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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.

However, the indicator can reveal whether a specific minimum temperature was attained at a particular location within the sterilizer chamber or the load. This temperature is the endpoint temperature and the indicator must be correctly selected for the minimum temperature of the process.

Single-parameter indicators should be supplemented by other means of monitoring the sterilization process.

5.5 Class 4: Multi-parameter indicators

A multi-parameter indicator shall be designed for two or more of the critical parameters and shall indicate exposure to a sterilization cycle at stated values of the chosen parameters. (ISO 11140-1, subclause 4.4)

The manufacturer states the conditions under which multi-parameter chemical indicators reach their endpoint. These indicators typically provide more information than either process (Class 1) or single parameter (Class 3) indicators. Chemical indicators are designed to reach their endpoint when preset critical parameters have been met.

Most multi-parameter indicators are based on a chemical and/or physical change that results in a colour change or in the migration of a chemical. These reactions take place at a defined rate at a stated temperature; usually the rate increases as the temperature of the process increases.

The ISO 11140-1 standard 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. See Table 1.

An example of multi-parameter indicator performance is given below. Although all parameters have been altered simultaneously in the example, in practice when the manufacturers test the indicators, they may vary one or more parameters while holding the remaining parameters at the stated value.

EXAMPLE Ethylene oxide sterilization indicator (Class 4: Multi-parameter indicator)

Stated values: 60 min at 900 mg/l

Table 1 provides the tolerances and limiting values (upper and lower limits of performance) for this Class 4 indicator. The tolerances from this table are 60 min $^{0}_{-25}$% and 900 mg/l $^{0}_{-25}$% when tested at a relative humidity greater than 30 %. Therefore, the indicator will not reach its endpoint if the time is less than 45 min [i.e. 60 — (60 × 0,25)], the gas concentration is less than 675 mg/l [i.e. 900 — (900 × 0,25)] and the relative humidity is less than 30 %. If the time is 60 min or longer, and the EO concentration is 900 mg/l or higher, and the relative humidity is greater than 30 %, the indicator must reach its endpoint.

An indicator with the above stated values responds as follows when exposed to the conditions below:

Exposed to the following conditions	Based on Table 1, an acceptable indicator
⩽ 44 min at ⩽ 650 mg/l	must show fail
⩾ 60 min at ⩾ 900 mg/l	must show pass

5.6 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 possible, 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). (ISO 11140-1, subclause 4.5)

Viable microorganisms are affected by all the complex interrelationships of the critical sterilization process parameters. Chemical indicators may not provide the same sort of biological integration of variables, but they do provide information about the conditions necessary to destroy microorganisms.

An important concept to grasp is that the often unstated goal of the chemical indicator manufacturer is to design a product that will provide as much information as a biological indicator. The assumption is that if we know the process conditions that provide kill to the biological indicator, and the chemical indicator can be prevented from reaching its endpoint until those conditions have been met, reaching the chemical indicator endpoint gives a level of assurance similar to that provided by the biological indicator.

An integrating indicator, by definition, will be affected simultaneously by a number of critical process parameters. Because the effects of the critical parameters on the integrating indicator are simultaneous, failure to reach the “endpoint” may not be assignable to a specific parameter also observable by the response of biological indicators.

Table 2 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 must maintain during testing.

That table is reproduced here:

Table 2 — Tolerances and limiting values for the response to critical parameters for Class 5 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] $^{0}_{-15}$ %	SV $^{0}_{-1}$ °C			0,85	1,0
Dry heat	SV $^{0}_{-20}$ %	SV $^{0}_{-5}$ °C				
Ethylene oxide	SV $^{0}_{-20}$ %	SV $^{0}_{-5}$ °C	SV $^{0}_{-15}$ %	> 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.

An example of integrating indicator performance is given below. Although all parameters have been altered simultaneously in the example, in practice when the manufacturers test the indicators, they may vary one or more parameters while holding the remaining parameters at the stated value.

EXAMPLE Steam sterilization indicator (Class 5: Integrating indicator)

Stated values: 3,5 min at 134 °C

Table 2 provides the tolerances (upper and lower limits of acceptability for the chemical indicator, when tested by the manufacturer) and limiting values (upper and lower limits of performance) for this Class 5 indicator. The tolerances from this table are 3,5 min $^{0}_{-15}$ % and 134 $^{0}_{-1}$ °C when tested in a saturated steam condition with a dryness value between 0,85 and 1,0. Therefore, to reach its endpoint, the time needed shall be at least 2,975 min [i.e. 3,5 — (3,5 × 0,15)] with a

temperature of 133 °C [i.e. (134 — 1)] and a dryness value between 0,85 and 1,0. Any time shorter than 2,975 min and any temperature below 133 °C must not result in the indicator reaching its endpoint. If the time is 3,5 min or longer, the temperature is 134 °C or higher, and the dryness value is between 0,85 and 1,0, the indicator must reach its endpoint.

