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Sterilization of health care products — Chemical indicators —

Part 1: General requirements

Stérilisation des produits de santé — Indicateurs chimiques —

Partie 1: Exigences générales

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ISO copyright office
Case postale 56 • CH-1211 Geneva 20
Tel. + 41 22 749 01 11
Fax + 41 22 749 09 47
E-mail copyright@iso.org
Web www.iso.org

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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. www.iso.org/directives

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For an explanation on the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the WTO principles in the Technical Barriers to Trade (TBT) see the following URL: Foreword - Supplementary information

The committee responsible for this document is ISO/TC 198, *Sterilization of health care products*.

This third edition cancels and replaces the second edition (ISO 11140-1:2005), which has been technically revised.

ISO 11140 consists of the following parts, under the general title *Sterilization of health care products — Chemical indicators*:

— *Part 1: General requirements*

— *Part 3: Class 2 indicator systems for use in the Bowie and Dick-type steam penetration test*

— *Part 4: Class 2 indicators as an alternative to the Bowie and Dick-type test for detection of steam penetration*

— *Part 5: Class 2 indicators for Bowie and Dick-type air removal tests*

ISO 11140-2 has been withdrawn and replaced by ISO 18472.

Introduction

This part of ISO 11140 specifies performance requirements and/or test methods for chemical indicators intended for use with sterilization processes employing steam, dry heat, ethylene oxide, γ or β radiation, low temperature steam and formaldehyde or vaporized hydrogen peroxide.

Additional requirements for indicators intended for use with other sterilization methods (e.g. other forms of moist heat sterilization) are not specifically provided in this part of ISO 11140; however, the general requirements will apply.

The requirements for specific test indicators (e.g. Bowie-Dick test indicators and indicator systems) are covered in other parts of ISO 11140.

Standards for sterilizers and for the validation and process control of sterilization describe performance tests for sterilizers and methods of validation and routine control, respectively.

This part of ISO 11140 is intended for manufacturers of chemical indicators and specifies the general requirements for chemical indicators. The categorization structure for chemical indicators is used solely to denote the characteristics and intended use of each type of indicator when used as specified by the manufacturer. This categorization has no hierarchical significance. The chemical indicators described in this part of ISO 11140 are categorized into six types. The chemical indicators within each of these categorizations are further subdivided by the sterilization process for which they are designed to be used. This part of ISO 11140 defines the requirements for Type 1 and Types 3 to 6. In subsequent parts of ISO 11140, the requirements for Type 2 indicators are categorized by their intended use. The use of the indicators and indicator systems, specified in this part of ISO 11140, is described in for example the ISO 11135, the ISO 17665- series, ISO 15882, EN 285, and EN 13060.

Resistometers are used to characterize the performance of the chemical indicators described in this part of ISO 11140, with the exception of Type 2 indicators. Requirements for resistometers are specified in ISO 18472. Resistometers differ from sterilizers. As sterilizers cannot duplicate resistometer conditions they should not be used to test the performance of chemical indicators. Sterilizers from different manufacturers and of different ages have significantly different cycle profiles; for example, prolonged preconditioning phases. Resistometers allow for precise control of the specific test cycle sequences in order to study the effect of process parameters on indicator performance under controlled, repeatable conditions. Guidance on the selection, use and interpretation of the results of chemical indicators is given in ISO 15882. Users of chemical indicators are expected to make reference to this part of ISO 11140.

Sterilization of health care products — Chemical indicators —

Part 1:
General requirements

WARNING — The use of this part of ISO 11140 can involve hazardous materials, operations and equipment. This part of ISO 11140 does not purport to address all of the safety problems associated with their use. It is the responsibility of the user of this part of ISO 11140 to determine the applicability of national or regional regulatory requirements and to establish appropriate occupational health and safety practices prior to use of any hazardous materials, operations and/or equipment.

1 Scope

This part of ISO 11140 specifies general requirements and test methods for indicators that show exposure to sterilization processes by means of physical and/or chemical change of substances, and which are used to monitor the attainment of one or more of the process parameter(s) specified for a sterilization process. They are not dependent for their action on the presence or absence of a living organism.

NOTE 1 Biological test systems are regarded as those test systems which are dependent for their interpretation on the demonstration of the viability of an organism. Test systems of this type are considered in the ISO 11138-series for biological indicators (BIs).

The requirements and test methods of this part of ISO 11140 apply to all indicators specified in subsequent parts of ISO 11140, unless the requirement is modified or added to by a subsequent part, in which case the requirement of that particular part will apply.

Relevant test equipment is described in ISO 18472.

NOTE 2 Additional requirements for specific test indicators/indicator systems (Type 2 indicators) are given in ISO 11140-3, ISO 11140-4 and ISO 11140-5.

