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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
A technical information report (TIR) is a publication of the Association for the Advancement of Medical Instrumentation (AAMI) Standards Board that addresses a particular aspect of medical technology.

Although the material presented in a TIR may need further evaluation by experts, releasing the information is valuable because the industry and the professions have an immediate need for it.

A TIR differs markedly from a standard or recommended practice, and readers should understand the differences between these documents.

Standards and recommended practices are subject to a formal process of committee approval, public review, and resolution of all comments. This process of consensus is supervised by the AAMI Standards Board and, in the case of American National Standards, by the American National Standards Institute.

A TIR is not subject to the same formal approval process as a standard. However, a TIR is approved for distribution by a technical committee and the AAMI Standards Board.

Another difference is that, although both standards and TIRs are periodically reviewed, a standard must be acted on—reaffirmed, revised, or withdrawn—and the action formally approved usually every five years but at least every 10 years. For a TIR, AAMI consults with a technical committee about five years after the publication date (and periodically thereafter) for guidance on whether the document is still useful—that is, to check that the information is relevant or of historical value. If the information is not useful, the TIR is removed from circulation.

A TIR may be developed because it is more responsive to underlying safety or performance issues than a standard or recommended practice, or because achieving consensus is extremely difficult or unlikely. Unlike a standard, a TIR permits the inclusion of differing viewpoints on technical issues.

CAUTION NOTICE: This AAMI TIR may be revised or withdrawn at any time. Because it addresses a rapidly evolving field or technology, readers are cautioned to ensure that they have also considered information that may be more recent than this document.

All standards, recommended practices, technical information reports, and other types of technical documents developed by AAMI are voluntary, and their application is solely within the discretion and professional judgment of the user of the document. Occasionally, voluntary technical documents are adopted by government regulatory agencies or procurement authorities, in which case the adopting agency is responsible for enforcement of its rules and regulations.

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.
# Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glossary of equivalent standards</td>
<td>iv</td>
</tr>
<tr>
<td>Committee representation</td>
<td>v</td>
</tr>
<tr>
<td>Foreword</td>
<td>viii</td>
</tr>
<tr>
<td>Introduction</td>
<td>ix</td>
</tr>
<tr>
<td>1 Scope</td>
<td>1</td>
</tr>
<tr>
<td>1.1 Inclusions</td>
<td>1</td>
</tr>
<tr>
<td>1.2 Exclusions</td>
<td>1</td>
</tr>
<tr>
<td>2 Normative references</td>
<td>1</td>
</tr>
<tr>
<td>3 Terms and definitions</td>
<td>1</td>
</tr>
<tr>
<td>4 Definition and maintenance of product families for dose setting, dose substantiation and sterilization dose auditing</td>
<td>3</td>
</tr>
<tr>
<td>4.1 General</td>
<td>3</td>
</tr>
<tr>
<td>4.2 Defining product families</td>
<td>4</td>
</tr>
<tr>
<td>4.3 Designation of product to represent a product family for performance of a verification dose experiment or a sterilization dose audit</td>
<td>4</td>
</tr>
<tr>
<td>4.4 Maintaining product families</td>
<td>5</td>
</tr>
<tr>
<td>4.5 Effect of failure on establishment of sterilization dose or of a sterilization dose audit on a product family</td>
<td>5</td>
</tr>
<tr>
<td>5 Selection and testing of product for establishing and verifying the sterilization dose</td>
<td>5</td>
</tr>
<tr>
<td>5.1 General</td>
<td>5</td>
</tr>
<tr>
<td>5.2 Nature of product</td>
<td>6</td>
</tr>
<tr>
<td>5.3 Sample Item Portion (SIP)</td>
<td>6</td>
</tr>
<tr>
<td>5.4 Sampling conditions</td>
<td>6</td>
</tr>
<tr>
<td>5.5 Microbiological testing</td>
<td>7</td>
</tr>
<tr>
<td>6 Methods of dose establishment</td>
<td>13</td>
</tr>
<tr>
<td>6.1 General</td>
<td>13</td>
</tr>
<tr>
<td>6.2 Selecting a method for the establishment of a sterilization dose</td>
<td>13</td>
</tr>
<tr>
<td>6.3 Establishing a maximum acceptable dose</td>
<td>13</td>
</tr>
<tr>
<td>Selection of a Dose Setting Method</td>
<td>14</td>
</tr>
<tr>
<td>Bibliography</td>
<td>16</td>
</tr>
</tbody>
</table>
Glossary of equivalent standards

International Standards adopted in the United States may include normative references to other International Standards. AAMI maintains a current list of each International Standard that has been adopted by AAMI (and ANSI). Available on the AAMI website at the address below, this list gives the corresponding U.S. designation and level of equivalency to the International Standard.

www.aami.org/standards/glossary.pdf
Committee representation

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.

At the time this document was published, the AAMI Radiation Sterilization Working Group had the following members:

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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.

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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 11737-1, Sterilization of medical devices—Microbiological methods—Part 1: Determination of a population of microorganisms on products


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