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Sterilization of health care products — Chemical indicators — Guidance for selection, use and interpretation of results

Stérilisation des produits de santé — Indicateurs chimiques — Directives pour la sélection, l'utilisation et l'interprétation des résultats

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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.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. 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.

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.

ISO 15882 was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

This second edition cancels and replaces the first edition (ISO 15882:2003), which has been technically revised.

Introduction

This International Standard provides guidance for users regarding the selection, use and interpretation of results of chemical indicators intended for use with sterilization processes employing steam, dry heat, ethylene oxide, γ or β radiation, low temperature steam and formaldehyde (LTSF), or vapourized hydrogen peroxide as documented in ISO 11140-1 [13]. The ISO 11140 [12], [13], [14], [15], [16] series of standards specifies performance requirements for chemical indicators. These standards are intended primarily for the use of manufacturers of chemical indicators. The guidance in this document is of a general nature; chemical indicators do not, of themselves, constitute a comprehensive monitoring programme with regard to the sterilization of health care products. Users' attention is drawn to the requirements for validation of sterilization processes specified in ISO 14937 [18] for general processes, the ISO 17665 [19], [20] series for moist heat sterilization, the ISO 11135 [5], [6] series for ethylene oxide sterilization, ISO 11137-1 [7] for radiation sterilization and ISO 20857 [22] for dry heat sterilization.

The actual use/frequency of chemical indicators might be regulated by international and or national standards as well as by local regulatory authorities.

The need for convenient and rapid means of detecting sterilization problems occurring during sterilization processes has brought about the development of sterilization process monitors generally referred to as “chemical indicators.” In this International Standard, users will find guidance on selection of the correct chemical indicator for their particular sterilization process and critical parameters as well as guidance on its appropriate use. The complexity of modern medical technology and the wide variety of sterilization processing techniques and equipment available have made effective sterility assurance programmes more challenging than ever before.

Sterilization of health care products — Chemical indicators — Guidance for selection, use and interpretation of results

1 Scope

1.1 This International Standard provides guidance for the selection, use and interpretation of results of chemical indicators used in process definition, validation and routine monitoring and overall control of sterilization processes. This International Standard applies to indicators that show exposure to sterilization processes by means of physical and/or chemical change of substances, and which are used to monitor one or more of the variables required of a sterilization process. These chemical indicators are not dependent for their action on the presence or absence of a living organism.

1.2 This International Standard does not consider indicators for use in those processes that rely on physical removal of microorganisms, e.g. filtration.

1.3 This International Standard is not intended to apply to indicators for use in combination processes, for example, washer disinfectors or CIP (cleaning in place) and SIP (sterilization in place).

2 Terms and definitions

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

NOTE A vocabulary of terms used for sterilization of health care products is provided in ISO/TS 11139[11].

2.1
chemical indicator
non-biological indicator
test system that reveals change in one or more pre-defined process variables based on a chemical or physical change resulting from exposure to a process

[ISO/TS 11139, definition 2.6]

2.2
endpoint
point of the observed change as defined by the manufacturer occurring after the indicator has been exposed to specified stated values

[ISO 11140-1, definition 3.3]

2.3
indicator
combination of the indicator agent and its substrate in the final form in which it is intended to be used

[ISO 11140-1 definition 3.5]

NOTE 1 An indicator system in combination with a specific test load is also termed an indicator.

NOTE 2 See Annex E.

2.4
indicator agent
indicator reagent
active substance(s) or combination of substances

[ISO 11140-1, definition 3.6]

NOTE See Annex E.

2.5
process challenge device
PCD
item designed to constitute a defined resistance to a sterilization process and used to assess performance of the process

[ISO/TS 11139, definition 2.33]

2.6
process challenge location
PCL
site which represents “worst case” conditions as they are given for sterilizing agent(s) in the goods to be sterilized

2.7
process parameter
specified value for a process variable

[ISO/TS 11139, definition 2.34]

NOTE 1 The specification for a sterilization process includes the process parameters and their tolerances.

