BS EN ISO 11138-1:2017

BSI Standards Publication

Sterilization of health care products — Biological indicators

Part 1: General requirements (ISO 11138-1:2017)

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National foreword

This British Standard is the UK implementation of EN ISO 11138-1:2017. It supersedes BS EN ISO 11138-1:2006 which is withdrawn.

The UK participation in its preparation was entrusted to Technical Committee CH/198, Sterilization and Associated Equipment and Processes.

A list of organizations represented on this committee can be obtained on request to its secretary.

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Sterilisation von Produkten für die Gesundheitsfürsorge - Biologische Indikatoren - Teil 1: Allgemeine Anforderungen (ISO 11138-1:2017)

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European foreword

This document (EN ISO 11138-1:2017) has been prepared by Technical Committee ISO/TC 198 "Sterilization of health care products in collaboration with Technical Committee CEN/TC 102 "Sterilizers and associated equipment for processing of medical devices", the secretariat of which is held by DIN.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by September 2017 and conflicting national standards shall be withdrawn at the latest by September 2017.

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This document supersedes EN ISO 11138-1:2006.

The standard is a full technical revision of the previous version. The following amendments have been made in comparison with EN ISO 11138-1:2006:

— Normative references and bibliography updated;

— Terms and definitions „F_{BIO}-value" und „packaging system" deleted;

— General manufacturing requirements (clause 4) including Table 1 revised, e.g. requirements on traceability added;

— requirements on carrier and the primary and secondary packaging revised;

— general resistance requirements (6.1.2 and 6.4.3) revised;

— requirements on software validation (7.4) and detection systems (7.5) added;

— for determination of growth inhibition by carriers and primary packaging materials exposed to sterilization processes the number of probes was increased and requirements revised (see Annex B).

EN ISO 11138 consists of the following parts, under the general title *Sterilization of health care products — Biological indicators*:

— *Part 1: General requirements*

— *Part 2: Biological indicators for ethylene oxide sterilization processes*

— *Part 3: Biological indicators for moist heat sterilization processes*

— *Part 4: Biological indicators for dry heat sterilization processes*

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

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Endorsement notice

The text of ISO 11138-1:2017 has been approved by CEN as EN ISO 11138-1:2017 without any modification.

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Foreword

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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 third edition cancels and replaces the second edition (ISO 11138-1:2006), which has been technically revised.

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

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Introduction

This document specifies general requirements for 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 of sterilization processes. Other parts of ISO 11138 provide additional specific requirements for biological indicators for defined sterilization processes.

A graphic description of a biological indicator and its components is presented in Table F.1. The presentation includes the two types of biological indicators which are covered by ISO 11138 (all parts). This shows that inoculated carriers can be presented directly to the sterilizing agent without prior packaging, or included in a primary package that permits access by the sterilizing agent.

The resistance characteristics depend on the type of test organism, its numbers, the method of preparation, the substrate upon which it is inoculated, environmental conditions during inoculation and drying and the effects of the primary package. Advice on selection, use and interpretation of results of biological indicators can be found in ISO 14161.

For any individual sterilization process, including those covered in relevant parts of ISO 11138, the resistance of the biological indicator will also depend on its microenvironment during testing. In theory, this could lead to an infinite variation in the preparation of biological indicators. Moreover, a sterilization process could be manipulated in infinite variety to suit each possible set of conditions to which products could be exposed. It has, therefore, been a routine practice to manufacture biological indicators that, when exposed to a set of conditions in a defined sterilization process, provide resistance characteristics expressed as D values and, where relevant, z values. Such values are set out in the relevant parts of ISO 11138.

The ISO 11138 series represents the current “state-of-the-art” according to the experts representing manufacturers, users and regulatory authorities involved in developing this document.

Biological indicators for specific sterilization processes not covered by reference test conditions in relevant parts of ISO 11138 should comply with the general requirements in this document, including the resistance testing procedures. Such biological indicators might not be well enough described, or might be used for novel sterilization processes, or might be represented by isolated bioburden microorganisms. If microorganisms other than risk group 1 (WHO 2004) are included in these biological indicators, appropriate safety measures (e.g. containment) are necessary.

