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Washer-disinfectors —

Part 5: Performance requirements and test method criteria for demonstrating cleaning efficacy

Laveurs désinfecteurs —

Partie 5: Exigences de performance et critères des méthodes d'essai pour démontrer l'efficacité du nettoyage

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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).

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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*, in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 102, *Sterilizers and associated equipment for processing of medical devices*, in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This first edition of ISO 15883-5 cancels and replaces ISO/TS 15883-5:2005, which has been technically revised. The main changes compared to the previous edition are as follows:

— new and previous terms and definitions were harmonized with ISO 11139:2018;

— considerations for selection of an appropriate test soil and test load have been included;

— performance requirements to demonstrate cleaning efficacy of a washer-disinfector were consolidated and specified;

— cleaning efficacy test and acceptance criteria for the type test and performance qualification test have been specified for a variety of analytes;

— alert and action levels were introduced for analytes to facilitate interpretation of cleaning validation data;

— examples of test soils relevant to certain procedures, as referenced in published literature, and suitable assay methods for detection or quantification of certain soil residuals have been included in Annex A;

— the immersion test protocol resulting from interlaboratory tests to evaluate cleaning performance of a protein-based test is specified in Annex B, together with examples of worksheets to assist laboratories performing the test in an Annex E;

— examples of protein detection methods were revised and transferred across from ISO 15883-1:2006 to informative Annex C;

— examples of haemoglobin detection methods were added to informative Annex D;

— extensive revision of the Bibliography.

A list of all parts in the ISO 15883 series can be found on the ISO website.

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

Testing of cleaning efficacy is a key aspect of establishing satisfactory performance of a washer-disinfector (WD). This testing includes type testing under simulated use conditions. In addition to type testing, performance qualification testing is performed under clinical use conditions.

The cleaning efficacy of washer-disinfectors has historically been demonstrated by referring to different test soils and methods that have been used in several different countries. This document gives requirements for standardized methods for demonstration of cleaning efficacy, including examples of test soils. The individual requirements for the various types of washer-disinfectors and processing procedures can vary, but this document provides the basis for the demonstration of cleaning efficacy.

Cleaning efficacy testing is performed in the WD and with associated accessories in two phases:

— type testing, under simulated use conditions, with defined test soils and their analytes, soiling methods and test surfaces/medical devices/product representative of design and intended applications;

— performance qualification testing under clinical conditions with load(s) that are soiled with the most challenging soil from clinical use.

This document excludes the verification of cleaning of product that could have been exposed to prions, the causative agent in transmissible spongiform encephalopathies such as Creutzfeldt-Jakob disease (CJD).

Washer-disinfectors —

Part 5: Performance requirements and test method criteria for demonstrating cleaning efficacy

1 Scope

This document specifies procedures and test methods used to demonstrate the cleaning efficacy of washer-disinfectors (WD) and their accessories intended to be used for cleaning of reusable medical devices.

NOTE 1 The requirements can be used for washer-disinfectors intended for use with other articles used in the context of medical, dental, laboratory, pharmaceutical and veterinary practice.

NOTE 2 This document does not apply to the activities to be performed by the manufacturers of reusable medical devices.

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 10993-1, *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process*

ISO 10993-5, *Biological evaluation of medical devices — Part 5: Tests for in vitro cytotoxicity*

ISO 15883-1:—[1)], *Washer-disinfectors — Part 1: General requirements, terms and definitions and tests*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 15883-1 and the following apply.

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

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

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

3.1
action level
value from monitoring that necessitates immediate intervention

[SOURCE: ISO 11139:2018, 3.5]

1) Under preparation. Stage at the time of publication: ISO/DIS 15883-1:2020.

3.2
alert level
value from monitoring providing early warning of deviation from specified conditions

[SOURCE: ISO 11139:2018, 3.11]

3.3
analyte
chemical substance that is the subject of chemical analysis

[SOURCE: ISO 11139:2018, 3.12]

3.4
clean
visually free of soil and below specified levels of *analytes* (3.3)

[SOURCE: ISO 11139:2018, 3.45]

3.5
clinical use
use of a health care product during a procedure on a patient

Note 1 to entry: This encompasses all steps prior to processing in a WD.