An indicator with the values stated above responds as follows when exposed to the conditions below:

Exposed to the following conditions	Based on Table 2, an acceptable indicator
$\leqslant$ 2,9 min at $\leqslant$ 132 °C	must show fail
$\geqslant$ 3,5 min at $\geqslant$ 134 °C	must show pass

5.7 Class 6: Emulating 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. (ISO 11140-1, subclause 4.6)

Table 3 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 must maintain during testing.

That table is reproduced here.

Table 3 — Tolerances and limiting values for the response to critical parameters for Class 6 indicators

Sterilization method	Time	Temperature	Gas concentration	Relative humidity	Saturation	
				Limiting values	Refers to the steam supply to the chamber	
	min.	°C	mg/l	%	LL[a]	UL[b]
Steam	SV[c] $^{0}_{-6}$ %	SV $^{0}_{-1}$ °C			0,85	1,0
Dry heat	SV $^{0}_{-20}$ %	SV $^{0}_{-1}$ °C				
Ethylene oxide	SV $^{0}_{-10}$ %	SV $^{0}_{-2}$ °C	SV $^{0}_{-10}$ %	SV $^{0}_{-10}$ %		

[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.

The tolerances defined in Table 3 are the most stringent of all the different classes of chemical indicators. Emulating indicators therefore provide the highest level of assurance in demonstrating that the critical parameters of the specified sterilization cycle have been met.

An example of an emulating indicator performance is given below. Although all parameters have been altered simultaneously in the example, in practice when the manufacturers test the indicators, they may vary one or more parameters while holding the remaining parameters at the stated value.

EXAMPLE Steam sterilization indicator (Class 6: Emulating indicator)

Stated values: 3,0 min at 134 °C

Table 3 provides the tolerances (upper and lower limits of acceptability for the chemical indicator, when tested by the manufacturer) and limiting values (upper and lower limits of performance) for this Class 6 indicator. The tolerances from this table are $3{,}0\ ^{0}_{-6}$ % min and $134\ ^{0}_{-1}$ °C when tested in a saturated steam condition with a dryness value between 0,85 and 1,0. Therefore, to reach its endpoint, the time needed shall be at least 2,8 min [i.e. 3,0 — (3,0 × 0,06)] with a temperature of 133 °C [i.e. (134 — 1)] and a dryness value between 0,85 and 1,0. Any time shorter than 2,8 min and any temperature below 133 °C must not result in the indicator reaching its endpoint. If the time is 3,0 min or longer, the temperature is 134 °C or higher, and the dryness value is between 0,85 and 1,0, the indicator must reach its endpoint.

An indicator with the above stated values will respond as follows when exposed to the conditions below:

Exposed to the following conditions	Based on Table 3, an acceptable indicator
⩽ 2,75 min at ⩽ 132 °C	must show fail
⩾ 3,0 min at ⩾ 134 °C	must show pass

6 Selection of chemical indicators

The user should select a chemical indicator that is appropriate for the particular process to be employed. The manufacturer does not intend chemical indicators for use in any process other than that specified. There are wide variations in sterilization processes and chemical indicator manufacturers are not able to foresee all possible uses of their product. Manufacturers, therefore, label chemical indicators according to their intended use. It is the responsibility of the users of chemical indicators to select, use, and interpret the results, as appropriate, for the particular sterilization process used. The stated value (parameters and values to which the indicator is designed to react) on the product and/or product insert will assist the user in this process.

Chemical indicators are used to demonstrate the attainment of one or more parameters of a sterilization process and are not in themselves sufficient to demonstrate the efficacy of a sterilization process. The demonstration of efficacy is a combination of physical monitoring and, where appropriate, the use of chemical and/or biological indicators. When any variable of a sterilization process is outside its specified limits, sterilizer function should be tested. It should be noted that measurements may be made during the cycle which need to be evaluated in the context of the overall cycle. Systems and/or procedures should be established to evaluate any deviations from the cycle process limits, and reasons for accepting any deviation should be fully documented.

Various types of chemical indicators are available, each with different response characteristics; that is, they differ in the sterilizing conditions they can detect and verify. The choice of a chemical indicator depends upon the specific needs, resources, and sterilization equipment of the individual facility.

Users should obtain data from manufacturers on the reliability, safety, and performance characteristics of their products. In addition, manufacturers of chemical indicators should provide written information on how to interpret indicator results, the reliability of the indicator in maintaining endpoint colour (if applicable) during storage of sterilized items, the sterilization conditions that the indicator has been designed and tested to detect, and the storage requirements for and shelf life of the indicator itself.

