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Sterilization of health care products — Biological and chemical indicators — Test equipment

Stérilisation des produits de santé — Indicateurs biologiques et chimiques — Appareillage d'essai

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see www.iso.org/iso/foreword.html.

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

This second edition cancels and replaces the first edition (ISO 18472:2006), which has been technically revised.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

To test the performance of biological and chemical indicators, specific test equipment is required. This document specifies the performance requirements for the test equipment to be used to establish the response of biological and chemical indicators to critical process variables. This document does not apply to test equipment for indicators used in irradiation, isolator/room biodecontamination (at atmospheric pressure), or low temperature steam and formaldehyde processes.

Resistometers constitute test equipment designed to create precise and repeatable sterilizing environments, allowing the evaluation of their effect on biological inactivation kinetics, chemical reactions, material degradation and product bioburden. Resistometers allow precise variation of the environmental conditions and cycle sequences in order to produce controlled physical studies. When used with the defined test methods given in the appropriate parts of ISO 11138 for biological indicators and ISO 11140 for chemical indicators, the results of these studies can be used to demonstrate conformance of biological indicators and chemical indicators to these standards.

Resistometers differ from conventional sterilizers. Instrumentation selection and control requirements for resistometers are based upon mathematical models in which rates of reaction, measurement accuracy and process control requirements are evaluated to quantify the effects induced by test equipment-controlled variables. The requirements for accurate measurement, precise control, and rapid rates of change approach limits of commercially available process control and calibration instrumentation measurement accuracy. The measurement and control requirements often prohibit practical validation of a resistometer using procedures that might be employed in a conventional heat or chemical sterilization system. Resistometers are considered test equipment rather than sterilizers; therefore, an understanding of instrumentation and process design is critical in clarifying requirements on precision and measurement accuracy. Practical design takes the following into consideration:

— achievable measurement and control;

— acceptable equipment induced variation in test results;

— economic design (utilizing tight process controls only where required);

— test method correlation with intended use;

— historical knowledge applied to test procedures and an understanding of micro-environmental physical phenomena;

— testing and analysis alternatives, when accurate quantitative determinations exceed physical measurement/control limits.

Sterilization of health care products — Biological and chemical indicators — Test equipment

1 Scope

This document specifies the requirements for test equipment to be used to:

— test biological indicators for steam, ethylene oxide gas and dry heat sterilization processes for conformity to the requirements given in ISO 11138 series;

— test chemical indicators for steam, ethylene oxide gas, dry heat and vaporized hydrogen peroxide sterilization processes for conformity to the requirements given in ISO 11140-1:2014.

This document also provides informative methods useful in characterizing the performance of biological and chemical indicators for intended use and for routine quality control testing.

This document does not specify requirements for test equipment for processes specifically for testing chemical and biological indicators intended to monitor isolator and room biodecontamination processes at atmospheric pressure.

ISO 11138-2:2017, ISO 11138-3:2017, ISO 11138-4:2017, and ISO 11140-1:2014 require the use of resistometers specified in this document, and these resistometers are used in conjunction with the test methods specified in the appropriate parts of ISO 11138 series and ISO 11140 series.

Resistometers for low temperature steam and formaldehyde indicators are not included in this document. Test methods using laboratory apparatus for low temperature steam and formaldehyde are included in ISO 11138-5:2017.

Test equipment for testing Type 2 (e.g. Bowie Dick) chemical indicators are specified in ISO 11140-3:2007, ISO 11140-4:2007, and ISO 11140-5:2007.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements 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 11138-1:2017, *Sterilization of health care products — Biological indicators — Part 1: General requirements*

ISO 11138-2:2017, *Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes*

ISO 11138-3:2017, *Sterilization of health care products — Biological indicators — Part 3: Biological indicators for moist heat sterilization processes*

ISO 11138-4:2017, *Sterilization of health care products — Biological indicators — Part 4: Biological indicators for dry heat sterilization processes*

ISO 11138-5:2017, *Sterilization of health care products — Biological indicators — Part 5: Biological indicators for low-temperature steam and formaldehyde sterilization processes*

ISO 11140-1:2014, *Sterilization of health care products — Chemical indicators — Part 1: General requirements*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 11138-1:2017, ISO 11138-2:2017, ISO 11138-3:2017, ISO 11138-4:2017, ISO 11138-5:2017, and ISO 11140-1:2014 and the following apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— IEC Electropedia: available at http://www.electropedia.org/

— ISO Online browsing platform: available at https://www.iso.org/obp

3.1
biological indicator
test system containing viable microorganisms providing a specified resistance to a specified sterilization process

[SOURCE: ISO 11139:2018, 3.29]

3.2
calibration
operation that, under specified conditions, in a first step, establishes a relation between the quantity values with measurement uncertainties provided by the measurement standards and corresponding indications with associated measurement uncertainties and, in a second step, uses this information to establish a relation for obtaining a measurement result from an indication

[SOURCE: ISO/IEC Guide 99:2007, 2.39, modified — NOTE 1, 2, and 3 have been deleted.]

3.3
chemical indicator
test system that reveals change in one or more pre-specified process variables based on a chemical or physical change resulting from exposure to a process

[SOURCE: ISO 11139:2018, 3.43]

3.4
come-down period
<resistometer> time elapsed from the termination of the exposure period to an established null reaction point

[SOURCE: ISO 11139:2018, 3.56]

3.5
come-up period
<resistometer> time elapsed from the introduction of the sterilizing agent to the attainment of the specified conditions

[SOURCE: ISO 11139:2018, 3.57]

3.6
indicator exposure period
duration between the initial attainment to the termination of the specified exposure conditions

[SOURCE: ISO 11139:2018, 3.140]

3.7
measurement accuracy
closeness of the agreement between a measured quantity value and a true quantity value of a measurand

Note 1 to entry: “Accuracy” is a qualitative concept.

Note 2 to entry: The term “precision” should not be used for “accuracy”.

[SOURCE: ISO/IEC Guide 99:2007, 2.13, modified — The terms “accuracy of measurement” and “accuracy” have been deleted. NOTE 1 and 2 have been modified. NOTE 3 has been deleted.]

3.8
measurement precision
closeness of agreement between indications or measured quantity values obtained by replicate measurements on the same or similar objects under specified conditions

Note 1 to entry: Measurement precision is usually expressed numerically by measures of imprecision, such as standard deviation, variance, or coefficient of variation under the specified conditions of measurement.

Note 2 to entry: The ‘specified conditions’ can be, for example, repeatability conditions of measurement, intermediate precision conditions of measurement, or reproducibility conditions of measurement.

Note 3 to entry: Measurement precision is used to define “measurement repeatability”, “intermediate measurement precision”, and “measurement reproducibility”.

Note 4 to entry: Sometimes “measurement precision” is erroneously used to mean measurement accuracy.

[SOURCE: ISO/IEC Guide 99:2007, 2.15, modified — The term “precision” has been deleted. The NOTEs have been modified.]