[SOURCE: ISO 11139:2018, 3.49, modified – Note 1 to entry has been added]

3.6
load
product, equipment, or materials to be processed together within an operating cycle

[SOURCE: ISO 11139:2018, 3.155]

3.7
product
tangible result of a process

EXAMPLE Raw material(s), intermediates(s), sub-assembly(ies), health care product(s)

[SOURCE: ISO 11139:2018, 3.217]

3.8
rinsing
removing process residues through displacement by, and dilution with, water

[SOURCE: ISO 11139:2018, 3.237]

3.9
simulated use
use that mimics the intended use of the medical device

3.10
soil
natural or artificial contamination on a device or surface following its use or simulated use

[SOURCE: ISO 11139:2018, 3.257]

3.11
surrogate product
item designed to represent product in process simulations and which is comparable with the actual product

[SOURCE: ISO 11139:2018, 3.291]

3.12
test soil
formulation designed for use as a substitute for a contaminant or debris found on a device after use

[SOURCE: ISO 11139:2018, 3.300]

3.13
washing
removal of contaminants from surfaces by means of an aqueous fluid

[SOURCE: ISO 11139:2018, 3.321]

4 Performance requirements

4.1 General

4.1.1 In addition to the requirements below (see 4.1.3 to 4.1.5), the relevant cleaning performance requirements of the subsequent parts of ISO 15883 that apply to the washer-disinfector type shall apply.

4.1.2 In addition to the tests specified in 4.1.4 and 4.1.5), the relevant cleaning tests of the subsequent parts of ISO 15883 that apply to the washer-disinfector type shall apply.

NOTE See for example ISO 15883-7[5].

4.1.3 The process conditions for cleaning, e.g. stages, temperatures, pressure, flow, process chemicals, quality and quantity of water, used to confirm conformance of the WD with the requirements of this standard shall be defined in accordance with ISO 15883-1:—, 4.1.12 and 8.2 b).

NOTE Refer to ISO 15883-1:—, 5.23 and ISO 15883-4 [4] for water quality.

4.1.4 Tests of cleaning efficacy shall be performed on the defined cleaning stages, including, where appropriate, flushing, rinsing, etc. (see 5.2). Cleaning stages shall be specified according to ISO 15883-1:—, 4.1. It shall be verified and documented that the full cleaning stage does not interfere with analyte detection. During tests of cleaning efficacy, the WD shall be operated without any disinfection or drying stage and should not affect the efficacy and safety of the WD process.

4.1.5 Cleaning efficacy testing shall be performed in the WD and with accessories specified for the particular load in two phases:

a) type testing under simulated use conditions with defined test soil(s), including the analyte(s) and representative test load(s) (see 4.4.1),

b) performance qualification testing with worst-case load(s) soiled by clinical use (see 4.4.1), or if justified (5.4.2), with surrogate product.

4.2 Test soil considerations

4.2.1 The rationale for the choice of test soil(s) and soiling method(s) shall be justified and documented. Test soil formulations may be chosen or developed based on a review of the literature and demonstration of its relevance based on the use of the medical device/product in clinical practice (see Annex A and the Bibliography).

NOTE The test soils for the load, chamber walls and load carriers can be different.

4.2.2 The protein-based test soil shall conform to the performance criteria specified in B.2.

NOTE Sample result sheets for data entry are provided in Annex E.

4.2.3 The choice of test soil, its method of application, and conditioning (e.g. drying) shall simulate worst-case clinical use conditions of the load.

a) Composition of the test soil shall include the analyte(s) representative of soiling likely to be encountered during intended use of the product at a quantity justified by 4.2.1, and if applicable, any associated procedural material(s) used on the product during its clinical use, that are intended to be cleaned (e.g. contrast media, lubricants, etc.).

b) The method of test soil application shall simulate the conditions of use of the product, for example, cauterization or heating that present a greater challenge to cleaning, and/or pressure gradients that could facilitate the penetration of material into various parts of the product. Parts of the product identified as the most difficult to clean shall be soiled (see 4.3).

c) After application of the test soil on the product or test pieces, consideration shall be given to transport and dwell time conditions (e.g. temperature, time, humidity) for the product from point of use to place of processing, and if applicable, any pre-treatment (see 5.1.2.2).

d) The composition of the soil shall be characterized and the most difficult soil elements (e.g. lipids, adhesives, insoluble proteins, etc.) shall be identified and considered in the validation strategy to ensure that the validation activities demonstrate effective removal of the soil.

