INTERNATIONAL STANDARD

ISO 18472

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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.

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 18472 was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

This first edition of ISO 18472 partially replaces ISO 11140-2.

Introduction

To test the performance of chemical and biological indicators, specific test equipment is required. This International Standard specifies the performance requirements for the test equipment to be used in order to establish the response of chemical and biological indicators to critical process variables. This International Standard does not apply to test equipment for irradiation indicators or low temperature steam and formaldehyde indicators.

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 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 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 accuracy. Practical design has to consider the following:

— 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

1.1 This International Standard specifies the requirements for test equipment to be used to test chemical and biological indicators for steam, ethylene oxide, dry heat and vaporized hydrogen peroxide processes for conformity to the requirements given in ISO 11140-1 for chemical indicators, or the requirements given in the ISO 11138 series for biological indicators. This International Standard also provides informative methods useful in characterizing the performance of biological and chemical indicators for intended use and for routine quality control testing.

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

NOTE Resistometers for formaldehyde indicators are not included in this International Standard. Test methods using laboratory apparatus for steam-formaldehyde are included in ISO 11138-5, ISO 11140-3 and ISO 11140-4.

1.2 This International Standard does not address the methods used to demonstrate compliance of biological or chemical indicators to ISO 11138 and ISO 11140, as these are covered in the appropriate parts of these standards. Indicators used with combination processes, such as washer-disinfection, are not covered by this International Standard.

NOTE Test equipment and methods necessary for ISO 11140-3, ISO 11140-4 or ISO 11140-5 are specified in those standards.

1.3 This International Standard does not address safety aspects of the test equipment because these are usually covered by specific regional, national or local regulations.

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

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

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

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

ISO 11140-4[1)], *Sterilization of health care products —Chemical indicators — Part 4: Class 2 indicators as an alternative to Bowie and Dick test for detection of steam penetration*

ISO 17665-1, *Sterilization of health care products — Moist heat — Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices*

IEC 60584 (all parts), *Thermocouples*

IEC 60751:1983, *Industrial platinum resistance thermometer sensors*

3 Terms and definitions

For the purpose of this document, the terms and definitions given in ISO 11138, ISO 11140 and the following apply.

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

[ISO/TS 11139:2006, definition 2.3]

3.2
calibration
set of operations that establish, under specified conditions, the relationship between values indicated by a measuring instrument or measuring system, or values represented by a material measure or a reference material, and the corresponding values realized by standards

[VIM 1993, definition 6.11]

3.3
chemical indicator
non-biological indicator
system that reveals change in one or more predefined process variables based on a chemical or physical change resulting from exposure to a process

[ISO/TS 11139:2006, definition 2.6]

3.4
come-up period
time elapsed from the introduction of the sterilizing agent to the attainment of the minimum specified exposure conditions

3.5
come-down period
time elapsed from the termination of the exposure period to an established null reaction point

3.6
exposure period
time from the initial attainment of the minimum specified exposure conditions to the termination of the exposure period

NOTE This phase of the cycle includes the stabilization period and the steady state period

1) To be published. (Revision of ISO 11140-4:2001)

3.7
measurement accuracy
closeness of the agreement between the result of a measurement and the true value of the measurement

NOTE 1 "Accuracy" is a qualitative concept.

NOTE 2 The term "precision" should not be used for "accuracy".

3.8
null reaction point
terminating set of conditions that are either specified in the document or have been established and demonstrated to produce no significant effect on the indicators

3.9
precision
degree of reproducibility of a measurement

3.10
reference standard
standard, generally having the highest metrological quality available at a given location or in a given organization, from which measurements are derived

3.11
resistometer
test equipment designed to create defined combinations of the physical and/or chemical variables of a sterilization process

NOTE Resistometers were formerly referred to as a Biological Indicator Evaluator Resistometer (BIER) or Chemical Indicator Evaluator Resistometer (CIER) test systems.

3.12
response time
time required for a 90 % change in sensor output when exposed to a step change in the variable being measured

NOTE 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 International Standard. Documentary evidence from the sensor manufacturer's stated response time is equally acceptable as proof of conformance.

3.13
saturated steam
water vapour in a state of equilibrium between condensation and evaporation

3.14
stabilization period
elapsed time from the attainment of the minimum specified exposure conditions until the end of the defined time to achieve steady state conditions

3.15
steady state period
that portion of the exposure period which begins after the stabilization period and terminates at the end of the exposure period, during which time all control parameters are within the specified limits

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, ISO 11138-3, ISO 11138-4 and ISO 11140-1, the resistometer utilized need only verify those limits necessary to characterize the chemical or biological indicators.

NOTE The following specifications 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.

4.2 Measurement and control capabilities

The following performance requirements define the measurement and control capabilities for steam, ethylene oxide, dry heat, and vaporized hydrogen peroxide resistometers.

4.3 Test methods

The equipment specified in this International Standard shall be used with the detailed test methods given in the appropriate parts of ISO 11138 and ISO 11140.