3.9
null reaction point
terminating set of conditions that have no significant effect on the indicator

3.10
record, verb
<data> collect, store and make accessible

[SOURCE: ISO 11139:2018, 3.223]

3.11
reference standard
measurement standard designated for the calibration of other measurement standards for quantities of a given kind in a given organization or at a given location

[SOURCE: ISO/IEC Guide 99:2007, 5.6, modified — The term name has been simplified.]

3.12
resistometer
test equipment designed to create specified combinations of the physical and/or chemical parameters of a sterilization process

[SOURCE: ISO 11139:2018, 3.233]

3.13
response time
τ_{90}
<sensor> period required for a 90 % change in sensor output when exposed to a step change in the variable being measured

Note 1 to entry: It may be necessary to determine the sensor response time using a faster data sampling rate than the minimum for the equipment specified in this document. Documentary evidence from the sensor manufacturer's stated response time is equally acceptable as proof of conformance.

[SOURCE: ISO 11139:2018, 3.234, modified — Note 1 to entry has been added.]

3.14
saturated steam
water vapour in a state of equilibrium between its liquid and gas phases

[SOURCE: ISO 11139:2018, 3.241]

3.15
stabilization period
elapsed time from the attainment of the minimum specified exposure conditions until the end of the specified time to achieve steady state conditions

[SOURCE: ISO 11139:2018, 3.261]

3.16
steady state period
<indicator> portion of the exposure period which begins after the stabilization period and terminates at the end of the exposure period

[SOURCE: ISO 11139:2018, 3.266]

3.17
sterilant
chemical or combination of chemicals used to generate a sterilizing agent

[SOURCE: ISO 11139:2018, 3.268]

4 Performance requirements for resistometers

4.1 Intended use

The resistometer is intended to be used to expose test samples under stated test conditions, and therefore shall be capable of producing cycle sequences as required for specific test methods. Depending upon the test methods defined in ISO 11138-2:2017, ISO 11138-3:2017, ISO 11138-4:2017 and ISO 11140-1:2014, the resistometer utilized need only verify those limits necessary to characterize the chemical or biological indicators being tested.

NOTE 1 The following requirements define the conditions to be achieved in the vessel in which the sample is to be placed, but the means by which these conditions are to be controlled are not addressed.

NOTE 2 Piping connected to the chamber can modify the total volume of the chamber.

4.2 Test methods

The equipment specified in this document shall be used with the detailed test methods given in ISO 11138-1:2017, ISO 11138-2:2017, ISO 11138-3:2017, ISO 11138-4:2017, and ISO 11140-1:2014.

The performance of resistometers can be influenced by the nature of the load being used. The performance requirements listed in Tables 2, 4, 6, and 8 shall be met during testing of indicators as well as during empty chamber conditions.

NOTE Tolerances might be compounded when taking into consideration the tolerances designated for the performance of the resistometer and the tolerances for performance testing of biological (ISO 11138-1:2017, ISO 11138-2:2017, ISO 11138-3:2017, ISO 11138-4:2017) and chemical (ISO 11140-1:2014) indicators.

4.3 Air leakage test

4.3.1 With the temperature stabilized and the chamber empty (except for fixed furniture and necessary monitoring sensors) start the test cycle. When the pressure in the chamber has reached or is below the value corresponding to the lowest operating vacuum of the test cycle air removal stages, close all the valves connected to the chamber and stop the vacuum pump. Observe and record the time, t_1, and the absolute pressure, p_1. Allow evaporation of condensate in the chamber for 300 s ± 10 s and then observe

and record the absolute pressure, p_2, in the chamber and the time, t_2. After a further 600 s ± 10 s, again observe and record the absolute pressure, p_3, and the time, t_3.

The resistometer may be equipped with a test cycle for air leakage that will carry out this procedure automatically and display the air leakage in kPa/min (mbar/min).

4.3.2 At the end of the test calculate the rate of pressure rise for the 600 s period.

NOTE 1 If the value of ($p_2 - p_1$) is greater than 2 kPa (20 mbar), this could be due to the initial presence of excessive condensate in the sterilizer chamber.

NOTE 2 In a closed vessel at 4 kPa pressure, the pressure changes by approximately 0,1 kPa (1 mbar) for each 10 °C change in temperature; over the range 20 °C to 140 °C; at 7 kPa (70 mbar) the change is approximately 0,2 kPa (2 mbar). The test can be compromised if the temperature changes by more than 10 °C during the period in which the chamber pressure is monitored.

NOTE 3 The leak test is relevant for steam, ethylene oxide gas and vaporized hydrogen peroxide resistometers.

4.4 Steam resistometer performance requirements

4.4.1 Measurement accuracy

The sensors used to measure temperature and pressure from within the steam resistometer shall have a response time as specified in Table 1. For temperature this step change shall be from 20 °C to 90 °C and for pressure this step change shall be from 10 kPa to 100 kPa. The measurement chains used to record time, temperature and pressure from within the steam resistometer shall be capable of operation with a resolution and measurement accuracy within the scale range specified in Table 1.

The measurement chains used may operate beyond the scale range specified as long as the limiting values within the scale range specified in Table 1 are attained.

These requirements shall apply to complete measurement chains including sensors and data processing.

Table 1 — Steam resistometer instrumentation requirements (measurement and recording)

Measurement	Unit	Scale range	Resolution	Measurement accuracy (+/−)[a]	Sensor response time[b] ms
Time	HH:MM:SS	Selectable	00:00:01	00:00:01	—
Temperature	°C	110 to 145	0,01	0,5	≤500
Pressure	kPa	0 to ≤100	0,01	1,0	≤200
	kPa	>100 to 420	0,01	1,6	≤200

[a] Measurement accuracy over the test condition range (see 3.7 and 4.1).

[b] See 3.13.

4.4.2 Data

Data from the measurements specified in Table 1 shall be provided at a sampling interval of not less than one data point per second and may be electronically archived.

If this data is required to be recorded, the recording interval is at the user's discretion.

4.4.3 Process control

The steam resistometer process control shall control the parameters to the tolerances as specified in Table 2.