4.2.4 The method of test soil extraction, recovery efficiency, and detection of analytes shall be validated and specified. Validation of the recovery shall demonstrate the ability to reduce analyte below the action level.

An appropriate percent recovery is greater than 70 %, unless otherwise justified (see 5.1.3.2).

4.3 Load considerations

4.3.1 Load(s), including their respective product that represent typical and worst-case, clinical use conditions, shall be defined and justified. Such load(s) shall be used for cleaning efficacy and process residuals for type testing and performance qualification tests [see also ISO 15883-1:—, 8.1 b) and ISO 15883-4[4]. The load(s) shall be considered appropriate for the type of washer-disinfector being tested.

NOTE For type testing and performance qualification testing, when justified, the load can be surrogate product, which could be used for tests if they are shown to be representative of the prescribed load.

4.3.2 Consideration shall be given to any applicable physical characteristics of the product type(s) and patient contact area, including but not restricted to:

— lumens;

— valves;

— crevices;

— hinges and joints;

— rough and irregular surfaces;

— material composition, including porosity;

— junctions and dead ends;

— internal moveable parts (e.g. cables).

These design characteristics are at a greater risk of accumulation and retention of soil and shall be specifically considered in the estimation and risk assessment of cleaning efficacy and cleaning endpoints of the entire product.

NOTE See ASTM F3357[18] for additional detail on medical device design and cleaning.

4.3.3 Any necessary pre-treatment of the product specified in its IFU, e.g. manual pre-cleaning or disassembly, shall be included as part of the test procedure.

4.4 Cleaning efficacy test criteria

4.4.1 General

Cleaning efficacy shall be determined by visual examination (see 4.4.2) and by the quantitative detection of protein (see 4.4.3.2, Note and Annex B).

For invasive medical devices, at least one other validated quantitative analytical test method shall be used to measure another analyte(s) in addition to protein for type testing.

Non-invasive medical devices shall require visual examination only.

NOTE 1 Some non-invasive medical devices can represent higher levels of risk e.g. infant formula bottles, contact tonometers.

NOTE 2 A validated qualitative method (see References [22], [52], [54], [70] and[88]) can be used for routine testing when the detection level of this method is below the alert level assay criteria given in 4.4.3.

NOTE 3 Typical analytes are given in 4.4.3.2 and 4.4.3.3 (also see Bibliography).

NOTE 4 Refer to ISO 14971[3] for approach to risk assessment to support justification.

4.4.2 Visual examination

Visual examination shall demonstrate the absence of visible soil on all observable surfaces of the load(s), following cleaning stage(s). This requirement does not apply where adequate visual inspection of the surfaces of the product is not possible due to its configuration.

NOTE Adequate visual inspection requirements can include:

— defined instructions for inspection;

— adequate illumination;

— inspection aids, if applicable (e.g. lighted magnification boroscope);

— viewing distance.

Refer to EN 13018[10] and ASTM E3106[16] for additional information on visual inspection.

4.4.3 Assay criteria

4.4.3.1 General

Acceptance criteria for analytes are specified in terms of both an alert level and an action level.

The alert and action levels for protein and other analytes are specified in 4.4.3.2 and 4.4.3.3. Their action levels are the maximum criteria for acceptable cleaning efficacy during testing, but the target values are given as the alert levels. When both alert and action levels are specified, if analytes are detected at values between the two levels, they shall be investigated, but considered to pass cleaning requirements.

For the purpose of conforming to the requirements of 4.2 and 6.10 in ISO 15883-1:—, the action level shall be used.

NOTE The analyte values in this document are expressed per unit area (cm^2). Some regional and national guidance specify maximum analyte values per medical device or per medical device side. It is not possible to directly compare numerical values expressed per cm^2 to those values expressed per medical device or per medical device side, unless the surface area of the medical device or medical device side are known, and the appropriate conversion made.