7 Use of chemical indicators

7.1 External chemical indicators

The purpose of an external chemical indicator is to differentiate between processed and unprocessed products, not to establish whether the parameters for adequate sterilization were met. In practice, this is achieved by the use of Class 1 process indicators on every package.

Sterilizer indicator tape, indicating labels, or an indicating printed legend should be affixed to or printed on all packages assembled in the facility intended for sterilization. An indicator should be attached to or printed on all commercially acquired packages if sterilization is to be performed by the facility. The tape, label or legend, needs to be examined after sterilization and also before use to make sure that it indicates that the item has been exposed to a sterilization process.

7.2 Internal chemical indicators

When a chemical indicator is used within each package, tray, or container being processed, it provides information concerning the attainment of critical parameters at that specific location. Many factors can affect the attainment of acceptable parameters, such as load contents, loading configurations, packaging technique and sterilizer malfunction.

The chemical indicator should be placed in that area of the package, tray or container considered least accessible to sterilizing agent penetration. This area may or may not be at the centre of the package, tray or container and may or may not be at the centre of the given sterilizer chamber. For unwrapped loads, at least one internal chemical indicator should be placed in the tray with the items to be sterilized.

The choice of the type of chemical indicator to be used as the internal chemical indicator should be from Class 3, 4, 5 or 6.

7.3 Indicators for specific test procedures

The steam penetration, or air removal, test is run in an empty sterilizer. The test pack can be either user-assembled, pre-made, one-time-use disposable, or limited-use disposable. The manufacturer's instructions should be followed for use of the device.

7.4 Indicators for use with process challenge devices

Process challenge devices (PCDs) have been developed to represent a defined challenge to the sterilization process. A PCD may have several configurations. It may be based on an actual or simulated product and may not resemble either. The chemical indicator should not interfere with the function of the PCD. Thus, a PCD serves as a "dummy" to replace the actual goods for a specific location and allows removal of the chemical indicator without destroying the goods to be sterilized. It may be desirable to use more than one PCD in a sterilization cycle.

The performance of PCDs should be correlated to specific sterilization methods, types of sterilizers, and load contents. There is no universal PCD that can be used for all sterilization types and methods. Different products, e.g. hollow loads (beakers, basins, tubing), porous loads (linens, dressings, textiles) and non-porous loads (solid and surgical instruments), may be represented by different PCDs.

PCDs are commercially available as prefabricated sets, often called chemical indicator test packs. Single-use chemical indicator test packs are manufactured by various companies and may be used instead of in-house PCDs. There are no recognized performance requirements for PCDs, therefore commercially available devices shall be demonstrated to be equivalent to the load that they are meant to represent. To obtain reliable results when using commercially available chemical indicator test packs, the placement in the sterilizer and within the load shall be validated to represent the most difficult-to-sterilize location, called the process challenge location (PCL).

Some important issues to consider when purchasing a PCD are as follows.

a) The device is so constituted that a chemical indicator can be placed in the position that is most difficult for the sterilant to reach.

b) The design of the device should relate to the type of goods to be sterilized and the sterilization procedure.

c) The chemical indicator should not interfere with the function of the device.

8 Interpretation of chemical indicators

8.1 General

A comprehensive sterility assurance programme incorporates every aspect of processing including: cleaning, decontamination, preparation and packaging, loading the sterilizer, sterilization, handling the item after sterilization, sterile storage, distribution, and handling to the point of use. Routine monitoring and control of the sterilization cycle is an important aspect of a comprehensive sterility assurance programme. Chemical indicators complying with the requirements of ISO 11140-1, which are used in accordance with the manufacturer's recommendations for use, can provide useful information about the sterilization cycle. The frequency and number of chemical indicators per load or cycle depends on national regulations or recommendations.

Chemical indicators should clearly differentiate between adequately and inadequately processed items. For this reason, the endpoint response should be appropriate and unambiguous. Examples of adequate and inadequate exposures should be available from the manufacturer and clearly understood by the user.

8.2 Chemical indicator responses

Chemical indicators cannot prove or assure that sterilization has occurred. A very common and dangerous mistake is the idea that if a chemical indicator has had a colour change, the item is sterile. This idea is both theoretically and factually incorrect. Chemical indicators should be viewed as an element of an overall sterility assurance programme.

8.3 Chemical indicators showing "Fail" response

If a chemical indicator fails to reach its endpoint, the facility should follow a documented protocol which may include, but not be limited to, lot identification, review of the physical monitoring information for the sterilization cycle, the results of chemical indicators elsewhere in the load, and, if applicable, the results of biological monitoring of the sterilizer. Chemical indicators are only one way to verify sterilizer and cycle performance.