Table 2 — Steam resistometer physical conditions

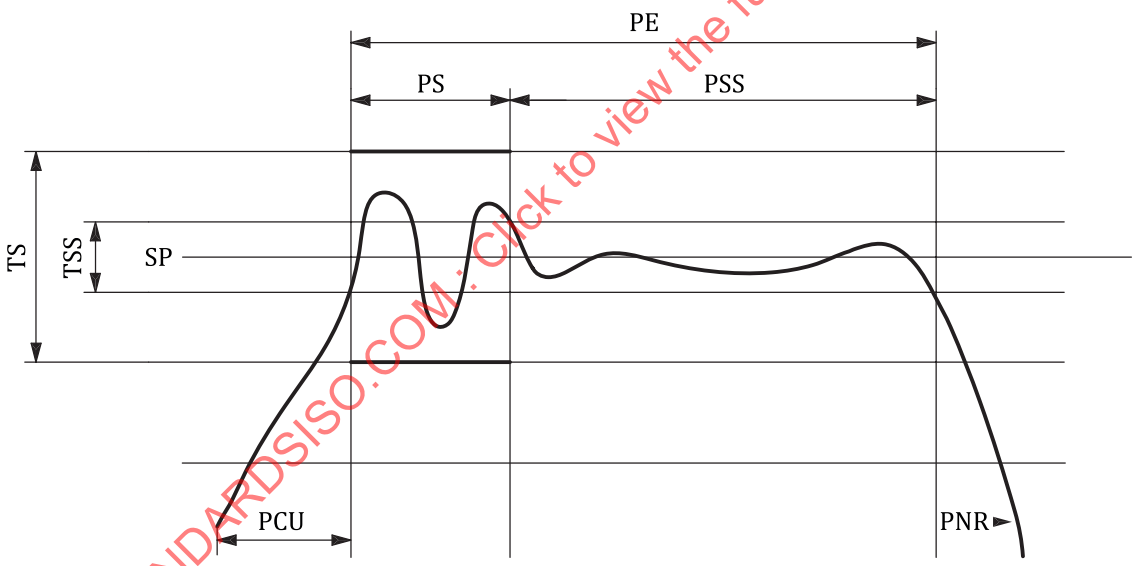
Parameter	Unit	Range	Tolerance (+/−)
Time	HH:MM:SS	Selectable	00:00:01
Temperature	°C	110 to 145	0,5[a], 1,0[d]
Pressure	kPa	>100 to 420	3,5[a,c]
	kPa	3 to ≤100	1,0
Time to achieve vacuum set point	HH:MM:SS	≤00:02:00[b]	–
Come-up period	HH:MM:SS	≤00:00:11	–
Come-down period	HH:MM:SS	≤00:00:11	–
Stabilization period (PS)	HH:MM:SS	≤00:00:10	

[a] During steady-state period (PSS) (see Figure 1).

[b] Some indicators can be adversely affected by prolonged exposure to dry heat and vacuum. The minimum practicable settings for evacuation should be used. The time taken should be as consistent as possible in order to minimize potential variability (e.g. desiccation can occur).

[c] Tolerance is at 121 °C. Tolerance will increase at higher temperatures based on steam tables, (i.e. 4,5 kPa at 132 °C, tolerances at other temperatures may be interpolated or extrapolated.)

[d] During stabilization period.



Key

PS	stabilization period	PNR	null reaction point example
PSS	steady-state period	SP	set point
PE	exposure period	TS	stabilization tolerance
PCU	come-up period	TSS	steady-state tolerance

Figure 1 — Stabilization time for temperature for steam resistometer

4.4.4 General steam resistometer requirements

4.4.4.1 The chamber shall be supplied with dry saturated steam with dryness of 0,9 or greater from a source external to the chamber.

NOTE A method to determine steam dryness which can be modified for use in steam resistometers is specified in EN 285.

4.4.4.2 Air admitted at the end of the cycle shall be filtered through a filter having the capability of removing not less than 99,5 % of 0,5 µm particles.

4.4.4.3 The sample holder shall allow the indicator to be exposed to the test conditions in the manner intended by the indicator manufacturer.

The various types of indicator may require customized sample holders. Sample holders might have to be constructed to hold test items in different vertical and horizontal attitudes to test performance differences.

NOTE Consult the indicator manufacturer for guidance when verifying label claim performance.

4.4.4.4 The null reaction point shall be specified and demonstrated by experimentation or by calculation using published data.

4.4.5 Air leakage test

4.4.5.1 When determined by the method given in 4.3, for vessels less than or equal to 55 l, the air leakage rate shall not be greater than 0,13 kPa/min.

4.4.5.2 When determined by the method given in 4.3, for vessels greater than 55 l, the air leakage rate shall not be greater than 0,13 kPa/min × $(54{,}8/V_c)$ where V_c is chamber volume in l.

4.4.6 Operation of steam resistometer

4.4.6.1 The chamber shall be designed such that the formation of condensate during any stage of the operating cycle does not adversely affect the required test conditions. To avoid excessive condensate formation during the operating cycle it might be necessary to provide thermostatic control of the inner surfaces of the resistometer so that they can be maintained at a specified temperature (e.g. the exposure period temperature).

4.4.6.2 Before initiating a test cycle, the inner surface of the chamber shall be heated to the test temperature.

4.4.6.3 The equipment shall be provided with means to evacuate the chamber to the vacuum set point to permit adequate air removal prior to admission of steam.

Steam admission/gravity displacement shall not be used to effect air removal from the chamber.

4.4.6.4 Data from controlled values shall be provided at an interface for recording purposes within a minimum frequency of 1 s.

NOTE 1 For additional applications of steam resistometers, see Annex A.

NOTE 2 For examples of resistometer test cycle documentation, see D.4.

4.5 Ethylene oxide gas resistometer performance requirements

4.5.1 Measurement accuracy

The sensors used to measure temperature, pressure and relative humidity from within the EO gas resistometer shall have a response time as specified in Table 3. For temperature this step change shall be from 20 °C to 90 °C and for pressure this step change shall be from 10 kPa to 100 kPa. The system

used to record time, temperature, vacuum, pressure, relative humidity and EO gas concentration from within the EO gas resistometer shall be capable of operation with a resolution and measurement accuracy within the scale range specified in Table 3.

The measurement systems used may operate beyond the scale range specified as long as the limiting values within the scale range specified in Table 3 are attained.

These requirements shall apply to complete measurement chains including sensors and data processing.

Table 3 — EO gas resistometer instrumentation requirements (measurement and recording)

Measurement	Unit	Scale range	Resolution	Measurement accuracy (+/−)[a]	Response time ms
Time	HH:MM:SS	Selectable	00:00:01	00:00:01	—
Temperature	°C	25 to 80	0,1	0,5	≤500
Pressure	kPa	0 to 100	0,1	±3,5	≤30
Relative humidity[b]	% RH	20 to 90	1	5	15 000
EO gas concentration	mg/l	25 to 1 200	—	5 % of the concentration targeted	—

[a] Measurement accuracy over the test condition range (see 4.1).

[b] If relative humidity is not determined by partial pressure.

4.5.2 Data

Data from the measurements specified in Table 3 shall be provided at a sampling interval of not less than one data point per second and may be electronically archived.

If this data are required to be recorded, the recording interval is at the user's discretion.

The percentage of relative humidity and ethylene oxide gas concentration shall be directly measured by using a suitable sensor, or determined from pressure measurements during steady-state stages of the operating cycle.

4.5.3 Process control

The EO gas resistometer process control shall control the parameters to the tolerances as specified in Table 4.

NOTE For calculation of EO gas concentration and relative humidity, see D.2 and D.3.

