Technical Information Report

AAMI TIR37: 2013

Sterilization of health care products—Radiation—Guidance on sterilization of biologics and tissue-based products

AAMI
Advancing Safety in Medical Technology

AAMI Technical Information Report

AAMI TIR37:2013
(Revision of AAMI TIR37:2007)

Sterilization of health care products—Radiation—Guidance on sterilization of biologics and tissue-based products

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Association for the Advancement of Medical Instrumentation

Abstract: This AAMI Technical Information Report (TIR) provides guidance for development, validation and routine control associated with the radiation sterilization processing of biologics and tissue-based products.

Keywords: sterilization, radiation, tissue

AAMI Technical Information Report

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Comments on this technical information report are invited and should be sent to AAMI, Attn: Standards Department, 4301 N. Fairfax Drive, Suite 301, Arlington, VA 22203-1633.

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www.aami.org/standards/glossary.pdf

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Association for the Advancement of Medical Instrumentation

Radiation Sterilization Working Group

This Technical Information Report (TIR) was developed by the AAMI Radiation Sterilization Working Group under the auspices of the AAMI Sterilization Standards Committee. Working Group approval of the TIR does not necessarily imply that all committee members voted for its approval.

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NOTE—Participation by federal agency representatives in the development of this document does not constitute endorsement by the federal government or any of its agencies.

Foreword

The dose setting methods described in the ANSI/AAMI/ISO 11137 series *Sterilization of health care products—Radiation,* Parts 1–3, were developed in the context of medical devices, and do not address the unique issues associated with biologics/tissues. These unique issues might potentially involve every aspect of a radiation sterilization validation, routine processing and maintenance of the sterilization process. This TIR addresses these unique issues and provides guidance on how to adapt current guidelines and standards for use with biologics/tissues.

As used within the context of this document, “should” indicates that among several possibilities, one is recommended as particularly suitable, without mentioning or excluding others, that a certain course of action is preferred but not necessarily required, or that (in the negative form) a certain possibility or course of action is undesirable but not prohibited; “may” is used to indicate that a course of action is permissible within the limits of the technical information report; “can” is used as a statement of possibility and capability; “must” is used only for those situations which cannot be otherwise, as in the example "Monday must follow Sunday."

Suggestions for improving this technical information report are invited. Comments and suggested revisions should be sent to Technical Programs, AAMI, 4301 N. Fairfax Drive, Suite 301, Arlington, VA 22203-1633.

NOTE—This introduction does not contain provisions of the AAMI TIR, *Sterilization of health care products—Radiation—Guidance on sterilization of biologics and tissue-based products* (AAMI TIR37:2013), but it does provide important information about the development and intended use of the document.

Introduction

The sources, types and radiation resistances of some microorganisms associated with biologics/tissues might be unique relative to the microorganisms associated with other health care products, such as medical devices. This TIR provides guidance to address issues that are unique to the radiation sterilization of biologics/tissues and to assist in substantiating a sterile label claim for these products. Except where indicated in this TIR, the requirements in the ANSI/AAMI/ISO 11137 series, ANSI/AAMI/ISO 11737-1, and ANSI/AAMI/ISO 11737-2, shall be followed, and AAMI TIR29 is guidance for characterizing the irradiation process and for establishing requisite process controls to ensure the irradiation system remains in a validated state.

The guidance contained in this TIR is only useful if the processing and other steps up to but not including sterilization have already been validated. Examples of steps that should be validated are microbiological testing, cleaning and disinfection, and sterilization of equipment used during processing, packaging and storage.

The key additions/changes in this second edition are as follows:

1. **Change of scope to "biologics and tissue-based products"**
   The scope of the document was changed from "human tissue-based products" to "biologics and tissue-based products" because much of the information in the document applies to all types of tissue-based products – not just human – as well as many biological products.

2. **Addition of information for selecting a dose establishment method (Annex A)**
   The most significant change to the document was the addition of Annex A, which gives guidance on how to select a dose establishment method that is suitable for a biologic or tissue-based product. These types of products have unique issues, such as availability of samples and tolerance to radiation; therefore, the Annex provides information about certain aspects of the various dose establishment methods and how these aspects might apply to the circumstances associated with a particular product. Some examples of the aspects discussed are the number of products required, availability of batches, bioburden levels versus sterilization dose, and the use of SIPs.

3. **Expansion of information on SIP use in dose establishment**
   The concept of SIP was originally developed for traditional medical devices to address issues of size and expected bioburden levels. Most biologics and tissue-based products not only can be tested in their entirety because of their size, but also do not have significant bioburden levels because they are processed in a way that reduces the bioburden. The use of SIPs is not recommended for these products, but guidance is given on what needs to be addressed if an SIP is used for testing.

4. **Addition of a clause on adopting a new product into a family**
   Because biologics and tissue-based products are processed in a way that results in very low bioburden, the product family concept is definitely applicable. Although other sterilization methods, such as ethylene oxide, address adopting a new product into a product family, none of the dose establishment documents have guidance about this. A new clause was added that gives guidance on how to assess a new product and show that it can be added to an existing family.

