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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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Contents

Page

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

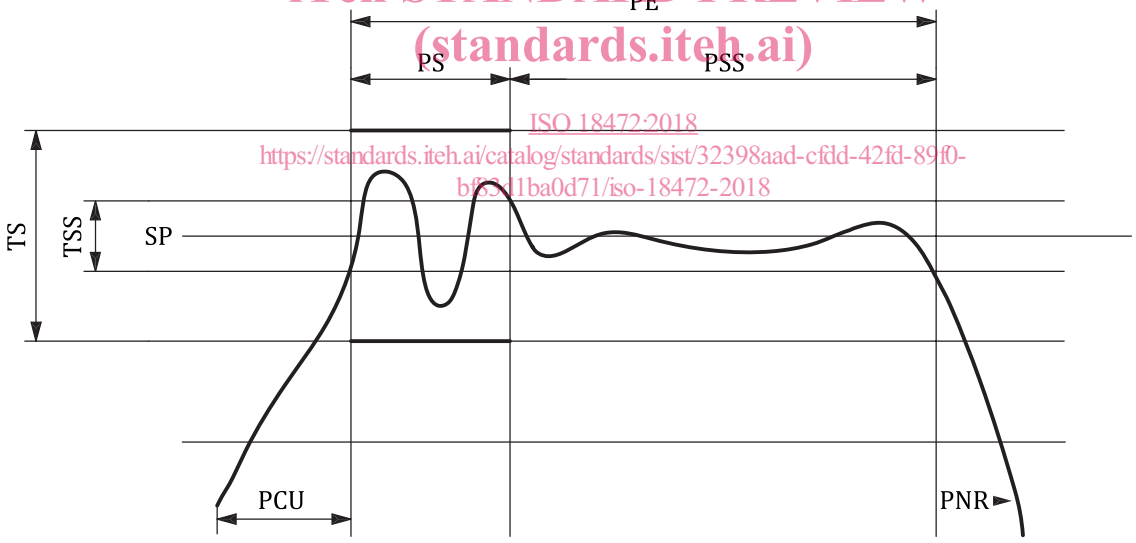
Parameter	Unit	Range	Tolerance (+/−)
Time	HH:MM:SS	Selectable	00:00:01
Temperature	°C	110 to 145	0,5[a], 1,0[d]
Pressure	kPa	>100 to 420	3,5[a,c]
	kPa	3 to ≤100	1,0
Time to achieve vacuum set point	HH:MM:SS	≤00:02:00[b]	–
Come-up period	HH:MM:SS	≤00:00:11	–
Come-down period	HH:MM:SS	≤00:00:11	–
Stabilization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