Standards exist providing requirements for the validation and control of sterilization processes (see Bibliography).

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

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INTERNATIONAL STANDARD ISO 11138-1:2017(E)

Sterilization of health care products — Biological indicators —

Part 1: General requirements

1 Scope

This document specifies general requirements for production, labelling, test methods and performance characteristics of biological indicators, including inoculated carriers and suspensions, and their components, to be used in the validation and routine monitoring of sterilization processes.

This document specifies basic and common requirements that are applicable to all parts of ISO 11138. Requirements for biological indicators for particular specified processes are provided in the relevant parts of ISO 11138. If no specific subsequent part is provided, this document applies.

NOTE National or regional regulations can apply.

This document does not apply to microbiological test systems for processes that rely on physical removal of microorganisms, e.g. filtration processes or processes that combine physical and/or mechanical removal with microbiological inactivation, such as use of washer disinfectors or flushing and steaming of pipelines. This document, however, can contain elements relevant to such microbiological test systems.

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 11135, *Sterilization of health-care products — Ethylene oxide — Requirements for the development, validation and routine control of a sterilization process for medical devices*

ISO 11737-1:2006, *Sterilization of medical devices — Microbiological methods — Part 1: Determination of a population of microorganisms on products*

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*

ISO 17665-1, *Sterilization of health care products — Moist heat — Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices*

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:

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

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

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

[SOURCE: ISO/TS 11139:2006, 2.3]

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

3.3
colony forming unit
CFU
individual visible units of growth of microorganisms arising from a single cell or multiple cells

3.4
culture collection number
unique identification of the test organism allocated by a scientifically recognized service culture collection

3.5
culture conditions
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 can include the temperature, time and any other conditions specified for incubation.

[SOURCE: ISO/TS 11139:2006, 2.10]

3.6
***D* value**
D_{10} value
time or dose required to achieve inactivation of 90 % of a population of the test microorganism under stated conditions

Note 1 to entry: Other critical process variable(s) exhibiting first order inactivation kinetics can achieve an inactivation of 90 % of a population of the test microorganism under stated conditions.

[SOURCE: ISO/TS 11139:2006, 2.11, modified]

3.7
inactivation
loss of ability of microorganisms to grow and/or multiply

[SOURCE: ISO/TS 11139:2006, 2.21]

3.8
inoculated carrier
supporting material on or in which a defined number of viable test organisms have been deposited

Note 1 to entry: See Annex F.

3.9
nominal population
manufacturer's stated number of viable microorganisms

Note 1 to entry: This is generally expressed in $\log_{10}$ function (e.g. 10^6).

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3.10
primary package
element of the packaging system which maintains the integrity of the product

Note 1 to entry: The packaging system protects the inoculated carrier from damage and contamination without preventing penetration of the sterilizing agent.

3.11
process challenge device
PCD
item designed to constitute a defined resistance to a sterilization process and used to assess performance of the process

[SOURCE: ISO/TS 11139:2006, 2.33]

3.12
resistometer
test equipment designed to create defined reference combinations of the physical and/or chemical variables of a sterilization process

[SOURCE: ISO 18472:2006, 3.11, modified]

3.13
secondary package
container in which biological indicators are packed for transport and storage

3.14
self-contained biological indicator
biological indicator presented in such a way that the primary package, intended for incubation, contains the incubation medium required for recovery of the test organism

3.15
survival-kill window
extent of exposure to a sterilization process under defined conditions where there is a transition from all biological indicators showing growth to all biological indicators showing no growth

3.16
survivor curve
graphical representation of the inactivation of a population of microorganisms with increasing exposure to a microbicidal agent under stated conditions

3.17
suspension
viable test organisms suspended in a fluid

Note 1 to entry: Suspension can be a biological indicator if ready to use in a sealed glass ampoule or may be an intermediate component used to produce an inoculated carrier or biological indicator.

