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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 — Lignes directrices pour le choix, l'emploi 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*.

Introduction

Performance requirements for manufacturers of chemical indicators are contained in the ISO 11140 series. This International Standard provides guidance regarding the selection, use and interpretation of results of chemical indicators used to monitor sterilization processes employing steam, ethylene oxide, γ- or β-radiation, steam-formaldehyde, or dry heat as documented in ISO 11140-1:1995 (amended 1998). The procedures described in this International Standard are of a general nature and do not, of themselves, constitute a comprehensive monitoring programme with regard to the sterilization of health care products. The intent of this International Standard is not to mandate the use of chemical indicators in a process, but to provide guidance for their proper selection and use. National standards should be consulted for information on the use of chemical indicators as well as the frequency of their 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. The need for convenient, inexpensive and rapid means of detecting sterilization problems 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, e.g. the choice of an appropriate chemical indicator, as well as guidance on its appropriate use.

Harmonization of the International and European standards on chemical indicators, ISO 11140 and EN 867, is in progress.

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

1 Scope

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 control of sterilization processes. This International Standard is applicable to chemical indicators for which International Standards exist (see ISO 11140 series).

This International Standard is not applicable to those processes that rely on physical removal of microorganisms, e.g. filtration.

This International Standard is not intended to apply to combination processes, for example, washer-disinfectors or flushing and steaming of pipelines.

2 Normative references

The following referenced documents are indispensable for the application 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 11138-2:1994, *Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization*

ISO 11138-3:1994, *Sterilization of health care products — Biological indicators — Part 3: Biological indicators for moist heat sterilization*

ISO 11140-1, *Sterilization of health care products — Chemical Indicators — Part 1: General requirements*

3 Terms and definitions

For the purposes of this document, the following terms and 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
chemical indicator
system that reveals a change in one or more predefined process variables based on a chemical or physical change resulting from exposure to a process

3.3
critical parameter
parameter identified as being essential to the sterilization process (and requiring monitoring)

3.4
indicator
combination of the indicator agent and its substrate in the form in which it is intended to be used

3.5
indicator agent
active ingredient or combination of ingredients

3.6
process challenge device
PCD
item designed to simulate product to be sterilized and to constitute a defined challenge to the sterilization process, and used to assess the effective performance of the process

3.7
process challenge location
PCL
site which represents “worst-case” conditions as they are given for sterilizing agent(s) in the goods to be sterilized

3.8
saturated steam
water vapor in a state of equilibrium between condensation and evaporation

3.9
stated value
value, or range of values, of a critical parameter to which the indicator is designed to react

3.10
resistometer
equipment designed to create defined combinations of the physicochemical variables of a sterilization process within defined limits

4 General considerations

4.1 All chemical indicators are intended to provide information about local conditions within the sterilizing chamber and thus to alert the user to potential sterilization process failures. The basic performance descriptor of any chemical indicator is its “endpoint” response, which is the observable change as specified by the manufacturer that occurs after the indicator has been exposed to certain predefined process conditions. This observable change generally involves either the melting of a chemical substance or a chemical reaction resulting in a colour change. Different classes of chemical indicators have been developed to suit different monitoring needs and to accommodate varying notions of what is the most useful information about the sterilization process. Some types are sensitive to certain specific problems, such as a temperature deficiency, while others can be less sensitive to an individual parameter but can simultaneously test the overall process. Even chemical indicators of the same basic type can differ in response characteristics, means of detecting exposure conditions, and reliability. This International Standard addresses the following classes of chemical indicator:

— Class 1: Process indicators

— Class 2: Indicators for use in specific tests

— Class 3: Single-parameter indicators

— Class 4: Multi-parameter indicators

— Class 5: Integrating indicators

— Class 6: Emulating indicators

The classification is based on defined performance characteristics (see ISO 11140-1) rather than on chemical or physical changes as related to specific sterilization processes.

For example, in a steam process, some of these products 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 the endpoint is not reached, the user should assume there is a sterilization processing problem. The user should investigate the cause of the problem. Possible causes are incorrect choice of packaging, improper packaging, improper loading technique, or sterilizer malfunction.

4.2 Though there are other factors that can influence the efficacy of a sterilization process, ISO 11140-1 identifies the critical sterilization parameters for each sterilization process as follows:

Process	Symbol	Critical parameters
Steam	STEAM	Time, temperature and saturated steam
Dry heat	DRY	Time and temperature
Ethylene oxide	EO	Time, temperature, humidity and EO concentration
Irradiation	IRRAD	Total absorbed dose
Steam formaldehyde	FORM	Time, temperature, humidity and formaldehyde concentration

If the use of the indicator is limited to a specific sterilization cycle, this information shall be 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.

4.3 Each indicator shall have a stated value (SV) printed on the product. This stated value, based on the manufacturer's chosen endpoint for the product, identifies the testing requirements for that specific class of chemical indicator. These conditions are attained using a resistometer.

The resistometer (see ISO 11140-2 for further information) is a special 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 sterilization exposure. Because standard sterilizers do not have the same response or accuracy of exposure conditions as found in resistometers, it is nearly impossible for a user to replicate manufacturer label claims.

4.4 Selection of the basic classes of chemical indicators that are best suited to a particular application are questions that can be answered only in the context of a basic understanding of the sterilization process, the possible problems that prevent sterilization, the performance characteristics of various classes of chemical indicators, and what constitutes an effective sterility assurance programme. 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 responds appropriately to the results.