Table 4 — EO gas resistometer physical design/control specifications

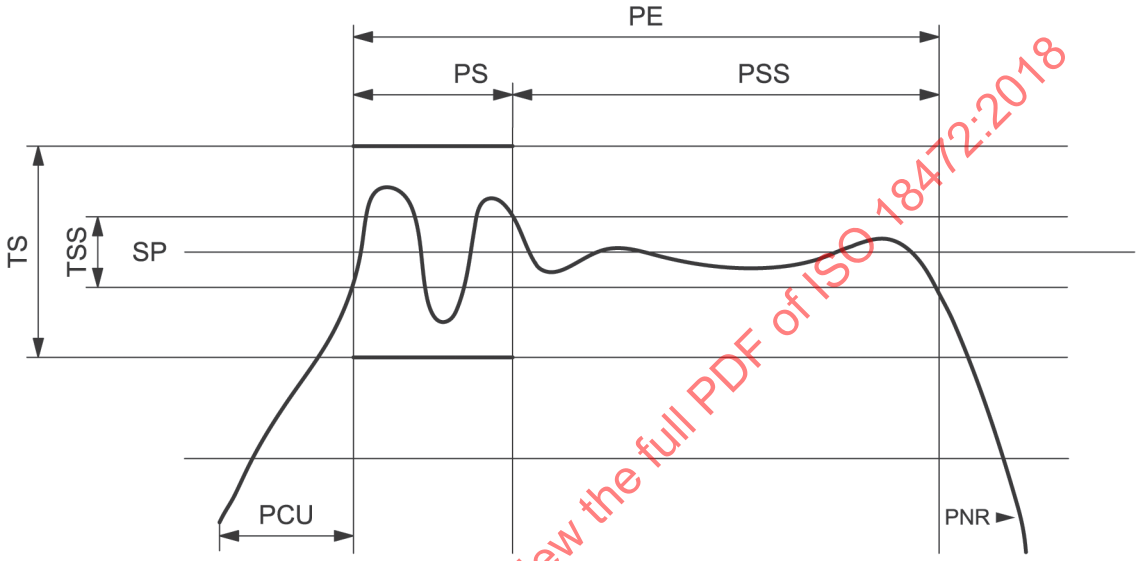
Parameter	Units	Range	Tolerance (+/−)
Time	HH:MM:SS	Selectable	00:00:01
Pressure	kPa	100 to 200	3,5
Pressure	kPa	4 to 100	1,0
EO gas concentration	mg/l	200 to 1 200	5 % of the targeted
Temperature	°C	>45 to 65	±1[a]
		29 to ≤45	±3[b]
Relative humidity	% RH	30 to 80	10
Time to achieve vacuum set point	HH:MM:SS	≤00:01:00	—

[a] During steady-state period (see Figure 2).

[b] During stabilization period.

Table 4 *(continued)*

Parameter	Units	Range	Tolerance (+/−)
Come-up period	HH:MM:SS	≤00:01:00	—
Come-down period	HH:MM:SS	≤00:01:00	—
Stabilization period	HH:MM:SS	≤00:02:00	—-
[a] During steady-state period (see Figure 2).			
[b] During stabilization period.			



Key

PS	stabilization period	PNR	null reaction point example
PSS	steady-state period	SP	set point
PE	exposure period	TS	stabilization tolerance
PCU	come-up period	TSS	steady-state tolerance

Figure 2 — Stabilization time for temperature for ethylene oxide gas resistometer

4.5.4 General ethylene oxide gas resistometer requirements

4.5.4.1 Means shall be provided to ensure that test samples are not contacted by liquid ethylene oxide or particles of polymer entering the chamber. Due to the potential for stratification, a mixing device may be used to facilitate homogeneous conditions within the chamber.

4.5.4.2 The test system including the chamber and door shall be provided with a means of maintaining the temperature of the inner surfaces above the dew point for the test temperature and relative humidity. The chamber environment shall be at thermal equilibrium control conditions before a cycle is initiated.

4.5.4.3 Air admitted at the end of the cycle shall be filtered through a filter having the capability of removing not less than 99,5 % of 0,5 µm particles.

4.5.4.4 The sample holder should allow the indicator to be exposed to the test conditions in the manner intended by the indicator manufacturer.

The various types of indicator may require customized sample holders. Sample holders might have to be constructed to hold test items in different vertical and horizontal attitudes in order to test performance differences.

NOTE The indicator manufacturer can be consulted for guidance when verifying label claim performance.

4.5.4.5 The null reaction point shall be specified and demonstrated by experimentation or by calculation using published data.

4.5.5 Air leakage test

When determined by the method given in 4.3, the air leakage rate shall not be greater than 0,13 kPa/min.

4.5.6 Operation of ethylene oxide gas resistometer

4.5.6.1 The chamber shall be designed such that the formation of condensate during any stage of the operating cycle does not adversely affect the required test conditions. In order to avoid condensation during the operating cycle it might be necessary to provide thermostatic control of the inner surfaces of the resistometer so that they can be maintained at a specified temperature above the dew point.

4.5.6.2 Before initiating a test cycle, the inner surface of the chamber shall be heated to the test temperature.

NOTE See Table 4 and Figure 2.

4.5.6.3 The equipment shall be provided with a means of evacuating the chamber to less than the vacuum set point to permit adequate air removal prior to admission of water vapour and ethylene oxide gas.

4.5.6.4 Data from controlled values shall be provided at an interface to record with a minimum frequency of 1 s.

NOTE 1 For additional applications of EO gas resistometers, see Annex B.

NOTE 2 For examples of resistometer test cycle documentation, see D.4.

4.6 Dry heat (heated air) resistometer performance requirements

4.6.1 Measurement accuracy

The sensors used to measure temperature from within the dry heat resistometer shall have a response time as specified in Table 5. For temperature this step change shall be from 20 °C to 90 °C and for pressure this step change shall be from 10 kPa to 100 kPa. The system used to record time and temperature from within the dry heat resistometer shall be capable of operation with a resolution and measurement accuracy within the scale range specified in Table 5.

The measurement systems used may operate beyond the scale range specified as long as the limiting values within the scale range specified in Table 5 are attained.

These requirements shall apply to complete measurement chains including sensors and data processing.

Table 5 — Dry heat resistometer instrumentation requirements (measurement and recording)

Measurement	Unit	Scale range	Resolution	Measurement accuracy (+/–)[a]	Response time ms
Time	HH:MM:SS	Selectable	00:00:01	00:00:01	—
Temperature	°C	120 to 200	0,1	0,5	≤500
[a] The measurement accuracy over the test condition range (see 4.1).					

4.6.2 Data

Data from the measurements specified in Table 5 shall be provided at a sampling interval of not less than one data point per second and may be electronically archived.