3.18
viable count
actual number of recoverable colony-forming units or other appropriate units

Note 1 to entry: See Annex A.

3.19
***z* value**
change in exposure temperature of a thermal sterilization process, which corresponds to a tenfold change in *D* value

Note 1 to entry: See ISO 11138-3 and ISO 11138-4.

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4 General manufacturing requirements

4.1 Manufacturing controls

4.1.1 Quality management systems

A formal quality system (e.g. ISO 13485, GMPs or other national or regional requirements) to cover all operations required by this document shall be established, documented and maintained. In particular, precautions at all stages of production to minimize contamination that would adversely affect the performance of the biological indicator shall be taken.

4.1.2 Traceability

4.1.2.1 Traceability of manufacturing components shall be maintained.

4.1.2.2 Manufacturing components shall include all materials incorporated in, or coming into direct contact with, the test organism suspension, the inoculated carrier and/or its primary package.

4.1.3 Finished product requirements

The finished product shall comply with the following requirements:

a) labelling (4.3);

b) manufacturing (Clause 5);

c) resistance characteristics (6.4);

d) storage and transport (4.4);

e) incubation (7.3).

NOTE 1 Advice on methods for the use of biological indicators is provided in ISO 14161.

NOTE 2 National and/or regional requirements might exist, for example, in the various national or regional pharmacopoeias.

4.1.4 Personnel

The procedures and methods in this document shall be carried out by suitably trained and experienced laboratory personnel (see e.g. ISO 13485).

4.2 Test organism

4.2.1 Strain

4.2.1.1 Test organisms shall be of a defined strain, available through a recognized culture collection, and shall be identified by appropriate test methods. A statement of traceability shall be provided to the purchaser upon request.

4.2.1.2 The test organism shall be a strain that is

a) suitable for handling without special containment facilities, does not need specific containment procedures for handling and does not have specific transport or mailing requirements (e.g. Risk Group 1, WHO 2004), and

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b) sufficiently stable to maintain its resistance characteristics for the duration of the stated shelf-life when transported and stored in accordance with label directions.

NOTE Traditionally, the test organisms of biological indicators have been bacterial spores, usually derived from *Bacillus* or *Geobacillus* species.

4.2.1.3 Test organisms other than bacterial spores may be used if they have been shown to provide appropriate resistance to the sterilization process.

4.2.2 Originating inoculum for suspension

4.2.2.1 The initial inoculum for each batch of test organism suspension shall be

a) traceable to the reference culture and available through a recognized culture collection, and

b) verified as to its identity and purity.

4.2.2.2 The methods used for maintaining test organism cultures shall be designed to protect them from contamination and to minimize any induced changes in the inherent properties of the test organisms.

4.2.2.3 Verification tests are specific for each strain of test organism and shall be documented and validated.

4.2.3 Test organism count

The viable test organism count of the suspension shall be determined in accordance with Annex A.

4.3 Information to be provided by the manufacturer (labelling)

4.3.1 The following information shall be provided on the label of each individual unit of suspension, inoculated carrier packaging and biological indicator:

— a unique code by which the manufacturing history can be traced;

— the name of the test organism;

— an indication of the sterilization process for which the suspension, inoculated carriers or biological indicators are suitable;

— the expiry date, expressed according to ISO 8601, e.g. YYYY-MM-DD;

— the manufacturer's name, trademark, address or other means of identification.

Internationally recognized symbols may be used where appropriate (see 4.1.3, ISO 15223-1, and ISO 11140-1).

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4.3.2 In addition to the information provided in 4.3.1, the information given in Table 1 shall be provided on or within the secondary packaging of each batch of product.

