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Sterilization of health care products — Chemical indicators —

Part 1: General requirements

Stérilisation des produits de santé — Indicateurs chimiques — Partie 1: Prescriptions générales

Reference number
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Contents

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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.

Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

International Standard ISO 11140-1 was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

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

— *Part 1: General requirements*

— *Part 2: Test methods*

— *Part 3: Penetration test systems for high density loads intended for use in porous load sterilizers employing parametric release*

— *Part 4: Penetration test systems for low density loads not intended for use in porous load sterilizers employing parametric release*

Introduction

This part of ISO 11140 specifies requirements for chemical indicators intended for use with sterilization processes employing steam, ethylene oxide, γ or β radiation, steam-formaldehyde, or dry heat.

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) will be covered in other parts of this International Standard.

Compliance with the performance requirements given in this document may be established using the test methods and equipment described in ISO 11140-2.

Sterilization of health care products — Chemical indicators —

Part 1:
General requirements

1 Scope

This part of ISO 11140 specifies performance requirements for indicators that show exposure to sterilization processes by means of physical and/or chemical change of substances.

NOTE 1 These indicators are used to monitor the presence or attainment of one or more of the parameters required for a satisfactory sterilization process, or are used in specific tests of sterilization equipment.

This part of ISO 11140 also includes acceptance criteria used to establish whether or not an indicator complies with it.

NOTE 2 Relevant test methods and equipment are described in ISO 11140-2.

NOTE 3 Additional requirements for (Class 2) penetration test indicators are given in ISO 11140-3 and ISO 11140-4.

2 Normative references

The following standards contain provisions which, through reference in this text, constitute provisions of this part of ISO 11140. At the time of publication, the editions indicated were valid. All standards are subject to revision, and parties to agreements based on this part of ISO 11140 are encouraged to investigate the possibility of applying the most recent editions of the standards indicated below. Members of IEC and ISO maintain registers of currently valid International Standards.

ISO 8601:1988, *Data elements and interchange formats — Information interchange — Representation of dates and times.*

ISO 9001:1994, *Quality systems — Model for quality assurance in design/development, production, installation and servicing.*

ISO 9002:1994, *Quality systems — Model for quality assurance in production and installation.*

ISO 11138-1:1994, *Sterilization of health care products — Biological indicators — Part 1: General requirements.*

ISO 11138-2:1994, *Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization.*

ISO 11138-3:—[1], *Sterilization of health care products — Biological indicators — Part 3: Biological indicators for moist heat sterilization.*

3 Definitions

For the purposes of all parts of ISO 11140, the following definitions apply.

3.1 endpoint: Observable change specified by the manufacturer that occurs after the indicator has been exposed to certain predefined physical conditions.

3.2 indicator: Combination of the indicator agent and its substrate in the form in which it is intended to be used.

NOTE 4 The different types of indicators are defined in clause 4.

3.3 indicator agent: Active ingredient or combination of ingredients.

1) To be published.

3.4 saturated steam: Steam with a dryness value between 0,85 and 1,0 (i.e. a liquid water content not exceeding 15 % (*m/m*) and where the temperature corresponds to the vaporization pressure).

3.5 critical parameters: Parameters identified as being essential to the sterilization process (and requiring monitoring).

3.6 stated value: Value or range of values of a critical parameter, to which the indicator is designed to react.

4 Classification of indicators

4.1 Class 1: Process indicators

Process indicators are intended for use with individual units, (e.g. packs, containers) to demonstrate that the unit has been exposed to the sterilization process and to distinguish between processed and unprocessed units.

4.2 Class 2: Indicators for use in specific tests

These indicators are designed for use in specific test procedures as defined in relevant sterilizer/sterilization standards.

NOTE 5 The requirements for specific test indicators (Class 2 indicators) will be provided in other parts of ISO 11140.