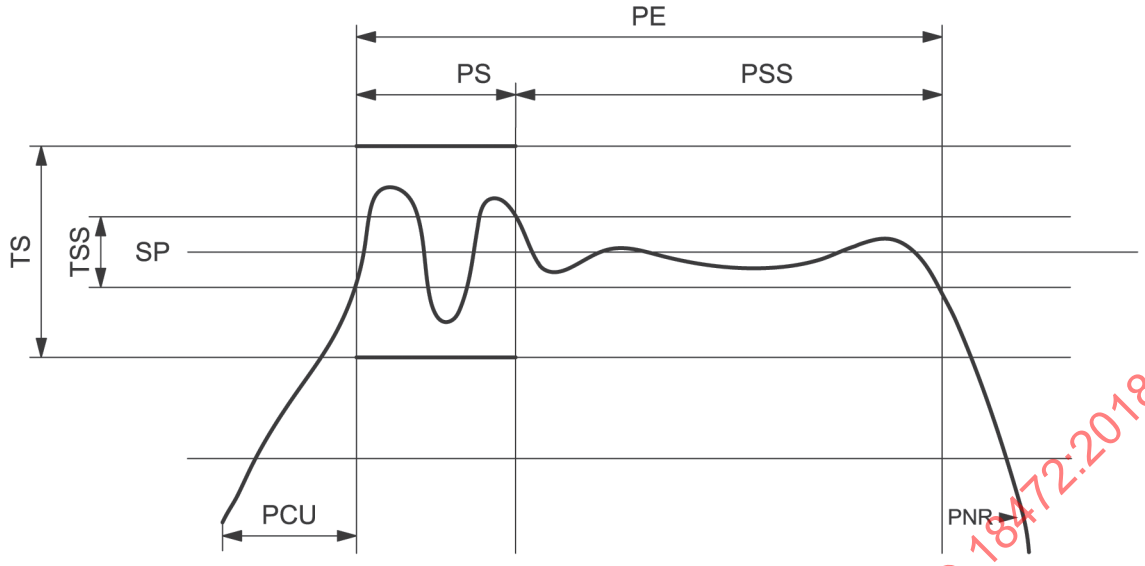
If this data is required to be recorded, the recording interval is at the user's discretion.

4.6.3 Process control

The dry heat resistometer process control shall control the parameters to the tolerances as specified in Table 6.

Table 6 — Dry heat resistometer physical design/control specifications

Parameter	Units	Range	Tolerance (+/–)
Time	HH:MM:SS	Selectable	00:00:02
Temperature	°C	120 to 200	2,5[a]
Come-up period	HH:MM:SS	≤00:01:00	—
Come-down period	HH:MM:SS	≤00:01:00	—
Stabilization period	HH:MM:SS	≤00:02:00	—
[a] After a 2 min stabilization time (see Figure 3).			



Key

PS	stabilization period	PNR	null reaction point example
PSS	steady-state period	SP	set point
PE	exposure period	TS	stabilization tolerance
PCU	come-up period	TSS	steady-state tolerance

Figure 3 — Stabilization time for temperature tolerance for dry heat resistometer

4.6.4 General dry heat (heated air) resistometer requirements

4.6.4.1 Test samples shall be loaded on to a suitable sample holder. The sample holder shall not adversely affect the performance of the indicator.

4.6.4.2 Test gas (generally air) shall be of the type for the indicator's intended use.

4.6.4.3 The null reaction point shall be specified and demonstrated by experimentation or by calculation using published data.

4.6.5 Operation of dry heat (heated air) resistometer

4.6.5.1 Before initiating a test cycle, the inner surface of the chamber shall be heated to the test temperature.

This can require thermostatic control of the inner surfaces of the chamber and/or door to be at the selected operating temperature.

4.6.5.2 Data from controlled values shall be provided at an interface for recording purposes within a minimum frequency of 1 s.

NOTE 1 For additional applications of dry heat resistometers, see Annex C.

NOTE 2 For examples of resistometer test cycle documentation, see D.4.

4.7 Vaporized hydrogen peroxide resistometer performance requirements

4.7.1 Measurement accuracy

The H_2O_2 resistometer shall be capable of measuring the following conditions within the limits given in Table 7.

The sensors used to measure temperature and pressure from within the H_2O_2 resistometer shall have a response time as specified in Table 7. For temperature this step change shall be from 20 °C to 90 °C and for pressure this step change shall be from 10 kPa to 100 kPa. The system used to record time, temperature, pressure and hydrogen peroxide concentration and water from within the resistometer shall be capable of operation with a resolution and measurement accuracy within the scale range specified in Table 7.

The measurement systems used may operate beyond the scale range specified as long as the limiting values within the scale range specified in Table 7 are attained.

These requirements shall apply to complete measurement chains including sensors and data processing.

Table 7 — Vaporized hydrogen peroxide resistometer instrumentation requirements (measurement and recording)

Measurement	Unit	Scale range	Resolution	Measurement accuracy (+/−)[a]	Response time ms[b]
Time	HH:MM:SS	Selectable	00:00:01	00:00:01	—
Temperature	°C	20 to 60	0,1	1,0	≤500
Pressure	kPa	0 to 102	0,01	0,25	≤30
Hydrogen peroxide vapour concentration	mg/l	1 to 10	0,1	0,3	—
Water concentration	mg/l	1 to 20	0,1	0,3	—

[a] Measurement accuracy over the test condition range (see 3.7 and 4.1).

[b] See 3.13.

NOTE A different method of measuring H_2O_2 can be used compared to the method used to measure H_2O.

4.7.2 Recording interval

Data from the measurements specified in Table 7 shall be provided at a sampling interval of not less than one data point per second and may be electronically archived.

If this data is required to be recorded, the recording interval is at the user's discretion.

The sterilizing agent concentration shall be measured using a suitable sensor. Pressure measurement shall not be used as the sole form of determining the sterilizing agent concentration.

4.7.3 Process control

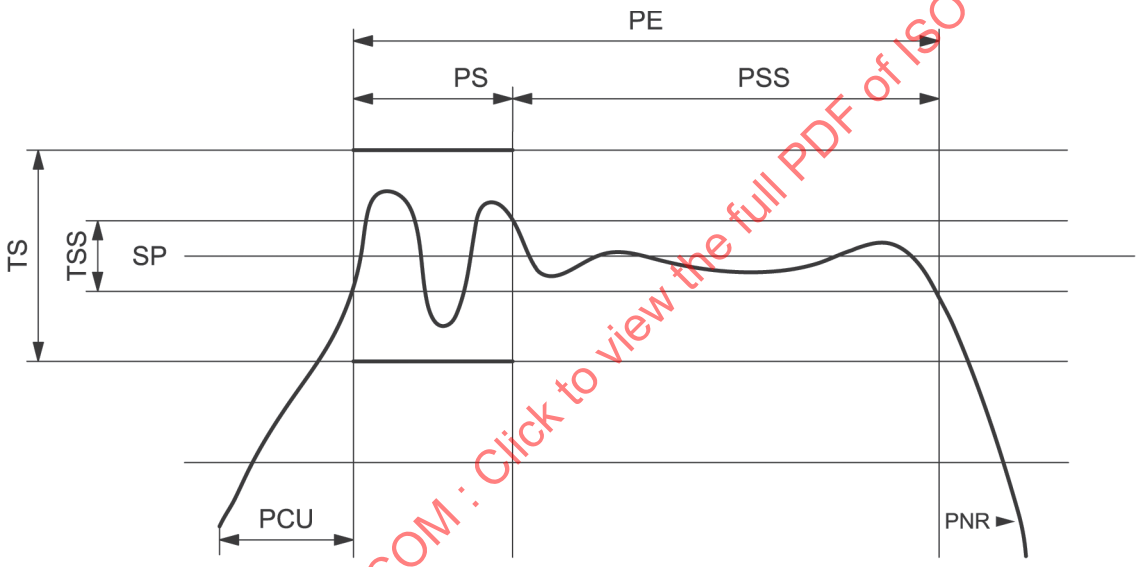
The vaporized hydrogen peroxide resistometer process control shall control the parameters to the tolerances as specified in Table 8.