NOTE 2 See Annex B.

2.8
process variable
condition within a sterilization process, changes in which alter microbicidal effectiveness

[ISO/TS 11139, definition 2.35]

EXAMPLES Time, temperature, pressure, concentration, humidity, wavelength.

NOTE See Annex B.

2.9
resistometer
test equipment designed to create defined combinations of the physical and/or chemical parameters of a sterilization process

2.10
saturated steam
water vapour in a state of equilibrium between condensation and evaporation

[ISO 11140-1 definition 3.11]

2.11
stated value
SV
value or values of a critical variable at which the indicator is designed to reach its endpoint as defined by the manufacturer

[ISO 11140-1, definition 3.12]

2.12
visible change
change defined by the manufacturer, which can be seen in the indicator after exposure to one or more critical variables of the process

NOTE Visible change is used to describe the response of class 1 process indicators.

[ISO 11140-1, definition 3.15]

3 General considerations

3.1 All chemical indicators are intended to provide information about conditions at the location of the indicator within the sterilizer, sterilizer load or PCD. This can alert the user to potential sterilization process failures.

3.2 The value of the information provided by a chemical indicator is dependent upon the class of indicator, number and location of the indicators, being representative of the conditions throughout the sterilizer chamber or load. Representative locations for a load configuration should be identified during process validation studies.

3.3 The basic performance descriptors of any chemical indicator are its visible change, graduated response or "endpoint" response. The endpoint response can, for example, involve either the melting of a chemical substance or a chemical reaction resulting in a specified colour change.

3.4 A number of different classes of chemical indicators have been developed to suit different monitoring needs and to provide information about the sterilization process. Some types are sensitive to certain specific problems, such as a failure to attain a required temperature. Others might not respond only to a single process variable, but might simultaneously respond to several process variables during the sterilization cycle.

Selection of the classes of chemical indicators that are best suited to a particular application should be made only in the context of:

— What characterizes effective sterilization?

— Which problems could prevent sterilization?

— What are the performance characteristics of the indicator(s)?

— What constitutes effective sterility assurance activities during product release?

Once an indicator is selected, it will be of value in sterility assurance only if it is used and interpreted correctly, and if the user takes appropriate action in response to the results.

3.5 Chemical indicators of the same class can differ in response characteristics and their means of detecting exposure conditions. Chemical indicator classification in ISO 11140-1[13] is based on defined performance characteristics (see, e.g., different stated values in that document) rather than on chemical or physical changes as related to specific sterilization processes. For example, in a steam process, some indicator types must be exposed to steam for a minimum length of time to achieve the endpoint, some must be exposed to a minimum temperature, some are affected by a combination of temperature and time of exposure, and still others are affected by time, temperature and saturated steam. In all cases, the user compares the response of the chemical indicator to an endpoint described by the manufacturer.

If a chemical indicator fails to reach its endpoint, the facility should follow a documented protocol to investigate the cause of the problem which could include, but not be limited to, the following items.

a) Was there a sterilizer malfunction that could account for the failure to achieve the endpoint?

b) Has there been a change(s) in the product and/or sterile barrier system?

c) Has the loading density increased or decreased within the sterile barrier system?

d) Has the sterilization processing container/configuration changed (e.g. number of cartons has increased or decreased, or the configuration was not the same as that used during validation)?

e) Was sterilizer calibration and/or routine maintenance conducted appropriately?

f) Was the correct sterilizer process chosen for the product sterilized?

g) Was the chemical indicator handled under manufacturer's recommended practices?

h) Have there been changes in the utilities supplied to the sterilizer that could materially affect cycle execution (pressure, flow rate, non-condensable gases in the steam supply, etc.)?

NOTE For more information, the requirements and guidance provided in the specific process standards, ISO/TS 17665-2[20], ISO 20857[22], ISO 11137-1[7], EN 14180[24] and EN 15424[25] is valid.

3.6 Although other factors can influence the efficacy of a sterilization process, ISO 11140-1[13] identifies the variables for each sterilization process in Table 1. A specific chemical indicator can respond to one, some, or all of the variables, as indicated by its class (see Clause 5) and manufacturer's instructions for use.

