Patient Safety Through Redundant Safeguards

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 exhaustive 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 after before processing begins, removes potentially unsuitable tissue from process
- Sterility confirmation: Performed at packaging, confirms sterility achieved during processing
- Environmental controls: Monitors cleanliness of processing environment

Stage 3: Processing for Patient Safety

Sterilized through BioCleanse®:

Bone constructs, tendons and milled tissue

“"The efficacy of the sterilization method (BioCleanse) is supported by the absence of reports of bacterial or viral allograft-associated infections in tissue processed by this method."
- New England Journal of Medicine (June 2004)

Sterilized through Demineralization Process:

Demineralized bone products

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

BioCleanse Validated to Inactivate

*Demineralization Process is validated to inactivate these viruses.

<table>
<thead>
<tr>
<th>Relevant and Model Viruses</th>
<th>Spores</th>
<th>Vegetative Bacteria and Fungi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Immunodeficiency Virus (HIV)*</td>
<td>Clostridium sporogenes</td>
<td>Staphylococcus aureus</td>
</tr>
<tr>
<td>Hepatitis B Virus (HBV)*</td>
<td>Bacillus stearothermophilus</td>
<td>Escherichia coli</td>
</tr>
<tr>
<td>HCV Model (BVDV)*</td>
<td></td>
<td>Enterobacter cloacae</td>
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<tr>
<td>Hepatitis A Virus (HAV)</td>
<td></td>
<td>Pseudomonas aeruginosa</td>
</tr>
<tr>
<td>Parvovirus (PPV)*</td>
<td></td>
<td>Candida albicans</td>
</tr>
<tr>
<td>Herpes Virus Model (PrV)*</td>
<td></td>
<td>Staphylococcus epidermis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acinetobacter calcoaceticus</td>
</tr>
</tbody>
</table>

Following processing, grafts distributed by RTI undergo at least one of the following final steps to confirm safety.

Final Safety Assurance Steps
- Post-processing sterility culturing: Grafts subject to sterility cultures before final release
- Terminal sterilization through Sterrad®: Grafts sterilized in final package to achieve 10⁶ sterility level
- Low-temperature, low-dose gamma sterilization: Grafts sterilized in final package to achieve 10⁶ 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.