125 MAY STREET | EDISON, NJ 08837 | MTFBIOLOGICS.ORG

June 2023

Re: Understanding Sterility

To Whom It May Concern:

There are several different ways a human tissue graft may be sterilized. This memo is intended to clarify MTF's position on the sterilization of acellular human matrices.

Measuring Tissue Sterilization

Sterilization is measured by a sterility assurance level (SAL), which the Association for the Advancement of Medical Instrumentation (AAMI) defines as the probability of a single viable microorganism remaining on an item after sterilization.

- AAMI states that an SAL of 10^{-6} is appropriate for medical devices, equating to a 1 in a million chance that a viable microbe remains on the device
- The FDA considers an SAL of 10^{-3} appropriate for some biologic medical devices, which is an estimated 1 in 1,000 probability of the presence of a viable microbe (AAMI, 2007)
- The FDA does not require a specific SAL level for tissue banks
- The AATB and the FDA require that any SAL claims be validated

Sterilization Methods

Aseptic processing

US Pharmacopeia (USP) guidance governs sterilization for pharmaceutical-grade medical products that cannot undergo terminal sterilization (e.g. injectable medications and sterile solutions).

A tissue bank may choose to clean, disinfect, and aseptically process bone and soft tissue rather than use terminal sterilization because of the potential deleterious effect of terminal sterilization on tissue. The tissue bank must use a validated cleaning and disinfection method with strict adherence to aseptic technique.

In these cases, sterility testing is performed on the processed tissue in accordance with the USP <71> Sterility Test. The test demonstrates that the tissue itself is not inhibitory to the growth of microbial contaminants. Tissue that is processed through aseptic means and passes all the appropriate testing related to the USP guidance can be labeled as "sterile per USP <71>."

Terminal sterilization

Many tissue banks use a terminal sterilization step and claim to achieve a SAL of 10^{-6}. Under some circumstances an SAL of 10^{-3} may be claimed. In terminal sterilization, tissue is sterilized in its final package. If this claim is validated, the FDA allows the bank to use the word "sterile" on its packaging. Allografts may be terminally sterilized by several methods, including ethylene oxide, gamma radiation, electron (E)-beam radiation, and hydrogen peroxide plasma.

The most common sterilization technique used for tissue is gamma radiation. Many tissue banks use a low to moderate dose of gamma radiation to sterilize their tissues in their final packaging. High levels of gamma radiation has been shown to be detrimental to tissue integrity.

What is USP<71> Sterility Testing?

The United States Pharmacopeia (USP) is a non-governmental, official, public-standards-setting authority for prescription and over-the-counter medicines, and other healthcare products manufactured or sold in the United States. The FDA relies on USP standards and testing protocols for both medical devices and human tissue. USP <71> is a standard for sterility testing method that is used for many aseptically processed pharmaceuticals and other substances that cannot be terminally sterilized. **Many supplies and solutions that are typically used in the OR are tested for sterility using this method.** For example: IV solutions including sterile saline, some chemotherapy drugs and some pharmaceuticals are tested in this manner.

MTF's USP<71> Sterility Process

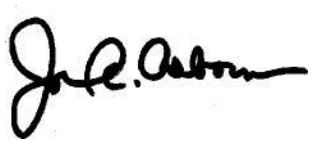
In order to maintain the most natural collagen matrix, MTF chooses to process ADM tissues aseptically and to avoid terminal sterilization. MTF's stringent criteria allows for only the highest quality incoming dermal tissue. Once received, the tissues are very carefully cleaned and disinfected in a patented multistep process that is validated to remove contaminants (bacteria, viruses, fungi, etc.) to achieve an SAL of 10^{-6}.

MTF dermal grafts are packaged in sterilized packaging, and representative samples are tested for sterility per USP<71> before they are released for transplantation. At least 10% or four grafts, whichever is greater, of each batch are tested for a panel of microbes. Only if all grafts are negative for bacteria is that batch of grafts released. If even one graft fails the entire batch is discarded

MTF chooses to process dermal grafts aseptically in order to maintain tissue integrity and to provide the best clinical outcomes possible.

If you have any questions, please do not hesitate to contact me at (732)-661-0202, extension 2209 or email MTF Regulatory Affairs at Regulatory_Customer_Inquiry@mtf.org

Sincerely,



Joel C. Osborne
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