5. **Expansion of information about MPN testing**
   Many times biologics and tissue-based products are good candidates for most probable number (MPN) testing, due to their low bioburden and ability to be tested/diluted by weight or volume. Additionally, MPN testing can result in a more sensitive bioburden test with much lower bioburden levels, which allows very low sterilization doses to be established. For these reasons, the information about using MPN testing was expanded upon.

6. **Addition of information on loading patterns for irradiation**
   In the new section 5.6.2 (previously 5.5.2), information was added about loading patterns for irradiation. Guidance was included on using a different container for shipment versus irradiation.

Sterilization of health care products—Radiation—Guidance on sterilization of biologics and tissue-based products

1 Scope

1.1 Inclusions

This technical information report (TIR) provides guidance for development, validation and routine control associated with the radiation sterilization processing of biologics and tissue-based products.

NOTE Although the scope of this document is limited to human biologics and tissue-based products, it provides guidance that might be applicable to other products.

1.2 Exclusions

This TIR does not address validation requirements for eliminating and/or inactivating viruses and prions or sterilization of cell/tissue by-products. Guidance on inactivating viruses and prions can be found in ANSI/AAMI/ISO 22442-3:2007. This TIR also does not address handling or safety issues for cell/tissue by-products.

2 Normative references

The following normative documents contain provisions which, through reference in this text, constitute provisions of this TIR. For dated references, subsequent amendments to, or revisions of, any of these publications do not apply. However, parties to agreements based on this TIR are encouraged to investigate the possibility of applying the most recent editions of the normative documents indicated below. For undated references, the latest edition of the normative document referred to applies. AAMI maintains a register of currently valid AAMI technical documents.

ANSI/AAMI/ISO 11137-1, *Sterilization of health care products—Radiation—Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices*

ANSI/AAMI/ISO 11137-2, *Sterilization of health care products—Radiation—Part 2: Establishing the sterilization dose*

ANSI/AAMI/ISO 11137-3, *Sterilization of health care products—Radiation—Part 3: Guidance on dosimetric aspects*

ANSI/AAMI/ISO 11737-1, *Sterilization of medical devices—Microbiological methods—Part 1: Determination of a population of microorganisms on products*

ANSI/AAMI/ISO 11737-2, *Sterilization of medical devices—Microbiological methods—Part 2: Tests of sterility performed in the validation of a sterilization process*

This document is intended to be used in conjunction with ANSI/AAMI/ISO 11137-1 and 11137-2.

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

3.1
bacteriostasis/fungistasis (B/F) test (also called the method suitability test or sterility test validation)
test performed with selected microorganisms to demonstrate the presence or absence of substances that inhibit the multiplication of microorganisms.

NOTE For the purposes of this type of testing, the B/F test is considered the validation for the test of sterility and MPN tests.

3.2
batch
defined quantity of product, intended or purported to be uniform in character and quality, that has been produced during a defined cycle of manufacture.

[ANSI/AAMI/ISO TIR11139:2006, definition 2.1]

NOTE For the purposes of this document, a group of tissue products can be described using terms such as donor, processing batch and sterilization batch.

3.3
bioburden
population of microorganisms on or in product and/or sterile barrier system.

[ANSI/AAMI/ISO TIR11139:2006, definition 2.2]

3.4
biologics
a preparation that is synthesized from living organisms, or their products, and used as a diagnostic, preventive or therapeutic agent.

3.5
companion tissue
tissue from the same donor(s) that is not intended to be used for transplantation.

NOTE For the purposes of this document, companion tissue should be processed in the same manner as tissue that is used for transplantation. Companion tissue is representative of tissue intended for transplantation but is only used for evaluation and/or testing purposes.

3.6
culture conditions
combination of growth media and manner of incubation used to promote germination, growth and/or multiplication of microorganisms

NOTE The manner of incubation may include the temperature, time and any other conditions specified for incubation.

[ANSI/AAMI/ISO TIR11139:2006, definition 2.10]

3.7
donor identification
unique code assigned to all tissue and companion tissue that originates from the same donor.

3.8
human tissue-based products
human cells, tissues, or cellular or tissue-based products (HCT/Ps)
articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient. Examples of HCT/Ps include, but are not limited to, bone, ligament, skin, dura mater, heart valve, cornea, hematopoietic stem/progenitor cells derived from peripheral and cord blood, manipulated autologous chondrocytes, epithelial cells on a synthetic matrix, and semen or other reproductive tissue.

[FDA 21 CFR 1271.3(d)]

3.9
processing
any activity performed on an HCT/P other than recovery, donor screening, donor testing, storage, labeling, packaging, or distribution, such as testing for microorganisms, preparation, sterilization, steps to inactivate or remove adventitious agents, preservation for storage, and removal from storage.

[FDA 21 CFR 1271.3(*ff)*]

NOTE For the purposes of this document, cellular-based products are not included.

3.10
processing batch
product that has been processed in the same manner and at the same time.

NOTE for HCT/Ps, the processing batch is from a single donor source.