2 Normative references

The following documents, in whole or in part, are normatively referenced in this document and are indispensable for its application. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 8601:2004, *Data elements and interchange formats — Information interchange — Representation of dates and times*

ISO 11135:2014, *Sterilization of health-care products — Ethylene oxide — Requirements for the development, validation and routine control of a sterilization process for medical devices*

ISO 11137-1:2006, *Sterilization of health care products — Radiation — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*

ISO 11137-2:2013, *Sterilization of health care products — Radiation — Part 2: Establishing the sterilization dose*

ISO 11137-3:2006, *Sterilization of health care products — Radiation — Part 3: Guidance on dosimetric aspects*

ISO 11138-1:2006, *Sterilization of health care products — Biological indicators — Part 1: General requirements*

ISO 11138-2:2006, *Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes*

ISO 11138-3:2006, *Sterilization of health care products — Biological indicators — Part 3: Biological indicators for moist heat sterilization processes*

ISO 11138-4:2006, *Sterilization of health care products — Biological indicators — Part 4: Biological indicators for dry heat sterilization processes*

ISO 11138-5:2006, *Sterilization of health care products — Biological indicators — Part 5: Biological indicators for low-temperature steam and formaldehyde sterilization processes*

ISO 11140-3:2007, *Sterilization of health care products — Chemical indicators — Part 3: Class 2 indicator systems for use in the Bowie and Dick-type steam penetration test*

ISO 11140-4:2007, *Sterilization of health care products — Chemical indicators — Part 4: Class 2 indicators as an alternative to the Bowie and Dick-type test for detection of steam penetration*

ISO 11140-5:2007, *Sterilization of health care products — Chemical indicators — Part 5: Class 2 indicators for Bowie and Dick-type air removal tests*

ISO 17665-1:2006, *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/TS 17665-2:2009, *Sterilization of health care products — Moist heat — Part 2: Guidance on the application of ISO 17665-1*

ISO/TS 17665-3:2013, *Sterilization of health care products — Moist heat — Part 3: Guidance on the designation of a medical device to a product family and processing category for steam sterilization*

ISO 18472:2006, *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.

3.1
bleed
unintentional lateral migration of the indicator agent beyond the margins within which the indicator agent was applied

3.2
critical process variable
variable identified as being essential to the attainment of sterilization and monitored by the chemical indicator

3.3
endpoint
point of the observed change defined by the manufacturer, occurring after the indicator has been exposed to specified stated values

3.4
exposure period
time from the attainment of the specified exposure conditions to its termination

3.5
graduated response
progressive observable change occurring on exposure to one or more critical process variables allowing assessment of the level achieved

3.6
indicator
combination of the indicator agent and its substrate that reveals change in one or more process variables based on a chemical or physical change resulting from exposure to a process

Note 1 to entry: An indicator intended to be used only in combination with a specific test load is also termed an indicator (both together becoming an indicator system).

Note 2 to entry: See Annex E.

3.7
indicator agent
active substance(s) or combination of substances

Note 1 to entry: See Annex E.

3.8
indicator system
combination of an indicator and a specific test load

3.9
off-set
transfer of indicator agent to a material in intimate contact with the surface of the indicator

3.10
process parameter
specified value for a critical process variable

Note 1 to entry: The specification for a sterilization process includes the process parameters and their tolerances.

[SOURCE: ISO/TS 11139:2006, 2.34]

3.11
saturated steam
water vapour in a state of equilibrium between condensation and evaporation

3.12
stated value
SV
value or values of a critical process variable at which the indicator is designed to reach its endpoint as defined by the manufacturer

3.13
substrate
carrier or support material on to which the indicator agent is applied

Note 1 to entry: See Annex E.

3.14
visible change
change defined by the manufacturer, which can be seen in Type 1 indicators after exposure to one or more critical process variables of the process

4 Categorization

4.1 General

The chemical indicators or indicator systems described in this part of ISO 11140 are for use in three main applications:

a) to allow differentiation between unprocessed and processed items;

b) in specific tests and/or procedures, e.g. the Bowie-Dick test;

c) placement inside individual load items in order to assess attainment of the process parameter(s) and attainment of the respective parameter(s) at the point of placement.

The six indicator types described in the main body of this part of ISO 11140 are categorized according to their performance requirements. Table 1 describes three categories according to their intended use. The chemical indicators within each of these categorizations are further subdivided by the sterilization process for which they are designed to be used. These categorizations have no hierarchical significance. Attainment of the chemical indicator's end point should not be regarded as an indication of attainment of an acceptable sterility assurance level, but rather one of many factors which should be taken into consideration when judging the acceptability of a sterilization process.