4.3 Class 3: Single parameter indicators

A single parameter indicator shall be designed for one of the critical parameters (see 3.5 and 5.1) and shall indicate exposure to a sterilization cycle at a stated value of the chosen parameter.

4.4 Class 4: Multi-parameter indicators

A multi-parameter indicator shall be designed for two or more of the critical parameters (see 3.5 and 5.1) and shall indicate exposure to a sterilization cycle at stated values of the chosen parameters.

4.5 Class 5: Integrating indicators

Integrating indicators are indicators designed to react to all critical parameters over a specified range of sterilization cycles. The stated values are those required to achieve a stated inactivation by referring to a stated test organism with stated D and, if applicable, z values (as described for biological indicators for ethylene oxide sterilization in ISO 11138-2 and for biological indicators for moist heat sterilization in ISO 11138-3).

4.6 Class 6: Emulating indicators (cycle verification indicators)

Emulating indicators are indicators designed to react to all critical parameters over a specified range of sterilization cycles, for which the stated values are based on the settings of the selected sterilization cycles.

5 General requirements

The requirements given in this clause shall apply to all indicators unless specifically excluded or amended in a subsequent clause or in an additional part of ISO 11140.

5.1 For the different sterilization processes, the following parameters are defined as being critical:

STEAM	Time, temperature and saturated steam
DRY HEAT	Time and temperature
ETHYLENE OXIDE (EO)	Time, temperature, humidity and EO concentration
IRRADIATION	Total absorbed dose
STEAM-FORMALDEHYDE	Time, temperature, humidity and formaldehyde concentration

NOTE 6 Other factors may also influence the efficacy of the sterilization process.

5.2 The manufacturer shall establish, document and maintain a formal quality system in accordance with ISO 9001 and/or ISO 9002 to cover all operations required to produce a product conforming with this part of ISO 11140.

5.3 The change that occurs after exposure of the indicator to the specified conditions shall be clearly observable.

5.4 Each indicator shall be clearly marked with the type of sterilization process for which it is intended to be used.

The abbreviated description of the process shall be in accordance with the following:

STEAM	All steam sterilization processes
DRY	All dry heat sterilization processes
EO	All ethylene oxide sterilization processes
IRRAD	All ionizing irradiation sterilization processes
FORM	All steam-formaldehyde sterilization processes

These descriptions are symbols and should not be translated.

Where the size and format of the indicators do not permit this information to be stated, it shall be stated clearly in either a separate instruction or a packaging unit.

5.5 If the use of the indicator is limited to specific sterilization cycles, this information shall be stated or coded on the product (e.g. STEAM 15 min 121 °C).

5.6 Each package of indicators or the technical information leaflet supplied with the package shall state:

a) the change that is intended to occur, and for colour change indicators where the colour change cannot be adequately described, samples of the expected colour range for both changed and unchanged indicators;

b) the critical parameter(s) to which the indicator will respond and, where applicable, their values;

c) the type (classification) of the indicator, stated as process indicator, specific test indicator, single parameter indicator, multi-parameter indicator, integrating indicator or emulating indicator;

d) the storage conditions;

e) the manufacturing date and shelf life or expiry date under the specified storage conditions, expressed in accordance with ISO 8601 (i.e. YYYY-MM-DD);

f) a number or code that allows the manufacturing history to be traced;

g) instructions for use essential to ensure proper functioning of the indicator;

h) any interfering substances or conditions that are likely to be encountered or to occur during the intended use of the indicator and which are known to affect adversely the performance of the indicator;

i) any additional safety precautions required during and/or after use;

j) the name and address of the manufacturer or supplier;

k) the storage conditions for the indicator after use, if the indicator is intended to be retained as part of a record;

l) the nature of any change that can occur when completely/incompletely changed indicators are stored according to the manufacturer's instructions; and

m) the interaction between responses to the critical parameters detected, if any.

5.7 The manufacturer shall retain documentary evidence that the indicator does not release any substance known to be toxic in sufficient quantities to cause either a health hazard or a hazard to the intended properties of the product being sterilized, before, during or after the sterilization process for which it is designated.

