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Sterilization of health care products — Biological indicators —

Part 5: Biological indicators for low-temperature steam and formaldehyde sterilization processes

Stérilisation des produits de santé — Indicateurs biologiques —

Partie 5: Indicateurs biologiques pour la stérilisation à la vapeur d'eau et au formaldéhyde à basse température

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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).

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For an explanation on 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 the following URL: www.iso.org/iso/foreword.html.

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

This second edition cancels and replaces the first edition (ISO 11138-5:2006), which has been technically revised.

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

Introduction

ISO 11138-1 specifies production, labelling, test methods and performance requirements for the manufacture of biological indicators including inoculated carriers and suspensions intended for use in validation and monitoring sterilization processes. This document gives specific requirements for those biological indicators intended for use in low-temperature steam and formaldehyde sterilization processes.

Annex B gives rationale for the liquid-phase test method for low-temperature steam and formaldehyde biological indicators.

The ISO 11138 series represents the current "state-of-the-art" according to the experts representing manufacturers, users and regulatory authorities involved in developing the standard. The intent is not to promote the use of biological indicators where such use is not advised, but to provide common requirements for the production of those biological indicators that are known to be in use today.

A standard exists providing general requirements for the validation and control of low-temperature steam and formaldehyde sterilization processes (see ISO 25424).

NOTE It is possible that some countries or regions have published other standards covering requirements for sterilization or biological indicators.

Advice on selection, use and interpretation of results when using biological indicators can be found in ISO 14161.

Sterilization of health care products — Biological indicators —

Part 5: Biological indicators for low-temperature steam and formaldehyde sterilization processes

1 Scope

This document specifies requirements for test organisms, suspensions, inoculated carriers, biological indicators and test methods intended for use in assessing the performance of sterilization processes employing low-temperature steam and formaldehyde as the sterilizing agent.

NOTE 1 Requirements for validation and control of low-temperature steam and formaldehyde sterilization processes are provided by ISO 14937.

NOTE 2 Requirements for work place safety can be provided by national or regional regulations.

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*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 11138-1 and the following apply.

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

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

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

3.1
low-temperature steam and formaldehyde sterilization
process incorporating forced air removal, which allows exposure of wrapped goods to steam at sub-atmospheric pressure, and thus at temperatures less than 100 °C, with the admission of formaldehyde gas, keeping the sterilizing agent in a steady state throughout the hold time

4 General requirements

The requirements of ISO 11138-1 apply.

5 Test organism

5.1 The test organisms shall be spores of *Geobacillus stearothermophilus* or other strains of microorganisms of demonstrated equivalent performance as required by this document.

NOTE 1 *Bacillus stearothermophilus* has been reclassified as *Geobacillus stearothermophilus*.

NOTE 2 *Geobacillus stearothermophilus* NCIB 8224, DSM 6790, ATCC 7953, ATCC 10149 and ATCC 12980 have been found to be suitable[1)].

5.2 If a test organism other than *Geobacillus stearothermophilus* is used, the suitability of the resistance of that test organism shall be determined.

6 Suspension

The requirements of ISO 11138-1 apply.

7 Carrier and primary packaging

7.1 The suitability of the carrier and primary packaging materials for biological indicators for use in low-temperature steam and formaldehyde sterilization processes shall be demonstrated in accordance with the requirements of ISO 11138-1:2017, 5.2 and Annex B.

NOTE Carriers based on filter paper might not be suitable because of the chemisorption of formaldehyde on cellulose surfaces.

7.2 The exposure conditions to determine compliance shall be the following:

a) minimum exposure temperature: greater than or equal to 5 °C above the manufacturer's stated maximum exposure temperature;

b) maximum exposure temperature: as stated by the manufacturer; if not stated by the manufacturer, the maximum exposure temperature shall be greater than or equal to 100 °C;

c) exposure time: greater than or equal to 160 min.

NOTE These conditions have been selected to represent a realistic challenge to the carrier while remaining within the practical limits of a low-temperature steam and formaldehyde sterilization process.

8 Inoculated carriers and biological indicators

The requirements of ISO 11138-1 apply.

9 Population and resistance

9.1 The resistance characteristics shall be stated according to ISO 11138-1:2017, 6.4.

9.2 The viable count shall be stated with increments less than or equal to $0{,}1 \times 10^{n}$ per unit (e.g. per ml of suspension, per inoculated carrier or per biological indicator).

9.3 For inoculated carriers and biological indicators, the viable count shall be greater than or equal to $1{,}0 \times 10^{5}$.

1) These are examples of suitable products available commercially. This information is given for the convenience of users of this document and does not constitute an endorsement by ISO of these products.

9.4 The resistance shall be expressed as the *D* value in mins at 60 °C. The *D* value of each batch/lot of biological indicators or inoculated carriers shall be stated in minutes to one decimal place at 60 °C.

9.5 Suspensions, inoculated carriers or biological indicators containing *Geobacillus stearothermophilus* spores shall have a D_{60} value of greater than or equal to 6 min when tested according to the conditions in Annex A. Other microorganisms shall have *D* values supporting the application.

9.6 The resistance characteristics specified in this document and any other part of ISO 11138 shall be defined using the specific critical variables associated with the referenced sterilization process.

