 323 - 332.

** US Food and Drug Administration (FDA) Center for Biologics Evaluation and Research (CBER). 1998. "Q5A Viral Safety Evaluation of Biotechnology Products Derived From Cell Lines of Human or Animal Origin."

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