NOTE The claimed performance tolerances for chemical and biological indicators are based on the specified exposure conditions without allowance for the operational tolerances of the test equipment.

4.4 Leak test

4.4.1 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 condensation 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 fitted with a test cycle for air leakage that will carry out this procedure automatically and display the air leakage in kPa/min (mbar/min).

4.4.2 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.

4.5 Steam resistometer performance requirements

4.5.1 Measurement accuracy

The sensors used to measure temperature, vacuum and pressure from within the steam resistometer shall have a response time as specified in Table 1. The system used to record time, temperature, vacuum and pressure from within the steam resistometer shall be capable of operation with a resolution and accuracy within the scale range specified in Table 1.

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

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

Table 1 — Steam resistometer instrumentation requirements

Measurement	Unit	Scale range	Resolution	Accuracy (+/–)[a]	Sensor response time ms
Time	HH:MM:SS	Selectable	00:00:01	00:00:01	—
Temperature	°C	110 to 145	0,1	0,5	⩽ 500
Vacuum	kPa	0 to 100	0,1	1,0	⩽ 30
Pressure	kPa	100 to 420	0,1	3,5	⩽ 30

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

4.5.2 Recording interval

The measurement system shall have a recording interval for each of the measurements specified in Table 1 of not less than one data point per second.

The data may be electronically archived and the print interval can be at the user's discretion.

4.5.3 Process control

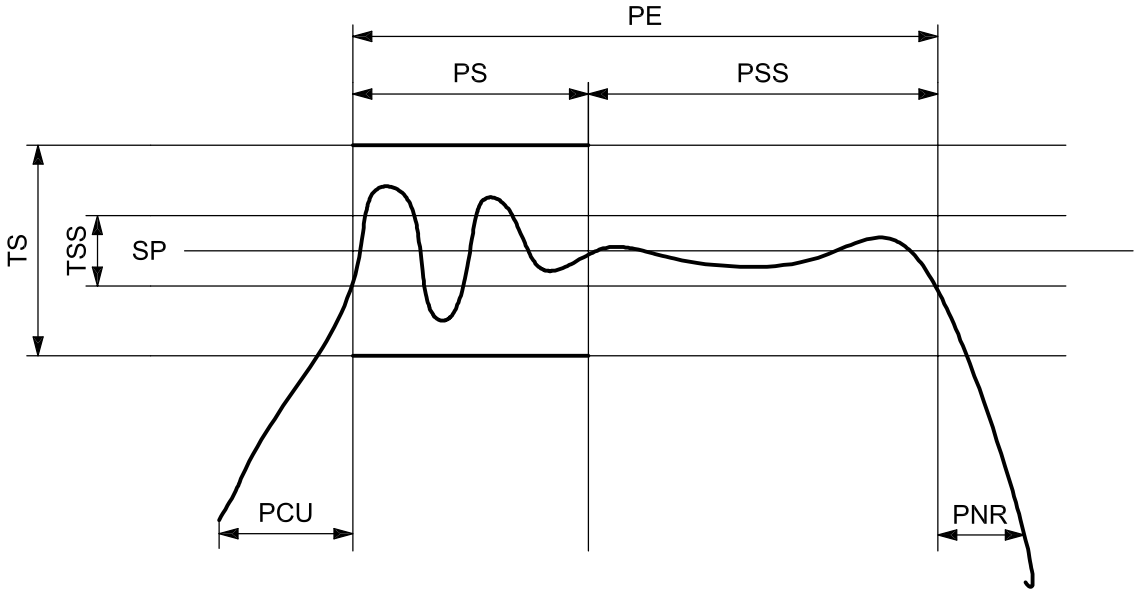
The steam resistometer process control shall be capable of producing the conditions given in Table 2.

Table 2 — Steam resistometer physical design/control specifications

Parameter	Unit	Range	Tolerance (+/–)
Time	HH:MM:SS	Selectable	00:00:01
Temperature	°C	110 to 145	0,5[a]
Pressure	kPa	100 to 420	3,5[a]
Vacuum	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	⩽ 00:00:10	–
Come-down period	HH:MM:SS	⩽ 00:00:10	–
Stabilization period		⩽ 00:00:10 HH:MM:SS	1,0 °C

[a] During steady state period (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).



Key

PS	stabilization period	PNR	null reaction point
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

4.5.4 General steam resistometer requirements

4.5.4.1 The chamber shall be supplied with saturated steam from a source external to the chamber. The steam supply shall meet the requirements of ISO 11140-4. Means shall be provided to ensure that the test items are not wetted by entrained water droplets in the steam supply.

4.5.4.2 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.

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

4.5.5 Air leakage test

When determined by the method given in 4.4, the air leakage rate shall not be greater than 0,13 kPa/min × (54,8/V_c) where V_c is the chamber volume in litres.

4.5.6 Operation of steam 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 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 phase temperature).