If the use of the indicator is limited to a specific sterilization cycle, this information is stated or coded on the product. For example, "STEAM 15 min 121 °C" means that the indicator is for use in a 15 min, 121 °C steam sterilization cycle. The box around the word "STEAM" signifies that the indicator can only be used in the steam sterilization process.

Table 1 — Variables for sterilization processes

Process	Symbol[a]	Variables
Steam	STEAM	Time, temperature and water (as delivered by saturated steam)
Dry heat	DRY	Time and temperature
Ethylene oxide	EO	Time, temperature, humidity, and EO concentration
Irradiation	IRRAD	Total absorbed dose
Low temperature steam and formaldehyde (LTSF)	FORM	Time, temperature, water (as delivered by saturated steam) and formaldehyde concentration
Vapourized hydrogen peroxide	VH2O2	Time, temperature, hydrogen peroxide concentration, and, if applicable, plasma

[a] These are symbols and are not intended to be translated.

3.7 Class 3, 4, 5 and 6 indicators will have one or more stated value (SV) identified by the manufacturer. These stated values identify the parameters that the indicator is designed to react to, and the level of exposure required to achieve the stated visible change, graduated response or endpoint. Details of the SV will be provided on the indicator, on the indicator packaging, or in information provided with the product. Visible change is used to describe the response of class 1 process indicators. Graduated response is the progressive observable change occurring on exposure to one or more process variables allowing assessment of the level achieved.

The SV's are based on the outcome of tests carried out in a resistometer by a manufacturer.

The resistometer (ISO 18472[21] gives further information) is a test vessel that is designed for very rapid attainment of the particular critical parameters of the sterilization process. These parameters are very closely controlled during the exposure phase. Because sterilizers typically do not have the same response

characteristics or accuracy of exposure conditions as found in resistometers, it is very difficult for a user to replicate manufacturer label claims using a sterilizer. Third party independent laboratories with resistometers may be used to verify manufacturers' label claims. Since chemical indicators are tested at specific conditions, inadvertent or intentional exposure to parameters (for example longer time, lower temperature and/or lower sterilant concentration) outside of those specified by the manufacturer can lead to misleading results.

All chemical indicators in classes 3, 4, 5 and 6 have SV(s) at which they will reach their endpoints. A sterilization process is defined by a minimum value with an upper limit, e.g. for a moist heat process a minimum temperature is specified with an upper limit of + 3 °C. The SV(s) of the chemical indicator will normally be linked to the minimum sterilization parameters for the process employed to process health care products.

The response of the chemical indicator to a fail condition is verified by exposing the chemical indicators to conditions lower than the SVs as specified in the accompanying tables.

4 Classes of chemical indicator

4.1 General

Chemical indicators are classified by their intended use. The chemical indicators described in ISO 11140-1[13] are classified into six groups. The chemical indicators within each of these classifications are further subdivided by the sterilization process for which they are designed to be used. The classification structure is used solely to denote the characteristics and intended use of each type of indicator when used as defined by the manufacturer. This classification has no hierarchical significance.

Chemical indicators are used to detect whether or not certain critical process variables have reached a predetermined level in a given sterilization process. The classification denotes the performance characteristics and intended use of the indicator only.

The performance characteristics of each class enable the respective chemical indicators to convey different types of information and therefore perform different functions.

All chemical indicators are based on either a chemical and/or physical change that results in a colour change or in the migration of a chemical.

The following descriptions for each class of chemical indicator will start with an italicized quote taken directly from ISO 11140-1[13], which has been used to define that specific class of chemical indicator.

4.2 Class 1: Process indicators

Process indicators are intended for use with individual units (e.g. packs, containers) to indicate that the unit has been directly exposed to the sterilization process, and to distinguish between processed and unprocessed units. They shall be designed to react to one or more of the critical process variables (ISO 11140-1:2005, 4.2).