Table 1 — Information to be provided by the manufacturer

Information requirement	Suspension	Inoculated carrier	Biological indicator
The nominal volume of suspension, in ml	Required	—	—
The process for which the product is suitable for use, the resistance and the procedure and carrier used to determine the resistance[a]	Required	Required	Required
The specified storage conditions	Required	Required	Required
Disposal instructions	Required	Required	Required
Instructions for use, especially data about the medium, incubation and other conditions to be used for recovery of test organisms after exposure to the sterilization process	Required	Required	Required
The number of test organisms per ml (suspension), or per unit (inoculated carrier or biological indicator)[a]	Required	Required	Required
The number of product units in the secondary pack	—	Required	Required
A reference to this document	Required	Required	Required

[a] Test methodology used to determine resistance and population should be supplied by the manufacturer upon request.

4.3.3 If a specific instrument is required to detect outgrowth of the biological indicator, the instrument manufacturer shall specify use of that instrument and provide a certificate of calibration and information on the required recalibration procedures.

4.3.4 If applicable, information shall be provided on required maintenance service of the specified instrument including detailed instructions of how to perform the maintenance, service and its frequency.

4.4 Storage and transport

4.4.1 Storage and transport conditions for the test organism suspension shall be maintained such that the test organism suspension complies with the requirements of this document and, where relevant, a subsequent part of ISO 11138.

4.4.2 If inoculated carriers are packaged for storage or transport, they shall be packaged in a way that does not adversely affect the nominal population or performance of individual inoculated carriers.

4.4.3 Storage and transport conditions for inoculated carriers shall be maintained such that the inoculated carriers comply with the requirements of this document and where relevant, a subsequent part of ISO 11138.

4.4.4 Individually-packaged biological indicators shall be placed in a secondary package for transport and storage. Packaging for transport and storage shall ensure that biological indicators comply with this document and, where relevant, a subsequent part of ISO 11138.

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5 Specific manufacturing requirements

5.1 Suspensions

5.1.1 Culture medium and incubation conditions shall consistently produce test organism suspensions that meet the performance requirements of this document and any relevant subsequent part of ISO 11138.

5.1.2 The suspending medium for the test organism suspension shall not adversely affect the stability of the test organism and shall be compatible with the procedures and materials employed in the manufacture of inoculated carriers and biological indicators.

5.1.3 The method of harvesting and subsequent treatment of suspensions to be used in the inoculation of carriers shall ensure that residues do not adversely influence the performance of the inoculated carrier or biological indicator.

5.2 Carrier, primary and secondary packaging

5.2.1 The materials of the carrier and the primary and secondary packaging shall not contain any contamination (physical, chemical or microbial) that would adversely affect the performance of the biological indicator.

5.2.2 The carrier, the primary and secondary packaging, and the specified storage conditions shall be designed so that the performance characteristics of the biological indicator meet the requirements of this document throughout the stated shelf life of the product. The purchaser shall be provided with a statement of the maximum and minimum values of each dimension of the carrier on request.

5.2.3 During and after the sterilization process, the carrier and the primary packaging shall not retain or release any substance to such an extent that, on transfer to the incubation medium, under the culture conditions, the growth of low numbers of surviving test organisms will be inhibited. Testing shall comply with Annex B.

5.2.4 The carrier, the primary packaging, and the secondary packaging shall withstand planned transport and handling at the point of use, without damage or breakage.

5.2.5 Raw materials used for the carrier and the primary packaging shall withstand exposure to the sterilization process for which they are intended in such a way that the performance characteristics of the inoculated carrier or biological indicator are maintained. Compliance shall be tested by observation of the carrier and the primary packaging exposed to the extreme ranges and rates of change of the chemical and physical variables of the sterilization process.

NOTE Reference sterilization conditions can be found in relevant parts of ISO 11138.

5.3 Inoculated carrier

5.3.1 The inoculated carrier shall be made of materials that will withstand exposure to the sterilization process without distortion, melting, corrosion or other failure that would impair the use of the inoculated carrier.

5.3.2 Only one strain of test organism shall be used in a batch of inoculated carriers, unless the manufacturer has demonstrated that the use of multiple strains does not significantly affect test organism performance in the specified sterilization process.

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