Table 8 — Vaporized hydrogen peroxide resistometer physical design/control specifications

Parameter	Units	Range	Tolerance (+/−)
Time	HH:MM:SS.S	Selectable	00:00:01,0
Temperature	°C	20[b] to ≤45 >45 to 60	3,0[a,b] 1,0
Pressure	kPa	0 to 102	0,25
Hydrogen Peroxide concentration	mg/l	1 to 5	0,3
Come-up period	HH:MM:SS	≤00:00:10	—
Come-down period	HH:MM:SS	≤00:00:10	—
Stabilization period	HH:MM:SS	≤00:00:10	—

[a] This value may be limited by ambient temperature.

[b] During stabilization period.



Key

PS stabilization period
PSS steady-state period
PE exposure period
PCU come-up period
PNR null reaction point example
SP set point
TS stabilization tolerance
TSS steady-state tolerance

Figure 4 — Stabilization time for temperature for hydrogen peroxide resistometer

4.7.4 General vaporized hydrogen peroxide resistometer requirements

4.7.4.1 Air admitted at the end of the cycle shall be filtered through a filter having the ability to remove not less than 99,5 % of 0,5 µm particles.

4.7.4.2 The sample holder should allow the indicator to be exposed to the test conditions in the manner intended by the indicator manufacturer.

The various types of indicator may require customized sample holders. Sample holders may have to be constructed to hold test items in different vertical and horizontal attitudes in order to test performance.

NOTE Consult the indicator manufacturer for guidance when verifying label claim performance.

4.7.4.3 The test system, including the chamber and the door, shall be provided with means to maintain the temperature of the inner surfaces above the dew point for the test temperature. The chamber environment shall be at thermal equilibrium with control set points before a cycle shall be initiated.

4.7.4.4 The contact surface of the chamber and the sample holder shall be constructed from materials that do not interfere with the sterilizing agent concentration.

NOTE Consideration can be given to desorption of hydrogen peroxide from all inner surfaces and materials, including the chamber, the door, fixed furniture and sample holder, before initiation of the next cycle.

4.7.4.5 The null reaction point shall be specified and demonstrated by experimentation or by calculation using published data.

4.7.5 Air leakage test

When determined by the method given in 4.3, the air leakage rate shall not be greater than $5{,}0 \times 10^{-3}$ kPa/min (0,05 mbar/min).

4.7.6 Operation of vaporized hydrogen peroxide resistometer

4.7.6.1 The chamber shall be designed such that the formation of condensate during any stage of the operating cycle does not adversely affect the required test conditions. In order to avoid excessive condensate formation during the operating cycle it might be necessary to provide thermostatic control of the inner surfaces of the resistometer so that they can be maintained at a specified temperature (e.g. the exposure period temperature).

NOTE Any water condensate in the chamber may absorb large amounts of gaseous hydrogen peroxide and thus influence hydrogen peroxide vapour concentration.

4.7.6.2 Before initiating a test cycle, the inner surface of the chamber shall be heated to the test temperature.

4.7.6.3 The equipment shall be provided with a means of evacuating the chamber to less than the vacuum set point to permit air removal prior to admission of hydrogen peroxide.

4.7.6.4 Data from controlled values shall be provided at an interface for recording purposes within a minimum frequency of 1 s. Water concentration in mg/l shall be recorded.

NOTE For examples of resistometer test cycle documentation, see D.4.

5 Calibration

Calibration shall be carried out using a working or reference standard that is traceable to the national standard or primary standard.

NOTE Calibration procedures are provided in ISO/TR 10013.

Annex A
(informative)

Additional performance characterization — Steam

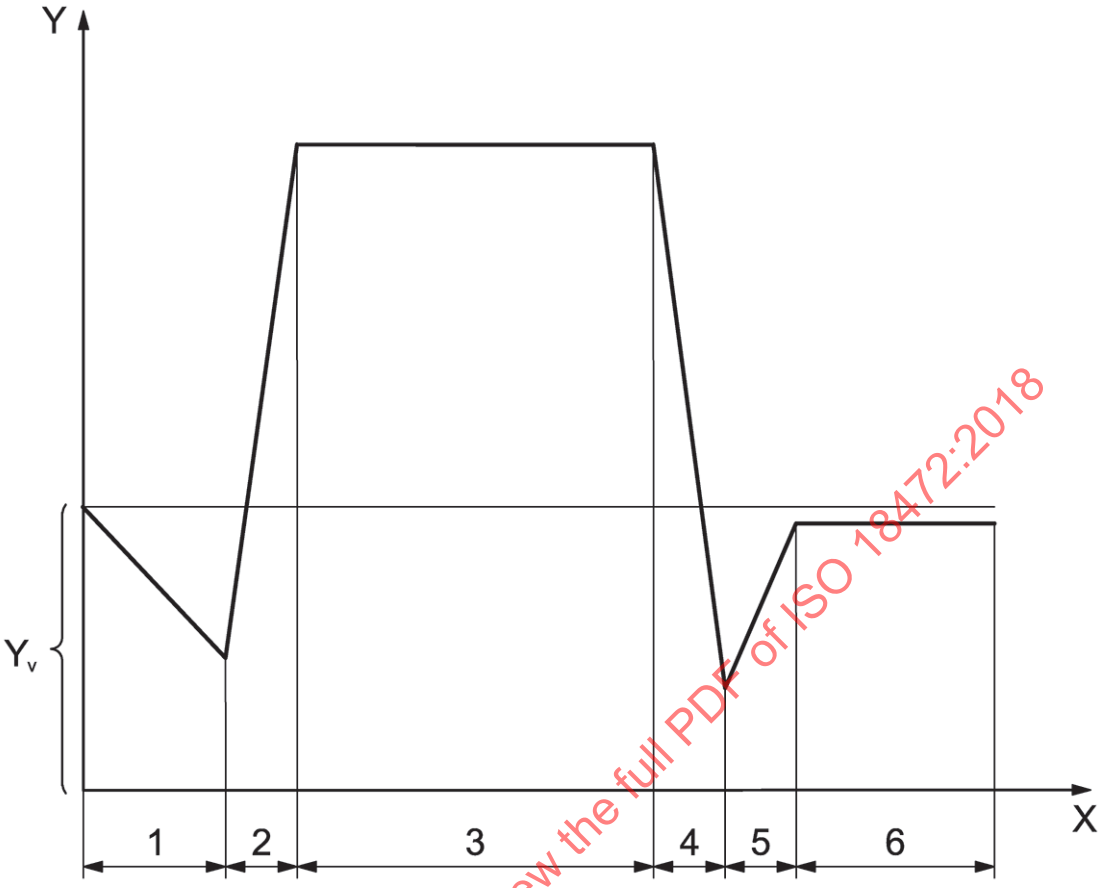
A.1 General

There are many factors that can influence the performance of the biological and chemical indicators used to evaluate different types of steam sterilization processes. Tests are performed on a routine basis as prescribed in ISO 11138-3:2017 and ISO 11140-1:2014 to characterize indicator performance. In addition to these normative tests, other tests also may be used to verify that indicators are suitable for their intended applications.