This class of indicator is used to identify packs yet to be processed, i.e., identifying packs yet to be processed versus those processed and ready for distribution if the sterilization cycle ran correctly and if indicators of a higher class show that the conditions required for sterilization were met. A “pass” response of a class 1 process indicator is not intended to indicate attainment of the conditions required for sterilization.

Process indicators are typically applied to, or visible from, the outside of packages. Examples of process indicators include indicator tape and packaging material with a chemical indicator printed on it. These chemical indicators are typically external and exposed directly to the sterilizating agent without the interference imposed by packaging, and will typically “fail” only when there is gross malfunction. Process indicators are intended to exhibit a visual change after exposure to what could be a sub-optimal sterilization cycle.

For the irradiation process ISO 11140-1[13] only describes process indicators for use in γ and β irradiation. For example, Table 1 from ISO 11140-1:2005, Clause 8 contains the tolerances (upper and lower limits of performance acceptability for the steam process indicator, when tested by the manufacturer) that need to be met for each critical parameter. That table is reproduced below.

Table 2 — Test and performance requirements for class 1 process indicators for STEAM

Test environment	Test time	Test temperature	No change or a change that is markedly different from the visible change as specified by the manufacturer	Visible change as specified by the manufacturer
Saturated steam	3,0 min ± 5 s	121 °C (+3/0 °C)	Acceptable result	Unacceptable result
Saturated steam	10,0 min ± 5 s	121 °C (+3/0 °C)	Unacceptable result	Acceptable result
Saturated steam	0,5 min ± 5 s	134 °C (+3/0 °C)	Acceptable result	Unacceptable result
Saturated steam	2 min ± 5 s	134 °C (+3/0 °C)	Unacceptable result	Acceptable result
Dry heat	30 min ± 1 min	140 °C (+2/0 °C)	Acceptable result	Unacceptable result
NOTE The dry heat test is designed to ensure that process indicators for steam require the presence of steam in order to respond.				

4.3 Class 2: Indicators for use in specific tests

Class 2 indicators are intended for use in specific test procedures as defined in relevant sterilizer/sterilization standards (ISO 11140-1:2005, 4.3).

Chemical indicators widely recognised in class 2 are used to perform the Bowie and Dick-type test. This can be carried out using test sheets specified in ISO 11140-3[14] in combination with the standard textile pack specified in EN 285[23]. Chemical indicators for conducting the alternative Bowie and Dick-type steam penetration test are specified in ISO 11140-4[15]. Chemical indicators for conducting the Bowie and Dick-type air removal test are specified in ISO 11140-5[16] and either used in combination with a standard textile test pack or alternatively as a ready-to-use pack. Also see Annex A.

The presence of moisture is critical to the effectiveness of the steam sterilization process. The presence of residual air will impede steam penetration and therefore the presence of moisture on the surfaces to be sterilized. Class 2 Bowie and Dick-type indicators are intended to demonstrate the rapid and even penetration of steam and by implication the adequacy of air removal. This condition is generally demonstrated by a uniform colour change on the indicator sheet. Causes of failure could include the presence of non-condensable gases in the steam (for example fabric conditioning agents used in the laundering of the textile pack) or inadequate air removal or air leaks.

Because Bowie and Dick-type indicators are designed to react to a specified exposure that could be different from those required to achieve effective sterilization, they are not appropriate for use as routine sterilization cycle indicators. Extending the exposure time for the Bowie and Dick-type test, or disregarding the manufacturer's recommendations for how to conduct the Bowie and Dick-type test will entirely defeat the purpose of the test by causing misleading results.

For background information on the Bowie and Dick test, see Annex A.

4.4 Class 3: Single variable indicators

A single variable indicator shall be designed to react to one of the critical variables and is intended to indicate exposure to a sterilization process at a stated value (SV) of the chosen variable (ISO 11140-1:2005, 4.4).

A single variable indicator is intended to respond to only one critical process variable of the sterilization process. The variable and its stated value will be provided by the indicator manufacturer and that indicator can only be used to monitor that process variable.