In the absence of relevant International Standards, regional or national requirements shall apply.

5.8 The endpoint condition of an indicator that has been exposed to a sterilization process during which all the values of critical parameters required to produce an endpoint reaction were met or exceeded shall not change to an extent that could lead to an interpretation other than that apparent on removal from the sterilizer when stored as specified by the manufacturer for up to six months.

Incompletely changed indicators can deteriorate on storage, either returning to the unchanged conditions or slowly changing to the defined endpoint condition. If such deterioration can occur, this information should be stated in the technical information supplied by the manufacturer. Such indicators may not be suitable for use as permanent records.

6 Additional requirements for process (Class 1) indicators

NOTE 7 Process indicators may be printed on packaging material or presented as self-adhesive labels, packaging tapes, tags, insert label, etc.

6.1 Process indicators for steam sterilization

6.1.1 After exposure to a previously stabilized condition of dry heat at 140 °C ± 2 °C for 30 min ± 1 min, the indicator shall show either no change or a change that is markedly different from the change occurring after exposure to a steam sterilization process.

6.1.2 The endpoint indicating exposure to a steam sterilization process shall not occur until the indicator has been exposed to saturated steam for not less than 3 min at 121 °C $^{+3}_{0}$ °C, or for 30 s at 134 °C $^{+3}_{0}$ °C.

6.1.3 The indicator shall provide clear visual evidence of exposure to the process after being subjected to dry saturated steam for not more than 10 min at 121 °C $^{+3}_{0}$ °C, and not more than 2 min at 134 °C $^{+3}_{0}$ °C.

6.2 Process indicators for dry heat sterilization

6.2.1 The endpoint indicating exposure to a dry heat sterilization process shall not occur until the indicator has been exposed to a previously stabilized condition of 160 °C $^{+5}_{0}$ °C for not less than 20 min.

6.2.2 The endpoint indicating exposure to a dry heat sterilization process shall occur when the indicator has been exposed to a previously stabilized condition of 160 °C $^{+5}_{0}$ °C for a time not exceeding 40 min.

6.3 Process indicators for ethylene oxide sterilization

6.3.1 After exposure to 60 °C ± 2 °C at greater than 85 % relative humidity (RH) for not less than 90 min, the indicator shall show either no change or a change that is markedly different from the change occurring after exposure to the ethylene oxide sterilization process.

This test is done without ethylene oxide being present and therefore should not be carried out in an ethylene oxide sterilizer where traces of the gas may be present.

6.3.2 The endpoint indicating exposure to an ethylene oxide sterilization process shall not occur until the indicator has been exposed to (600 ± 30) mg/l ethylene oxide and (60 ± 10) % RH at 30 °C ± 1 °C for not less than 5 min.

6.3.3 The endpoint indicating exposure to an ethylene oxide sterilization process shall occur when the indicator has been exposed to (600 ± 30) mg/l ethylene oxide and (60 ± 10) % RH at 30 °C ± 1 °C for a period not exceeding 30 min.

The reaction of some ethylene oxide indicators can be impaired by the presence of carbon dioxide or other gas. Where the formulation is such that this may occur, the indicator should be tested in a system employing not less than 80 % carbon dioxide or other gas in admixture with the ethylene oxide.

6.4 Process indicators for ionizing irradiation sterilization

6.4.1 After exposure to ultraviolet light (235 nm to 280 nm) with a surface intensity of not less than 3,3 W/m² for not less than 120 min, the indicator shall show either no change or a change that is markedly different from the change occurring after exposure to an ionizing radiation sterilization process.

6.4.2 The endpoint indicating exposure to an irradiation sterilization process shall not occur until the indicator has been exposed to an absorbed dose of at least 1 kGy.

6.4.3 The indicator shall show clear visual evidence of exposure to the process after being subjected to an absorbed dose not exceeding 5 kGy.