If the chamber temperature is higher than the pressure corresponding to saturated steam, a condition of superheated steam is present.

Superheated steam is a recognized fault condition in steam sterilization; this may be created in a resistometer by increasing the jacket temperature relative to the chamber temperature.

Figure A.1 graphically depicts the typical sequence of a steam resistometer used in saturated steam exposure processes.



Key

X time
Y steam pressure
Y_v vacuum
1 air removal: air is removed from the test chamber by evacuation to a selected vacuum level
2 come-up: steam is injected into the test chamber until the selected test temperature is attained
3 exposure period: the test chamber is maintained at the selected test temperature for the selected exposure period
4 come-down: the test chamber is exhausted to a selected level
5 air vent: the test chamber is vented to atmospheric pressure
6 cycle complete: test samples are manually removed from the chamber

Figure A.1 — Steam test sequence

A.2 Chamber air removal

There are demonstrable differences in indicator performance based upon residual air in the test system/indicator device. Varying the level of chamber air removal provides information relative to the change in performance expected for indicators with processes that use different vacuum levels and types of air removal prior to come-up to the selected sterilization temperature. If this range of tests is used, a range of depths of vacuum should be tested in order to characterize product performance.

A.3 Vacuum/pressurization rate

Alteration of the vacuum/pressurization rate can be utilized to evaluate device damage and resultant performance change related to the rate at which pressure changes in sterilization processes. During

resistometer testing, pressure changes occur at rates significantly faster than expected in normal applications. If the resistometer is capable of slower pressure changes, indicators may be tested using slower pressurization and evacuation phases. Observations that have been reported to produce changes in indicator performance might include:

a) indicating chemicals migrating by capillary action rather than wicking along the intended path;

b) ballooning of the primary package resulting in inconsistent synergistic inactivation characteristics (air/steam mixtures);

c) delamination;

d) dehydration/desiccation and sublimation;

e) rates of chemical reactions.

NOTE An observation view port or camera is helpful for visual observation of physical changes of the indicator that could affect performance of the indicator.

A.4 Range characterization

Indicators may be tested over the application range specified by the manufacturer in order to quantify performance characteristics. This type of testing will generally be as prescribed by the applicable normative standards for a given type of indicator, and can be performed whenever there is a change to the indicator design or manufacturing process.

A.5 Indicator orientation

How an indicator is staged within a resistometer can influence its performance. For example, placing a self-contained biological indicator (SCBI) on its side (versus standing it straight up or placing it upside down) has been shown to influence its resistance characteristics, most likely due to ingress and egress of steam due to vacuum and the configuration of the embodiment. Another example of how orientation can affect product performance is placement of a hot melt wicking indicator where the direction and extent of wicking action is augmented by gravity.

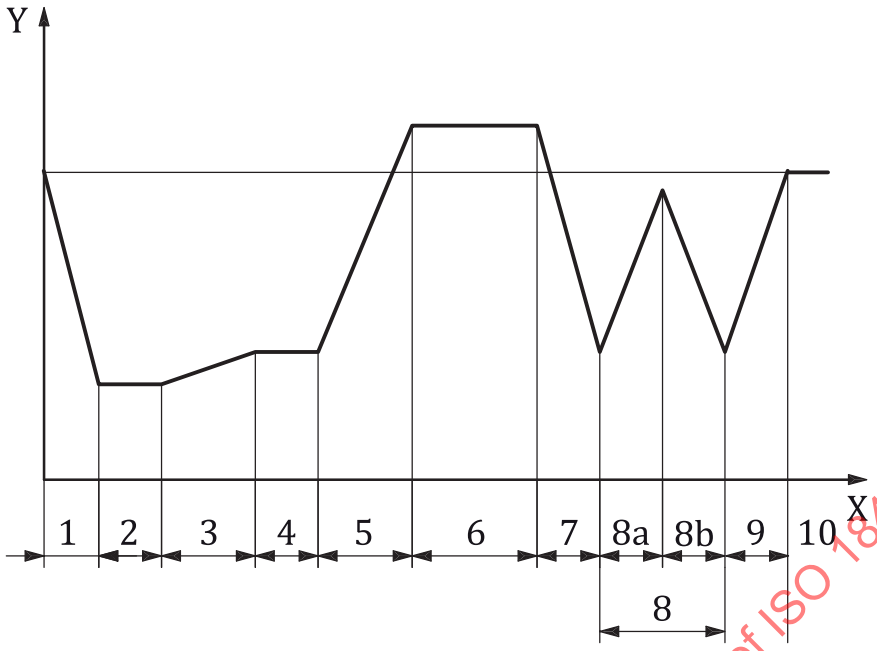
Annex B
(informative)

Additional performance characterization — Ethylene oxide gas

B.1 General

There are many factors that can influence the performance of the biological and chemical indicators used to evaluate different types of ethylene oxide gas sterilization processes. Tests are performed on a routine basis as prescribed in ISO 11138-2:2017 and ISO 11140-1:2014 to characterize indicator performance. In addition to these normative tests, other tests may also be used to verify that the indicators are suitable for their intended applications.

Figure B.1 graphically depicts the typical sequence of an ethylene oxide gas resistometer used in ethylene oxide gas exposure processes.



Key

X time
Y absolute pressure
1 pre-vacuum
2 vacuum hold
3 humidification
4 humidity dwell
5 sterilizing agent charge
6 exposure
7 exhaust/post vacuum
8 air wash: the test chamber is pressurized with air to a selected level (8a) and evacuated to a selected vacuum level (8b) for a selected number of times
9 air vent
10 cycle complete

Figure B.1 — Sequence of ethylene oxide gas resistometer used in ethylene oxide gas exposure processes

B.2 Chamber air removal

Residual air in the test system/indicator device can result in demonstrable differences in indicator performance. The chamber air removal test provides information relative to the change in performance expected for indicators with processes that use different vacuum levels and mechanical air removal techniques prior to admission of ethylene oxide gas. Results are compared to the performance requirements for the respective indicators.

B.3 Vacuum/pressurization rate

Alteration of the vacuum/pressurization rate can be utilized to evaluate device damage and resultant performance change related to the rate at which pressure changes in sterilization processes. During resistometer testing, pressure changes occur at rates significantly faster than expected in normal applications. If the resistometer is capable of slower pressure changes, indicators may be tested using

slower pressurization and evacuation phases. Observations that have been reported to produce changes in indicator performance might include:

— ballooning of the primary package;

— delamination.