Table 1 — Categories according to intended use

Intended use		Type	Category	Description (intended use)
Indicate exposure to a process to allow differentiation between unprocessed and processed items, and/or indicate gross failure of a sterilization process.		1	e1	"Exposure" or process indicator Requirements according to Type 1
Indicators for use in special applications, e.g. Bowie and Dick-type test.		2	s2	"Special" indicator (e.g. Bowie-Dick) Requirements in accordance with ISO 11140-3, ISO 11140−4, and ISO 11140−5.
Indicators to be placed inside individual load items and to assess attainment of the critical process variables at the point of placement.	This indicator only reacts to one critical process variable.	3	i3	"Internal" indicator Single variable indicator Requirements according to Type 3
	This indicator reacts to more than one critical process variable.	4	i4	"Internal" indicator Multivariable indicator Requirements according to Type 4
	This indicator reacts to all critical process variables.	5	i5	"Internal" indicator Integrating indicator Requirements according to Type 5
	This indicator reacts to all critical process variables.	6	i6	"Internal" indicator Emulating indicator Requirements according to Type 6

4.2 Type 1: process indicators

Process indicators shall be designed for use with individual items (e.g. packs, containers) to show that the unit has been directly exposed to the sterilization process and to distinguish between processed and unprocessed items.

4.3 Type 2: indicators for use in specific tests

Type 2 indicators are intended for use in specific test procedures as defined in relevant sterilizer/sterilization standards. The requirements for specific test indicators and indicator systems (Type 2 indicators) are provided in ISO 11140-3, ISO 11140-4, and ISO 11140-5.

4.4 Type 3: single critical process variable indicators

A single critical process variable indicator shall be designed to react to one of the critical process variables (see 5.2) and is intended to indicate exposure to a sterilization process at a stated value (SV) of the chosen critical process variable (see 5.7 and 5.8).

4.5 Type 4: multicritical process variable indicators

A multicritical process variable indicator shall be designed to react to two or more of the critical process variables (see 5.2) and is intended to indicate exposure to a sterilization process at SVs of the chosen critical process variables (see 5.7 and 5.8).

4.6 Type 5: integrating indicators

An integrating indicator shall be designed to react to all critical process variables (see 5.2). The SVs are generated to be equivalent to, or exceed, the performance requirements given in the ISO 11138- series for BIs. The minimum SV shall be related to the minimum values required to achieve sterilization as specified in International Standards ISO 11135, ISO 11137 (all parts), ISO 17665 (all parts), or by local regulatory agencies (see Clauses 11 and 12).

NOTE The SVs demonstrate how the indicator integrates over the temperature range.

4.7 Type 6: emulating indicators

An emulating indicator shall be designed to react to all critical process variables for specified sterilization processes. The SVs are generated from process variables of sterilization processes as specified in International Standards ISO 11135, ISO 11137 (all parts) and ISO 17665 (all parts), or by regulatory agencies (see Clause 13).

5 General requirements

5.1 The requirements given in this clause shall apply to all chemical indicators (CI) unless specifically excluded or amended in a subsequent clause or part of ISO 11140.

NOTE For ease of reading, only the term “indicator” is used hereinafter, although requirements do also apply to indicator systems.

5.2 For the different sterilization processes, the following critical process variables are defined as being critical:

STEAM	Time, temperature, moisture
DRY HEAT	Time and temperature
ETHYLENE OXIDE	Time, temperature, relative humidity and ethylene oxide (EO) concentration
RADIATION	Total absorbed dose
LOW TEMPERATURE STEAM AND FORMALDEHYDE	Time, temperature, moisture and formaldehyde concentration
VAPORIZED HYDROGEN PEROXIDE	Time, temperature, hydrogen peroxide concentration

5.3 The manufacturer shall establish, document and maintain a formal quality system to cover all operations required by this part of ISO 11140.

NOTE ISO 9001 and ISO 13485 describe requirements for quality systems for design, manufacture and testing.

5.4 Each indicator shall be clearly marked with the type of process for which it is intended to be used (see 5.6 and 5.7), and either

a) with a number indicating the type of indicator, i.e. 1 to 6, or

b) with a combination of a letter plus a number to indicate a category, i.e. e1, s2, i3, i4, i5, or i6.

For Type 3, 4, 5 and 6 indicators, each indicator shall be clearly marked with the SVs.

NOTE Some indicator manufacturers might use the category notation to provide additional guidance for the intended use of the chemical indicator.

Where the size or format of the indicator does not permit this information to be stated in a font of six characters per centimetre or larger, the information shall be provided on the label and/or instructions for use.

5.5 The indicator shall comply with the requirements of this part of ISO 11140 for the duration of the shelf-life as specified by the manufacturer (see Annex A).

5.6 Abbreviated descriptions of the process shall be in accordance with the following symbols:

STEAM

— all steam sterilization processes

DRY

— all dry heat sterilization processes