6.5 Process indicators for steam-formaldehyde sterilization

6.5.1 After exposure to saturated steam at 80 °C ± 2 °C for not less than 90 min, the indicator shall show either no change or a change that is markedly different from the change occurring after exposure to the steam-formaldehyde sterilization process.

This test is performed without formaldehyde being present and therefore should not be carried out in a steam-formaldehyde sterilizer where traces of the gas or its polymers may be present

6.5.2 After exposure to dry heat at 80 °C ± 2 °C for not less than 90 min, the indicator shall show either no change or a change that is markedly different from the change occurring after exposure to the steam-formaldehyde sterilization process.

6.5.3 The endpoint indicating exposure to the steam-formaldehyde sterilization process shall not occur until the indicator has been exposed to (10 ± 2) mg/l formaldehyde in steam at 70 °C ± 2 °C for not less than 5 min.

6.5.4 The endpoint indicating exposure to the steam-formaldehyde sterilization process shall occur when the indicator has been exposed to (10 ± 2) mg/l formaldehyde in saturated steam at 70 °C ± 2 °C for a time not exceeding 20 min.

6.5.5 For indicators produced for steam-formaldehyde sterilization cycles operating at temperatures below 65 °C, the tests described in 6.5.3 and 6.5.4 shall be carried out at the maximum temperature and formaldehyde concentration specified by the manufacturer of the indicator.

7 Additional requirements for single parameter (Class 3) indicators

7.1 Single parameter indicators shall be designed for one of the critical parameters listed in 5.1.

7.2 Single parameter indicators shall undergo a clearly detectable change indicating exposure to a sterilization cycle defined at a given value within the relevant tolerances listed in table 1.

7.3 The defined parameter shall be identified or coded on the product.

7.4 The stated value at which the indicator reaches its endpoint shall be identified or coded on the product.

8 Additional requirements for multi-parameter (Class 4) indicators

8.1 Multi-parameter indicators shall be designed for two or more of the critical parameters which affect the efficacy of the sterilization process to be monitored.

8.2 Multi-parameter indicators shall undergo a clearly detectable change indicating exposure to a sterilization cycle at defined parameters within the relevant tolerances listed in table 1.

8.3 The defined parameters shall be identified or coded on the indicator.

8.4 The stated values at which the indicator reaches its endpoint shall be identified or coded on the product.

9 Additional requirements for integrating (Class 5) indicators

9.1 Integrating indicators shall undergo a clearly detectable change indicating exposure to a sterilization cycle at defined parameters within the relevant tolerances given in table 2.

9.2 The stated values shall be identified or coded on the product.

9.3 The exposure required to effect the change in the indicator shall be related to the inactivation of a theoretical microorganism of stated D and z values (see 4.5). These values shall be not less than those specified in the appropriate parts of ISO 11138 for biological indicators for use in routine monitoring of the relevant sterilization process. The theoretical inactivation of the microorganism shall be stated as the fractional reduction in the population, expressed as the $\log_{10}$.

9.4 The manufacturer shall state clearly any factors of which he is aware that can adversely affect the efficacy of the sterilization process but which are not detected by the indicator, or not detected in a manner that will give assurance of satisfactory attainment of that critical parameter or attribute.

NOTE 8 An example of such a statement is as follows.

> "This indicator will not react in the absence of water vapour, but a successful indicator reaction does not necessarily indicate the presence of optimal levels of moisture. This should be verified by other means."

10 Additional requirements for emulating (Class 6) indicators

10.1 Emulating indicators shall undergo a clearly detectable change indicating exposure to a sterilization cycle at defined parameters within the relevant tolerances given in table 3.

10.2 The stated values shall be identified or coded on the product.

10.3 The manufacturer shall state clearly any factors of which he is aware that may adversely affect the efficacy of the sterilization process but that are not detected by the indicator, or not detected in a manner that gives assurance of satisfactory attainment of the critical parameter or attribute.