NOTE An observation view port or camera is helpful for visual observation of physical changes of the indicator that could affect performance of the indicator.

B.4 Range characterization

Indicators may be tested over the application range specified by the manufacturer to quantify performance characteristics. This type of testing will generally be as prescribed by the applicable normative standards for a given type of indicator, and can be performed whenever there is a change to the indicator design or manufacturing process.

Annex C
(informative)

Additional performance characterization — Dry heat

C.1 General

There are some factors that can influence the performance of the biological and chemical indicators used to evaluate different types of dry heat sterilization processes. Tests are performed on a routine basis as prescribed in ISO 11138-4:2017 and ISO 11140-1:2014 to characterize indicator performance. In addition to these normative tests, other tests may also be used to verify that the indicators are suitable for their intended applications.

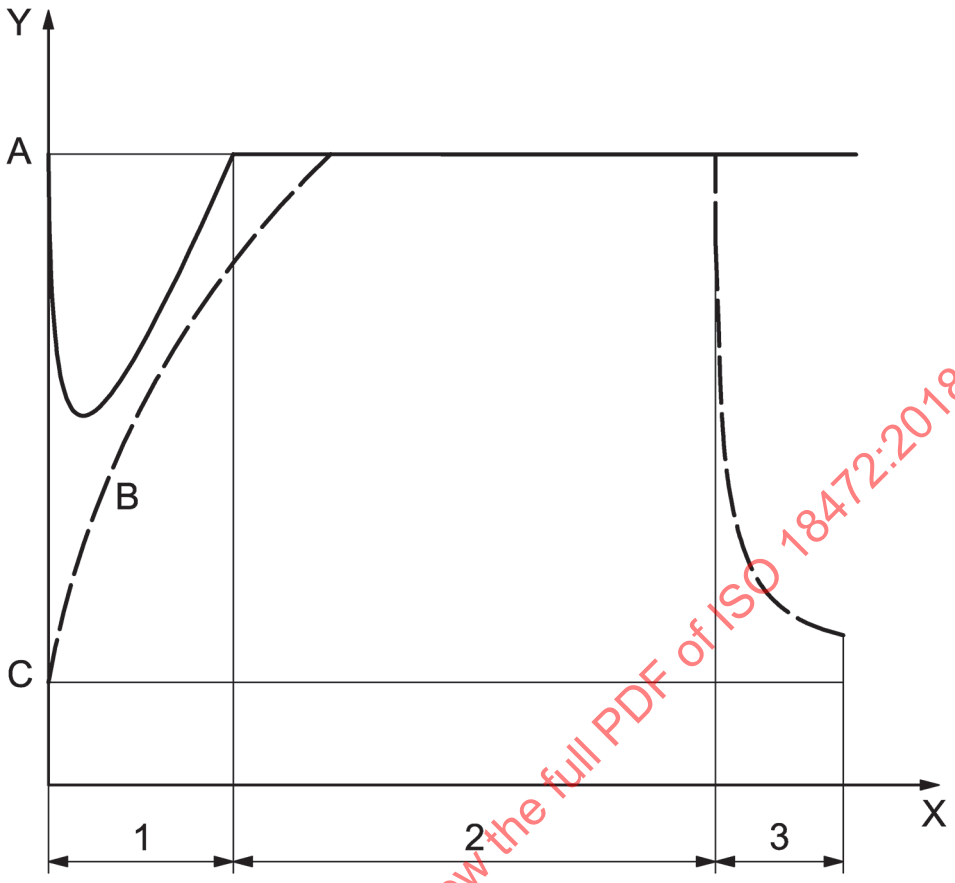
Figure C.1 graphically depicts the typical sequence of the resistometer used in a dry heat exposure process.

C.2 Specific variable response

Indicators that are designed to react to multiple variables or parameters may react partially or completely on exposure to only one of the critical process parameters. Indicators may be exposed to different combinations of these variables in order to observe the indicator response. This may include exposing the indicators to temperatures or conditions slightly outside of specified values.

C.3 Range characterization

Indicators may be tested over the application range specified by the manufacturer in order to quantify performance characteristics. This type of testing will generally be as prescribed by the applicable normative standards for a given type of indicator, and may be performed whenever there is a change to the indicator design or manufacturing process.



Key

X time

Y temperature

A exposure temperature

B sample temperature

C ambient temperature

1 sample placement: the test samples are placed in a preheated test environment that is designed to recover to the selected test temperature within the times specified in the normative references

2 exposure period: the test chamber is maintained at the selected test temperature for the selected exposure period

3 cycle complete: test samples are manually removed from the test environment

NOTE An observation view port or camera is helpful for visual observation of physical changes of the indicator that could affect performance of the indicator.

Figure C.1 — Sequence of dry heat resistometer used in dry heat exposure processes

Annex D
(informative)

Resistometer documentation and derivations

D.1 General

Resistometer documentation presents cycle information from each cycle that is performed. These data may be presented digitally or graphically, provided they meet the requirements of this document.

D.2 Calculation of relative humidity concentration

D.2.1 Relative humidity is the ratio of the mass or partial pressure in an environment to the mass or partial pressure that a saturated environment could hold at a given temperature, by definition. This ratio is usually expressed as percent relative humidity (% RH) by multiplying the ratio by 100. Measurement of relative humidity is typically determined by measuring the partial pressure of water vapour in an enclosed environment. Humidity determinations of ±5 % RH are reasonably obtained. Mathematically this is expressed as follows:

$$\%\,\mathrm{RH} = \frac{p_{H_2O}}{p^*_{H_2O}} \times 100 \qquad \text{(D.1)}$$

where

p_{H_2O} is the actual partial pressure of water vapour (at test temperature);

$p^*_{H_2O}$ is the saturation vapour pressure of water (at test temperature).

EXAMPLE

Test temperature: 54,4 °C

Saturation pressure at 54,4 °C (steam table): 15,3 kPa

Measured partial pressure (humidity added): 8 kPa

$$\%\,\mathrm{RH} = \frac{8\ \mathrm{kPa}}{15{,}3\ \mathrm{kPa}} \times 100\,\% = 52{,}3\,\%\ \mathrm{RH}$$

D.2.2 Primary measurement of relative humidity is best performed by direct measurement of physical properties using instrumentation that is easy to calibrate and that maintains measurement accuracy, such as temperature and pressure measurement devices. Direct measurement of humidity is typically performed by measurement of partial pressure at a temperature as described above or by dew point measurement.

Dew point is typically used for environmental monitoring, as the measurement/response time is usually too slow for control of fast processes. Dew point measurement uses a mirror that is chilled to a temperature at which the environmental humidity condenses. The formation of condensate on the surface of the mirror is detected using a photo sensor and light emitting source combination. The condensation temperature represents the saturation temperature or dew point. A dew point can be expressed in terms of relative humidity using the same format as above, but substituting the dew point