9.7 *D* values are determined according to methods given in ISO 11138-1:2017, Annexes C and D.

9.8 Determination of *D* value and survival-kill response characteristics are based on the process parameters in Annex A.

9.9 The survival-kill window should be calculated using the formulae in ISO 11138-1:2017, Annex E.

NOTE This information can be of value to the user when comparing different batches from the same manufacturer.

EXAMPLE Using the formulae in ISO 11138-1:2017, Annex E, with the minimum population and minimum *D* value requirements specified in this document, the survival-kill response characteristics are

— at 60 °C: survival time greater than or equal to 18 min and kill time less than or equal to 54 min.

Annex A
(normative)

Method for determination of resistance to low-temperature steam and formaldehyde

A.1 Principle

This method is based on a qualitative test on inoculated carriers immersed in an aqueous solution of formaldehyde. This method has been shown to provide more reproducible results than using a vapour phase, chamber method.

Specific requirements related to the test method are provided in A.3.

A.2 Inoculated carrier exposure conditions

A.2.1 The test system consists of test tubes filled with 10 ml of aqueous solution of formaldehyde and held in an automatically controlled temperature water bath. The test system shall be capable of maintaining the conditions specified for exposure periods between 1 min and 150 min to an accuracy of ±10 s.

A.2.2 The formaldehyde concentration of the aqueous solution shall be determined by use of analytical chemical methods.

A.2.3 The method shall be validated.

A.3 Procedure

A.3.1 Use an aseptic technique when performing this test in order to prevent adventitious contamination.

A.3.2 Completely immerse the inoculated carriers in the test tubes filled with the formaldehyde solution at a concentration of 1 mol/l ± 0,01 mol/l that has been pre-heated to 60 °C ± 0,5 °C.

A.3.3 Ensure that the inoculated carriers are completely immersed in the formaldehyde solution and do not float to the surface.

A.3.4 At the end of the specified exposure time, remove the inoculated carriers from the formaldehyde solution.

A.3.5 Eliminate the excess liquid and immerse the carriers in the test tubes filled with a filtered solution of 2 % Na_2SO_3 for at least 10 min at ambient conditions in order to inactivate formaldehyde residues on the carriers. Close the test tubes.

Care should be taken to minimize agitation in the formaldehyde, as well as in the neutralizer solution to prevent “wash off” of test organisms.

NOTE Histidine and cysteine have been shown to be effective neutralization agents.

A.3.6 The growth medium shall be specified and qualified to ensure recovery of the test organisms.

NOTE Soybean casein digest medium has been found suitable for this test.

A.3.7 Transfer the carriers into test tubes filled with 10 ml of the growth medium according to A.3.6. Close the test tubes.

A.3.8 Treat the test tubes for 60 min at 90 °C for heat activation of the spores.

A.3.9 At the end of the process, incubate the carriers (see ISO 11138-1:2017, Clause 7).

A.4 Determination of resistance

Resistance characteristics shall be determined according to methods given in ISO 11138-1:2017, Annexes C, D and E.

Annex B
(informative)

Rationale for the liquid-phase test method for low-temperature steam and formaldehyde biological indicators

B.1 General

In order to test indicators in a reproducible manner, specific test equipment (resistometers) and methods are used. For the low-temperature steam and formaldehyde process, it is extremely difficult to create a stable formaldehyde gas concentration in a resistometer, since defined amounts of formaldehyde injected into a vessel will dissolve in the small amounts of water droplets (condensate) present. The concentration of formaldehyde in this water is 1 000 times to 10 000 times higher in concentration than in the gas phase, depending on the temperature[5].

It is for this reason that this document utilizes a liquid-phase test method where the formaldehyde concentration is clearly defined and allows reproducible conditions.

B.2 The low-temperature steam and formaldehyde process

Even with constant steam conditions and stable formaldehyde gas concentrations, the sterilization process depends heavily upon the design of the sterilizer chamber and the nature of the load. The formaldehyde sterilization process can be considered simplistically in two steps:

a) as in steam sterilization processes, an aqueous condensate film is created on the surface of the load;

NOTE 1 This condensation will occur very rapidly.

b) since the concentration of formaldehyde at equilibrium between the gas and liquid phases is extremely different (1:1 000 to 1:10 000), the time taken for this equilibrium to occur will be relatively long.

NOTE 2 In practical situations, this can require a time frame from 10 min up to 2 h.

The lethality of the sterilization process thus depends heavily on the formaldehyde concentration in the liquid phase, i.e. surface condensate. It can be very difficult to determine in absolute terms the time taken for these equilibrium conditions to be achieved.

Bibliography

[1] ISO 14161, *Sterilization of health care products — Biological indicators — Guidance for the selection, use and interpretation of results*

[2] ISO 14937, *Sterilization of health care products -- General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices*

[2] ISO 25424, *Sterilization of medical devices — Low temperature steam and formaldehyde — Requirements for development, validation and routine control of a sterilization process for medical devices*

[3] EN 14180, *Sterilizers for medical purposes — Low temperature steam and formaldehyde sterilizers — Requirements and testing*

[4] Gömann J., Kaiser U., Menzel R. Reaction kinetics of the low-temperature-steam-formaldehyde (LTSF). *Sterilization Process. Zentr Steril.* 2000, 8 (5) pp. 290–296

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