4.4.3.2 Protein assay criteria

The protein assay criteria are:

— Alert level ≥ 3 µg/cm^2

— Action level ≥ 6,4 µg/cm^2

The maximum acceptable level of protein on a cleaned product shall be lower than the action level (see References [42],[51],[72],[76] and[85]), for each sample.

NOTE Protein detection methods can include those specified in Annex C, or as otherwise validated.

4.4.3.3 Assay criteria for other analytes

Other analytes, if used, and their acceptable levels on a cleaned product, include:

a) Total organic carbon (TOC)

1) Alert level ≥ 6 µg/cm^2 (see Reference [85])

2) Action level ≥ 12 µg/cm^2 (see Reference [67])

NOTE TOC is the quantity of carbon present in organic matter and determined as non-purgeable organic carbon.

b) Carbohydrate

1) Alert level ≥ 0,9 µg/cm^2

2) Action level ≥ 1,8 µg/cm^2 (see References [34],[40] and[53])

NOTE The method by Dubois et al.[53] varies in its detection of monosaccharides and therefore the level of detectable carbohydrate, depending on its composition. The alert and action levels provided were based on this limitation.

c) Haemoglobin

1) Alert level ≥ 1,0 µg/cm^2 (see Reference [73])

2) Action level ≥ 2,2 µg/cm^2 (see References [34],[35],[42] and[51])

NOTE Haemoglobin detection methods can include those specified in Annex D, or as otherwise validated.

d) Adenosine triphosphate (ATP)

1) Alert level ≥ 10 femtomoles (fmol) of ATP/cm^2 (see References [37] and[89])

2) Action level ≥ 22 femtomoles (fmol) of ATP/cm^2 (see References [36],[37] and[43])

NOTE Conversion of relative light units (RLU) to femtomoles can be obtained from the specific ATP monitoring equipment supplier.

e) Endotoxin

1) Alert level ≥ 2,2 EU/device (see References [12] and[33])

2) Action level ≥ 20 EU/device (see References [12],[32] and[33])

NOTE 1 Endotoxin is measured in endotoxin units (EU).

NOTE 2 The recommended endotoxin levels are ≤20 EU/device for implants and product that directly or indirectly contact the cardiovascular system and lymphatic system, and ≤2,15 EU/device for a product having intrathecal patient contact (see References [9],[12] and[33]).

NOTE 3 Additional endotoxin studies on medical devices can be found in References [41] and[50].

4.4.4 Process residuals

The cleaning stage(s), including any post-washing rinse(s) shall not leave any process residuals on the load that are potentially harmful during subsequent use or impair the following process stages (see 5.5).

NOTE Refer to process chemicals in ISO 15883-1:—, 4.6.

5 Testing for conformity

5.1 Cleaning test method validation

5.1.1 General

The cleaning test methods employed for both type tests (see 5.3) and performance qualification tests (see 5.4) shall be validated.

NOTE 1 Cleaning test method includes the test soil, soiling method, recovery method, and endpoint analysis.

NOTE 2 ISO/IEC 17025[6] requires test assay methods to be validated. Other references, such as ASTM E-2857,[15] I.C.H guidelines[21], and pharmacopoeias[26],[27],[28],[29], give guidance on requirements for the validation of various types of analytical test methods.

5.1.2 Load soiling method

5.1.2.1 The load soiling method, including its application and any treatment, shall simulate an equivalent challenge to the WD cleaning stage(s) as that presented by worst-case clinically soiled load(s), including the specified load carrier (see 4.2.3 and 5.2.1).

5.1.2.2 The load soiling method shall specify any conditioning, to include drying of soiled product for a defined time, temperature and humidity (i.e. dwell time) that will represent the use of the product being processed in the WD.

NOTE Refer to Köhnlein et al. 2008[62] as an example for conditioning.

5.1.3 Detection method(s)

5.1.3.1 The limit of detection, either directly or by extraction, shall be determined for each analyte and each method used for cleaning validation studies.

5.1.3.2 The test soil recovery efficiency shall be determined. The corresponding correction factor shall be calculated and applied to the results (see 4.2.4).