5 Classes of chemical indicator

5.1 General

With the exception of some indicators used in specific tests, chemical indicators are used to directly or indirectly detect whether or not one or more critical process parameters have reached a certain predetermined level in a given sterilization process. Which parameters need to be considered critical and how accurately they should be monitored depends on the tolerances given to specific sterilization parameters. For example, the temperature in moist heat sterilization is of greater importance than in ethylene oxide sterilization. The

requirements for the temperature accuracy of a chemical indicator intended for monitoring moist-heat sterilization processes are far stricter than those for a chemical indicator intended for use in monitoring an ethylene oxide sterilization process. In contrast to biological indicators, where many indicators are labelled for use in several different sterilization processes, chemical indicators are usually specific to a sterilization process.

The performance characteristics of each class enable the respective chemical indicators to convey different types of information, and therefore perform different functions. In general, progression from “process indicators” to “emulating indicators” will convey more information with greater specificity.

The following descriptions for each class of chemical indicator start with an italicized quotation taken directly from ISO 11140-1, which has been used to define that specific class of chemical indicator:

5.2 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. (ISO 11140-1, subclause 4.1)

This class is useful in aiding production flow (i.e. identifying loads yet to be processed versus those processed and ready for distribution).

Class 1 process indicators are typically applied to, or visible from, the outside of packages. Examples of Class 1 process indicators include sterilization tape and packaging printed with colour-changing chemically-indicating inks. Because these chemical indicators are typically external and exposed directly to the sterilization environment without the resistance imposed by packaging, they typically “fail” only when there is gross malfunction. Class 1 process indicators are intended to reach their endpoint after exposure to a sub-optimal sterilization cycle.

Chemical indicators intended for use in monitoring γ- or β-irradiation exist only as Class 1 process indicators.

5.3 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. (ISO 11140-1, subclause 4.2)

Bowie-Dick type indicators are commercially available as special test sheets or in disposable packs containing such test sheets. At this time, the only chemical indicator widely recognized in Class 2 are the Bowie-Dick type indicators which are defined in ISO 11140-3, ISO 11140-4 and ISO 11140-5. Class 2 Bowie-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 demonstrated by a uniform colour change on the indicator sheet. Causes of failure can include the evolution of volatile compounds within the test pack or the presence of non-condensable gases in the steam.

Because Bowie-Dick type indicators are designed to reach the endpoint after a specified exposure that can be different from that required to achieve effective sterilization, they may not be appropriate for use as routine sterilization cycle indicators. It should be noted that extending the exposure time for the Bowie-Dick test, or disregarding the manufacturer’s recommendations for how to conduct the Bowie-Dick test, can entirely defeat the purpose of the test by causing misleading endpoint development.

For background information on the Bowie-Dick Test, see Annex A.

5.4 Class 3: Single-parameter indicators

A single-parameter indicator shall be designed for one of the critical parameters and shall indicate exposure to a sterilization cycle at a stated value of the chosen parameter. (ISO 11140-1, subclause 4.3)

A single-parameter indicator is intended to respond to only one critical parameter of the sterilization process. The parameter and its stated value will be provided by the indicator manufacturer.

Care shall be taken when interpreting the results obtained from single-parameter indicators. Most sterilization processes have more than one critical parameter which must be attained if sterilization is to occur. Table 1 from ISO 11140-1:1995 contains tolerances (upper and lower limits of performance acceptability for the chemical indicator, when tested by the manufacturer) that need to be met for each critical parameter. The limiting values are the predetermined conditions that the manufacturer shall maintain during testing. That table is reproduced here:

Table 1 — Tolerances and limiting values for the response to critical parameters for Class 3 and Class 4 indicators

Sterilization method	Time	Temperature	Gas concentration	Relative humidity Limiting values	Saturation Refers to the steam supply to the chamber	
	min.	°C	mg/l	%	LL[a]	UL[b]
Steam	SV[c] $^{0}_{-25}$ %	SV $^{0}_{-2}$ °C			0,85	1,0
Dry heat	SV $^{0}_{-25}$ %	SV $^{0}_{-5}$ °C				
Ethylene oxide	SV $^{0}_{-25}$ %	SV $^{0}_{-5}$ °C	SV $^{0}_{-25}$ %	> 30 %		
Steam-formaldehyde	SV $^{0}_{-25}$ %	SV $^{0}_{-3}$ °C	SV $^{0}_{-20}$ %		0,85	1,0

[a] LL = lower limit (dryness value).

[b] UL = upper limit (dryness value).

[c] SV = stated value: reaction value identified for the product with respect to a critical parameter; it is either stated or coded on the product.

EXAMPLE 1 Time tolerance:

SV $^{0}_{-25}$ %

If SV = 4 min
SV + 0 = 4 min
SV — 25 % = 3 min

EXAMPLE 2 Gas concentration tolerance:

SV = $^{0}_{-25}$ %

If SV = 600 mg/l
SV + 0 = 600 mg/l
SV – 25 % = 450 mg/l

For example, a single-parameter indicator for temperature can only indicate the attainment of a stated temperature value and provides no information as to the total time at temperature. Also, it does not provide information on any other critical parameter, such as the presence of steam.