9 Chemical indicators in sterility assurance procedures

9.1 General

Chemical indicators, whether applied internally or externally to packages, are used to monitor sterilization processes to provide evidence that certain critical parameters have been achieved. Devices with visible soil, that have been improperly cleaned, or are otherwise contaminated can remain nonsterile even after processing in a correctly functioning sterilizer operating at commonly accepted sterilization parameters. If the device is not clean, it cannot be sterilized. Because chemical indicators do not respond to either cleanliness or microbial presence, they cannot measure either condition.

The processing department should have written procedures for all processes. Because the sterilization process is comprised of multiple steps which may include cleaning, decontamination, disassembly, inspection, re-assembly, packaging, terminal sterilization, storage and handling, it is imperative that means be established to differentiate the status of all items during each phase of the process.

The overall sterility assurance programme should include product (sterilized goods) identification and traceability; sterilizer calibration, maintenance and efficacy testing; and mechanical, chemical and biological monitoring of sterilization cycles. No single element of a sterility assurance programme, including the various sterilization monitors, can be relied upon, by itself, to assure sterility. Sterility assurance requires continuous attention to all aspects of sterilizer performance, the sterilization process, and continuous compliance with established policies and procedures.

Proper use of mechanical, biological and chemical sterilization monitors requires an understanding of what each type of monitor is designed to do and what each reveals about the sterilization cycle or process. Mechanical or physical sterilization monitors, which include time-, temperature- and pressure-recording devices and gauges, provide real-time assessment of the sterilization cycle conditions and allow many sterilizer malfunctions to be detected as soon as possible. However, mechanical indicators cannot determine if appropriate conditions were achieved throughout the sterilizer and cannot detect problems related to improper load configuration or package composition. Chemical indicators are designed to respond with a characteristic chemical or physical change to one or more of the process conditions (e.g. time, temperature, presence of saturated steam, humidity, ethylene oxide gas concentration, radiation dose) within the sterilizer chamber. An endpoint of a chemical indicator does not prove that the item accompanied by the indicator is sterile; it demonstrates that the item has been subjected to certain known processing conditions. Chemical indicators provide a rapid means to detect certain problems within the sterilizer before a potentially nonsterile product is released.

Chemical indicators can be helpful in diagnosing certain problems associated with the attainment of critical parameters associated with sterilization conditions. Effective use of chemical indicators requires a thorough understanding of the types of chemical indicators and what they can and cannot indicate about a sterilization process. Individual chemical indicators are usually specific to one type of sterilization process. However, different indicators of the same class and type, when exposed to a sterilization cycle, can show a different response.

A planned programme for the placement and evaluation of chemical indicators may:

— be part of the sterilizer installation, operating and performance qualification;

— be part of the process validation protocol;

— be part of the routine process-monitoring protocol;

— assist in the diagnosis of process malfunctions;

— assist in the detection of packaging problems (e.g. excessively large or dense packs);

— assist in the detection of loading problems (e.g. tipped basins that can trap air or water if not properly oriented);

— reveal unprocessed loads;

— assist in the detection of sterilizer malfunctions relating to air removal or temperature/dwell attainment; and,

— assist in the detection of problems with the sterilizing agent supply.

9.2 Record keeping

Chemical indicators or their results may be kept as part of the sterilization records. These results are part of a quality system (e.g. ISO 9000 series) and should be traceable to a specific sterilization cycle. The test results should be evaluated by a responsible trained person and should include date, sterilizer identification, load number and sterilizer parameters. Depending on national and/or local requirements, indicator results may be kept for varying periods of time. All chemical indicator results may be kept manually or electronically.

10 Labelling of chemical indicators

Labelling of chemical indicators should include all the information outlined in ISO 11140-1.

11 Personnel training

There should be written procedures for the handling and use of chemical indicators. Personnel responsible for the placement and retrieval of chemical indicators should be trained in the sterilization processes and the selection, use and interpretation of chemical indicators. This training should include all personnel in sterilization processing areas and anyone who will be using sterile supplies and thus interpreting chemical indicators. The correct interpretation of the chemical indicator endpoint is vital.

The training should be documented, and reviewed periodically.

12 Storage and handling

The manufacturer or supplier of the chemical indicator is responsible for providing information on the proper storage and handling of the product before and after exposure.

The performance of a chemical indicator can be affected by the conditions encountered during shipping or storage prior to its use, the method of use, the techniques employed after exposure to the sterilization process, and the stability of the chemical indicator following its exposure to the sterilization process. For these reasons, the recommendations of the chemical indicator manufacturer for storage and use should be followed. Failure to follow these recommendations could affect the integrity and performance of the chemical indicator and lead to incorrect assumptions regarding the efficacy of the sterilization process.

Chemical indicators should not be used beyond their expiration date.