NOTE ISO 11737-1[2] gives examples of methods of ascertaining bioburden recovery efficiencies and application of bioburden correction factors. These principles and general methods can also be applied regarding test soil recovery.

5.1.3.3 Negative and positive controls shall be conducted to identify interference of process conditions with the detection method (see 5.2.2).

5.1.4 Analyte assay method

The chosen analyte assay method shall be validated for each analyte used for cleaning validation studies.

5.2 Washer-disinfector requirements

5.2.1 The cleaning tests shall be performed on the defined washer-disinfector loads. The worst-case load shall include representative product and specified load carrier(s). Each type of load carrier with representative product shall be tested separately unless a justification is provided to do otherwise.

5.2.2 The WD cleaning stage(s) parameters and cleaning process chemicals shall be specified. Type testing shall be conducted under the specified worst-case parameters (e.g. temperature, time, process chemical concentration, services, pressure, and flow rate).

NOTE Services can include electricity, water, air, and steam supplies.

5.2.3 Cleaning validation shall be tested without any disinfection or drying stage (see ISO 15883-1:—, 6.10).

5.3 Cleaning type test

5.3.1 Principle

In addition to the requirements in this document, the relevant cleaning test requirements of the other applicable parts of ISO 15883 shall apply.

5.3.2 Reagents/materials

Coagulating blood or an alternative test soil meeting the criteria in 4.2 shall be used.

5.3.3 Procedure

5.3.3.1 The test load, washer-disinfector chamber walls and load carrier shall be soiled with test soil (see 4.2.1 and 4.3).

NOTE Refer to Annex A for examples of test soils.

5.3.3.2 Soiled surfaces shall be conditioned as described in 5.1.2.2.

5.3.3.3 Cleaning test stages shall be conducted in triplicate under the worst-case processing conditions as defined for the WD (see 5.2.2).

5.3.4 Acceptance criteria

Cleaning efficacy shall conform with the absence of visible soil as specified in 4.4.2 and with the action levels specified in 4.4.3 for the test load. Where practicable, cleaning efficacy should conform with the

alert levels in 4.4.3 for the test load. Visual examination may be sufficient for chamber walls and load carrier (see 4.4.2).

NOTE 1 The action levels are the acceptance criteria for cleaning efficacy during type testing, but the desired criteria are given as the alert levels.

NOTE 2 Photographic records can assist by capturing visual examination outcomes.

5.4 Cleaning performance qualification test

5.4.1 Principle

Testing shall be conducted in conformance with ISO 15883-1:—, 6.10.3 and the applicable part of ISO 15883.

5.4.2 Reagents/materials

The WD shall be tested using actual loads contaminated by clinical use. These loads shall be representative of those the WD is intended to process and include product that are known as difficult to clean.

For particular product, a surrogate product that simulates clinical use conditions may be used for cleaning efficacy. The use of surrogate product and test soils shall be justified (see 5.1 and 4.2) for applicability to clinical use conditions.

NOTE Surrogate product can be used to simulate product that are difficult to sample without destruction, or for which the extraction efficiency of the sampling method cannot be determined.

5.4.3 Procedure

5.4.3.1 Soiled surfaces shall be held under dwell time conditions representative of worst-case practices (e.g. time, temperature and humidity) prior to cleaning (see 5.1.2.2).

5.4.3.2 Cleaning tests shall be conducted on comparable loads in triplicate (see 5.2).

NOTE Based on a risk analysis, fewer replicates can be justified during requalification.

5.4.4 Acceptance criteria

Cleaning efficacy shall conform with the absence of visible soil specified in 4.4.2 and the action levels specified in 4.4.3 for the test load. Where practicable, cleaning efficacy should conform with the alert levels in 4.4.3 for the test load. Visual examination may be sufficient for chamber walls and load carrier (see 4.4.2).

NOTE Photographic records can assist by capturing visual examination outcomes.

5.5 Process residuals

5.5.1 General

The acceptable amount of process residuals shall be specified as part of risk analysis and cytotoxicity testing as part of type testing. Performance qualification requires periodic sampling of the product for process residuals (see ISO 15883-1:—, Table A.1).

In the case of a change to the process or the process chemicals, type testing and performance qualification shall be repeated.