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Sterilization of health care products — Biological indicators —

Part 8:
Method for validation of a reduced incubation time for a biological indicator

Stérilisation des produits de santé — Indicateurs biologiques —

Partie 8: Méthode de validation d'une période d'incubation d'indicateur biologique

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Contents

Page

Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

A list of all parts in the ISO 11138 series can be found on the ISO website.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

A biological indicator incubation time is the minimum period of cultivation required before making a final determination that a biological indicator is negative (shows no growth). The reference incubation time for biological indicators for established sterilization processes such as moist heat and ethylene oxide is 7 days (see ISO 11138-1:2017). In some instances where biological indicator results are needed as part of the product release process, a 7-day incubation time might not be practical. This is especially the case where biological indicators are used to monitor sterilization processes in hospitals or other health care facilities such as dental or general practitioner offices.

The purpose of a reduced incubation time is to demonstrate recovery of the surviving or injured spores to manifest as growth or no growth within the defined incubation period. The reduced incubation time is a function of the test method and conditions used to establish the incubation time and is independent of the process parameters for the sterilization method used to deliver the lethality.

Biological indicators with an incubation time of less than 7 days (a Reduced Incubation Time, or RIT) have been in use since the 1970s. The methodology to determine the RIT was originally created by the biological indicator manufacturers. Later, the United States Food and Drug Administration published guidance for manufacturers seeking regulatory clearance to market biological indicators to health care facilities in the United States (ref. Guidance for Industry and FDA Staff, Biological Indicator (BI) Premarket Notification [510(k)] Submissions, issued October 4, 2007, Attachment II). This guidance contained a protocol for validating an incubation time that was less than 7 days. This document was specific to regulations for commercial practices in a single country and did not address requirements for RIT methodology outside of that application. The purpose of this standard is to describe an internationally agreed approach to the validation of the reduced incubation time of a biological indicator.

Sterilization of health care products — Biological indicators —

Part 8:
Method for validation of a reduced incubation time for a biological indicator

1 Scope

1.1 This document specifies the requirements for a test method to be utilized to establish or confirm a reduced incubation time (RIT) that is shorter than the 7 day reference incubation time specified in 7.3.22 of ISO 11138-1:2017 for biological indicators used to monitor moist heat sterilization processes or ethylene oxide (EO) sterilization processes.

1.2 This document is applicable to manufacturers of biological indicators and to end users of biological indicators who intend to, if required by their quality system, establish, validate or confirm an RIT.

1.3 This document is not applicable to biological indicators used to monitor dry heat, low temperature steam formaldehyde (LTSF) or vaporized hydrogen peroxide (VH2O2) sterilization processes.

NOTE 1 The method described in this document to establish an RIT for biological indicators used to monitor moist heat or EO sterilization processes has been used extensively for many years. However, there is limited experience in use of this method to establish an RIT for biological indicators used to monitor dry heat, low temperature steam formaldehyde or vaporized hydrogen peroxide sterilization processes. This document, therefore, does not include these sterilization processes.

NOTE 2 For EO as a sterilizing agent, the stated RIT will be applicable for any EO cycle type, i.e. 100% EO, EO blends, etc.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 11138-1:2017, *Sterilization of health care products — Biological indicators — Part 1: General requirements*

ISO 18472, *Sterilization of health care products — Biological and chemical indicators — Test equipment*

3 Terms and definitions

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

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at http://www.electropedia.org/

3.1
biological indicator
test system containing viable microorganisms providing a specified resistance to a specified sterilization process

[SOURCE: ISO 11139:2018, 3.29]

3.2
carrier
supporting material on or in which test microorganisms are deposited

[SOURCE: ISO 11139:2018, 3.33]

3.3
culture condition
combination of growth media and manner of incubation used to promote germination, growth and/or multiplication of microorganisms

Note 1 to entry: The manner of incubation may include the temperature, time and any other conditions specified for incubation.

[SOURCE: ISO 11139:2018, 3.70]

3.4
fractional cycle
operating cycle in which the exposure phase is reduced compared with that specified for the sterilization cycle

[SOURCE: ISO 11139:2018, 3.123]

3.5
inoculated carrier
supporting material on or in which a defined number of viable test organisms have been deposited

[SOURCE: ISO 11139:2018, 3.144]

3.6
resistometer
test equipment designed to create specified combinations of the physical and/or chemical parameters of a sterilization process

[SOURCE: ISO 11139:2018, 3.233]

3.7
self-contained biological indicator
biological indicator presented such that the primary package, intended for incubation, contains the incubation medium required for incubation and recovery of the test organism

[SOURCE: ISO 11139:2018, 3.248]

4 General

4.1 When establishing, validating, or confirming a reduced incubation time (an incubation time of less than 7 days), the exposure shall be designed to achieve a fractional response in either

a) a resistometer meeting the requirements of ISO 18472;

b) a sterilizer process where all parameters are defined, controlled, and repeatable.

4.2 After successful RIT validation of the BI design per this standard, if ongoing lot-to-lot assessment of RIT is desired by the BI manufacturer as part of a quality control program,, this testing may follow other statistically valid sampling plans as determined by the BI manufacturer's Quality Systems requirements.

4.3 The reduced incubation time validation for a spore strip sold with recovery medium as a kit or a self-contained biological indicator does not have to be repeated by the end user as long as the end user uses the biological indicator with the same sterilizing agent and BI incubation temperature as that used in the validation, e.g. design validated and used in ethylene oxide. See ISO 11138-7:2019, 12.3.3. If an end user intends to use an RIT with a spore carrier/recovery medium combination or incubation conditions that have not been tested by a biological indicator manufacturer (e.g. a spore strip used with a recovery medium not supplied as part of a kit), the end user shall establish the RIT for that system using the method provided in this standard.

4.4 A requirement for end user verification of an RIT is determined by the quality system requirements of the end user. If an end user intends to confirm an RIT provided by the biological indicator manufacturer the end user shall follow the test method used by the biological indicator manufacturer.

4.5 The method described in this document shall be used to establish the RIT for a biological indicator design whose primary components include a spore carrier and a specific recovery medium (e.g. a spore strip supplied with recovery medium as a kit, or a self-contained biological indicator).

5 Selection and preparation of samples

5.1 Biological indicators used for testing by this method shall be randomly chosen from production equivalent lots of biological indicators.

5.2 Biological indicator sample holders should provide for adequate separation of the exposed biological indicators to avoid a shielding effect. The holder should be constructed and prepared for use (e.g. pre-warmed) in such a way that it does not influence exposure conditions.

NOTE Some examples of properties of the holder include:

a) chemically non-reactive with the sterilizing agent;

b) a good heat conductor;

c) the mass ratio of the holder to the exposed samples is kept to a minimum;

d) made in the form of mesh, as opposed to solid materials.

6 Exposure and culturing

6.1 Identify the fractional cycle exposure conditions in which 30% to 95% of the biological indicators exposed are expected to be positive after 7 days of incubation.

NOTE 1 Other process variables (e.g. temperature, dose or concentration)) can be modified to achieve the fractional response.

NOTE 2 Different fractional cycles can be used provided each set achieves 30-95% positives.

6.2 Obtain a minimum of 100 biological indicators from each of 3 different lots (for a total sample size of 300 biological indicators). Expose the biological indicators to the fractional cycles determined in 6.1 using sample sets of the minimum number required.

6.3 Place the biological indicator samples in the chamber to allow all of the samples equal exposure to the sterilization conditions.

